CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

BLA 103-948/S-5151

Trade Name: Lemtrada

Generic Name: alemtuzumab injection

Sponsor: Genzyme Corporation

Approval Date: September 18, 2015

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 103-948/S-5151

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 103-948/S-5151

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103948/S-5151

SUPPLEMENT APPROVAL

Genzyme Corporation
Attention: Mara Kochaba
Manager, Regulatory Affairs
500 Kendall Street
Cambridge, MA 02142

Dear Ms. Kochaba:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received July 22, 2015, submitted under section 351(a) of the Public Health Service Act for Lemtrada (alemtuzumab) injection.

We acknowledge receipt of your amendment dated September 10, 2015.

This "Changes Being Effected" sBLA provides for modifications to the approved REMS.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Lemtrada was originally approved on November 14, 2014. The REMS consists of a communication plan, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of an updated Lemtrada logo throughout the REMS, the addition of an option to complete and submit most of the required REMS forms online (with the exception of the Lemtrada REMS Patient Enrollment Form and the Lemtrada REMS Prescription Ordering Form), and revisions to the REMS website that provide the ability to search for certified prescribers and healthcare facilities within the US and its territories.

Your proposed modified REMS, submitted on September 10, 2015, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on November 14, 2014.

There are no changes to the REMS assessment plan described in our November 14, 2014, letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any of goal or element of the REMS, as described in section 505-1(g)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA).

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A). This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication.

b) A determination of the implications of a change in the benefit-risk profile for the current REMS.

c) If the new indication for use introduces unexpected risks: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use: A statement about whether the REMS was meeting its goals at the time of that the last assessment and if any modifications of the REMS have been proposed since that assessment.

e) If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use: Provision of as many of the currently listed assessment plan items as is feasible.

f) If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. If you are not proposing REMS modifications, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the

submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 103948 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 103948 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 103948/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 103948/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 103948/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103948/S-000 REMS ASSESSMENT

PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR BLA 103948

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

If you do not submit electronically, please send 5 copies of REMS-related submissions.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Nahleen Lopez, Regulatory Project Manager, at (240) 402-2659.

Sincerely,

{See appended electronic signature page}

Alice Hughes, MD
Deputy Director for Safety
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ALICE HUGHES
09/18/2015

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 103-948/S-5151

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Initial REMS approval: 11/2014

Last revision: 09/2015

BLA 103948 LEMTRADA® (alemtuzumab)

CD52-directed cytolytic antibody

Genzyme Corporation

500 Kendall Street, Cambridge, MA 02142

Phone: 1-800-745-4447

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the LEMTRADA REMS is to mitigate the risks of autoimmune conditions, infusion reactions, and malignancies associated with LEMTRADA by:

Helping to ensure informed decisions about the safe use of LEMTRADA by:

- Informing patients about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA and the need for baseline and periodic monitoring; and
- Informing healthcare providers about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA, the need to counsel patients, and the need for baseline and periodic monitoring.

Helping to ensure the safe use of LEMTRADA by:

- Ensuring that only certified prescribers prescribe LEMTRADA;
- Ensuring that LEMTRADA is dispensed only in certain healthcare settings, by certified pharmacies, and certified infusion sites, which have on-site access to equipment and personnel trained to manage infusion reactions; and
- Ensuring that only enrolled and authorized patients receive LEMTRADA;
- Ensuring that certified prescribers submit documentation of periodic monitoring of patients who receive LEMTRADA to identify autoimmune conditions and malignancies

II. REMS ELEMENTS

A. Communication Plan

Genzyme will implement the following communication plan to healthcare providers likely to diagnose, treat, and manage patients with multiple sclerosis. The communication plan will include:

1. REMS Letter for Healthcare Providers

Genzyme will send a *REMS Letter for Healthcare Providers* within 60 days of approval of the LEMTRADA REMS and again at 12 months, 24 months, and 36 months from the date of the REMS approval. The REMS Letters will address the risk of autoimmune conditions, infusion reactions, and malignancies associated with LEMTRADA as well as support the implementation of the LEMTRADA REMS program. A copy of or a link to the Prescribing Information will accompany each *REMS Letter for Healthcare Providers*.

Genzyme will use email as the primary method to disseminate the REMS Letter. If an email is marked as unopened, Genzyme will send a second email within 30 calendar days. If the second email is marked as unopened, Genzyme will mail the REMS Letter within 30 calendar days. If an email address is not available or if the email is undeliverable, Genzyme will mail the REMS Letter within 30 calendar days.

Genzyme will send the *REMS Letter for Healthcare Providers* to prescribers who have written at least one prescription within the previous 2 years for a prescription drug indicated for the treatment of multiple sclerosis.

2. REMS Website

Genzyme will ensure that the website (www.LemtradaREMS.com) will be available for the duration of the REMS. Genzyme will ensure that the website will:

- Contain information on the LEMTRADA REMS
- Provide access to all approved REMS materials and the Prescribing Information
- Provide the option to complete and submit all approved REMS materials online (except the LEMTRADA REMS Patient Enrollment Form and the LEMTRADA REMS Prescription Ordering Form)
- Provide the ability to search for a REMS certified prescriber or infusion site within the U.S. and its territories
- Allow for the review of patient authorization and enrollment status, and prescriber and infusion site certification status

The following are part of the REMS and are appended:

- The *REMS Letter for Healthcare Providers* (print and email versions)
- The LEMTRADA REMS Website

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe LEMTRADA are specially certified.

a. To become specially certified to prescribe LEMTRADA in the LEMTRADA REMS Program, healthcare providers must:

   i. Review the Prescribing Information for LEMTRADA.

   ii. Review the *LEMTRADA REMS Program Overview* and *LEMTRADA REMS Education Program for Prescribers* and successfully complete the *LEMTRADA REMS Knowledge Assessment*.

   iii. Enroll in the LEMTRADA REMS Program by completing and signing the *LEMTRADA REMS Prescriber Enrollment Form* and submitting it to the LEMTRADA REMS Program.

b. As a condition of certification, prescribers must agree to:

   i. Enroll each patient in the LEMTRADA REMS Program by:

      1) Informing the patient about the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies, and the need for baseline and periodic monitoring, by counselling on and providing each patient with *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and a *LEMTRADA Patient Safety Information Card*.

      2) Completing the *LEMTRADA REMS Patient Enrollment Form* for each patient and providing a completed copy to the patient. The completed form must be submitted to the LEMTRADA REMS Program and a copy should be stored in the patient's records.

   ii. Submit a *LEMTRADA REMS Prescription Ordering Form* for each LEMTRADA prescription to the LEMTRADA REMS Program.

   iii. Perform the baseline and periodic monitoring described in the Prescribing Information.

   iv. Submit a *LEMTRADA REMS Patient Authorization and Baseline Lab Form* to the LEMTRADA REMS Program indicating completion of each patient's baseline laboratory testing within 30 days prior to the patient's infusion date.

   v. Complete the *LEMTRADA REMS Patient Status Form* 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the completion of the patient's last infusion of LEMTRADA and submit the completed form to the LEMTRADA REMS Program.

   vi. Report any adverse events suggestive of autoimmune conditions, infusion reactions, and malignancies to Genzyme.

   vii. Notify Genzyme if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care.

c. Genzyme will:

   i. Ensure that healthcare providers who prescribe LEMTRADA are specially certified, in accordance with the requirements described above.

ii. Ensure that prescriber enrollment and documentation of training can be submitted by fax to (1-855-557-2478) to the LEMTRADA REMS Program or online via the LEMTRADA REMS website (www.LemtradaREMS.com).

iii. Ensure that healthcare providers are notified when they have been certified by the LEMTRADA REMS Program.

iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe LEMTRADA in the LEMTRADA REMS Program. Genzyme will ensure that the healthcare provider's certification requirements are met and may de-certify non-compliant healthcare providers if the requirements do not continue to be met.

v. Send a *LEMTRADA REMS Patient Status Reminder Letter* electronically or by mail 6 months after each patient's first LEMTRADA infusion, and every 6 months thereafter for 48 months, to certified prescribers enrolled in the LEMTRADA REMS Program, who must submit a completed *LEMTRADA REMS Patient Status Form* for an enrolled patient who has received LEMTRADA within the last 48 months.

vi. Provide the *LEMTRADA REMS Prescriber Enrollment Form*, *LEMTRADA REMS Patient Enrollment Form*, *LEMTRADA REMS Program Overview*, *LEMTRADA REMS Education Program for Prescribers*, *LEMTRADA REMS Patient Status Form*, *LEMTRADA REMS Prescription Ordering Form*, *LEMTRADA REMS Patient Authorization and Baseline Lab Form*, *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and the Prescribing Information to healthcare providers who (1) attempt to prescribe LEMTRADA and are not yet certified, or (2) inquire about how to become certified.

vii. Ensure that the REMS materials listed below are available on the LEMTRADA REMS Program Website (www.LemtradaREMS.com) and can be accessed or by calling the REMS call center (1-855-676-6326).

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Education Program for Prescribers*
- *LEMTRADA REMS Knowledge Assessment*
- *LEMTRADA REMS Prescriber Enrollment Form*
- *LEMTRADA REMS Patient Enrollment Form*
- *LEMTRADA REMS Patient Status Form*
- *What You Need to Know About LEMTRADA Treatment: A Patient Guide*
- *LEMTRADA REMS Prescription Ordering Form*
- *LEMTRADA REMS Patient Authorization and Baseline Lab Form*

- The LEMTRADA REMS Website
- *LEMTRADA REMS Patient Status Reminder Letter*

2. LEMTRADA is dispensed only in certain healthcare settings, by pharmacies and infusion sites that are specially certified.

a. To become specially certified to dispense LEMTRADA in the LEMTRADA REMS Program,

i. Each pharmacy must:

1) Designate an authorized representative to complete enrollment by submitting the completed *LEMTRADA REMS Pharmacy Enrollment Form* on behalf of the pharmacy.

2) Ensure the authorized representative will oversee implementation and compliance with the LEMTRADA REMS Program requirements by:

a. Reviewing the *LEMTRADA REMS Program Overview.*

b. Ensuring that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the *LEMTRADA REMS Program Overview*.

c. Putting processes and procedures in place, and following such processes and procedures, to ensure the following verifications and safe use conditions are met prior to dispensing LEMTRADA:

i. The *LEMTRADA REMS Prescription Ordering Form* is received for each prescription.

ii. LEMTRADA is dispensed to certified infusion sites only.

iii. The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by calling the LEMTRADA REMS Program prior to dispensing LEMTRADA.

d. Complying with request to be audited to ensure all training, processes and procedures are in place and being followed for the LEMTRADA REMS Program and appropriate documentation is available upon request.

e. Agreeing to renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

ii. Each infusion site must:

1) Designate an authorized representative to complete enrollment by submitting the completed *LEMTRADA REMS Healthcare Facility Enrollment Form* on behalf of the infusion site.

2) Ensure the authorized representative will oversee implementation and compliance with the LEMTRADA REMS Program requirements by:

   a. Reviewing the *LEMTRADA REMS Program Overview* and *LEMTRADA REMS Education Program for Healthcare Facilities.*

   b. Ensuring that all relevant staff involved in the dispensing and administration of LEMTRADA are educated and trained using the *LEMTRADA REMS Program Overview* and the *LEMTRADA REMS Education Program for Healthcare Facilities*.

   c. Putting processes and procedures in place, and following such processes and procedures, to ensure the following verifications and safe use conditions are met prior to, during, and following dispensing LEMTRADA:

      i. The *LEMTRADA REMS Prescription Ordering Form* is received for each prescription.

      ii. The prescriber is certified and the patient is enrolled and authorized to receive LEMTRADA by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website (www.LemtradaREMS.com) prior to dispensing LEMTRADA.

      iii. Patients are counseled about the risk for infusion reactions and provided with *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to dispensing LEMTRADA.

      iv. The infusion site is equipped with the necessary equipment and personnel to manage infusion reactions.

      v. LEMTRADA is not dispensed outside of the authorized representative's certified infusion site.

      vi. Monitoring patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.

      vii. Completing a *LEMTRADA REMS Infusion Checklist* for each patient at the conclusion of each treatment course and submitting the form within 5 business days either by fax (1-855-557-2478) or via the LEMTRADA REMS website (www.LemtradaREMS.com) to the LEMTRADA REMS Program.

      viii. Renewing enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

3) Ensuring that unused vials of LEMTRADA are returned to a distributor within 50 business days from the date of submission of the *LEMTRADA Patient Authorization and Baseline Lab Form.*

4) Complying with request to be audited to ensure that all training, processes and procedures are in place and are being followed for the LEMTRADA REMS Program and appropriate documentation is available upon request.

b. Genzyme will:

i. Ensure that LEMTRADA is dispensed only by pharmacies and infusion sites that are specially certified in accordance with the requirements described above.

ii. Ensure that pharmacy and infusion site enrollment and certification can be submitted by fax (1-855-557-2478) or via the LEMTRADA REMS website (www.LemtradaREMS.com) to the LEMTRADA REMS Program.

iii. Ensure that pharmacies and infusion sites are notified when they have been certified by the LEMTRADA REMS Program.

iv. Ensure that certified pharmacies and certified infusion sites are provided access to the database of certified health care providers and enrolled and authorized patients by contacting the LEMTRADA REMS Program (1-855-676-6326); infusion sites also have the option to view this information via the LEMTRADA REMS website (www.LemtradaREMS.com).

v. Contact certified infusion sites if a completed *LEMTRADA REMS Infusion Checklist* has not been received by the LEMTRADA REMS Program within 40 days from the date of submission of the *LEMTRADA Patient Authorization and Baseline Lab Form*.

vi. Verify annually that the authorized representative is the current designated authorized representative for the certified pharmacy and certified infusion site.

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Healthcare Facility Enrollment Form*
- *LEMTRADA REMS Pharmacy Enrollment Form*
- *LEMTRADA REMS Education Program for Healthcare Facilities*
- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Infusion Checklist*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

3. **LEMTRADA will be dispensed[1] to patients only in certain health care settings, specifically, certified infusion sites that have the necessary on-site equipment and personnel to manage infusion reactions.**

   Genzyme will ensure that LEMTRADA will only be available to be dispensed to patients in an infusion site that has the necessary on-site equipment and personnel to appropriately manage serious infusion reactions (including anaphylaxis, cardiac and respiratory emergencies) and is certified in the LEMTRADA REMS Program.

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Healthcare Facility Enrollment Form*
- *LEMTRADA REMS Infusion Checklist*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*
- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Education Program for Healthcare Facilities*

4. **LEMTRADA will be dispensed to patients with evidence or other documentation of safe-use conditions.**

   a. To become enrolled in the LEMTRADA REMS Program, each patient must sign a *LEMTRADA REMS Patient Enrollment Form* indicating that he/she has:

      i. Been counselled with and provided *What You Need to Know About LEMTRADA Treatment: A Patient Guide*;

      ii. Been counselled by the prescriber regarding the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions and malignancies;

      iii. Been counselled by the prescriber regarding the need for baseline and periodic monitoring recommendations contained in the LEMTRADA Prescribing Information;

      iv. Been counselled with and provided a *LEMTRADA Patient Safety Information Card*.

   b. Genzyme will:

[1] For the purposes of this REMS, dispensed to patients only in certain health care settings includes dispensing and administration in health care settings, specifically infusion sites.

i. Ensure that the certified prescriber is able to submit the completed *LEMTRADA REMS Patient Enrollment Form* to the LEMTRADA REMS Program by fax (1-855-557-2478).

ii. Ensure that each patient treated with LEMTRADA is enrolled in the LEMTRADA REMS Program before LEMTRADA is dispensed to the patient, by verification prior to dispensing and administration (see Section B.2.).

iii. Ensure that LEMTRADA is dispensed to patients only if there is evidence or other documentation that they have met the following safe use conditions:

1) Patients have been counselled with and provided a *LEMTRADA Patient Safety Information Card*, *What You Need to Know about LEMTRADA Treatment: A Patient Guide*, and *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide,* on the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies.

2) Patients have completed the *LEMTRADA REMS Patient Enrollment Form*.

iv. Send a *LEMTRADA REMS Patient Reminder Letter* to patients enrolled in the LEMTRADA REMS Program. These monthly communications will be sent to patients who have received LEMTRADA within the last 48 months, reminding the patient to obtain the needed periodic monitoring as described in the Prescribing Information, and will include a request for the patient's preferred method of contact for receiving future monthly reminders.

The following materials are part of the REMS and are appended:

- *What You Need to Know about LEMTRADA Treatment: A Patient Guide*
- *LEMTRADA Patient Safety Information Card*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*
- *LEMTRADA REMS Patient Reminder Letter*

C. Implementation System

An implementation system will be established for the LEMTRADA REMS Program to monitor and evaluate whether the elements to assure safe use are meeting the program's goals.

1. Genzyme will ensure that LEMTRADA is only distributed to certified pharmacies and certified infusion sites by:

a. Ensuring that distributors who distribute LEMTRADA to certified pharmacies and certified infusion sites comply with the program requirements for distributors. In order for a distributor to distribute LEMTRADA, the distributor must:

i. Put processes and procedures in place to verify, prior to distributing LEMTRADA, that the pharmacies and infusion sites are certified by calling the LEMTRADA REMS Program (1-855-676-6326).

ii. Train all relevant staff on the LEMTRADA REMS Program requirements.

iii. Agree to be audited to ensure that all processes and procedures are in place and are being followed for the LEMTRADA REMS Program.

iv. Agree to provide distribution data to the LEMTRADA REMS Program.

b. Ensuring that distributors maintain patient level distribution records of all shipments of LEMTRADA to certified pharmacies and certified infusion sites and agree to provide the data to the LEMTRADA REMS Program.

c. Genzyme will monitor and audit the distributors within 180 days after the distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the LEMTRADA REMS Program. Corrective action will be instituted by Genzyme if noncompliance is identified.

2. Genzyme will maintain a list of pharmacies and infusion sites which are certified to dispense and/or administer LEMTRADA in the LEMTRADA REMS Program. Genzyme will ensure that the pharmacies' and infusion sites' certification requirements are met and may de-certify non-compliant pharmacies and infusion sites if the requirements do not continue to be met. This list is available by telephone (1-855-676-6326) for certified prescribers of LEMTRADA. A list of certified prescribers and infusion sites is also available via the LEMTRADA REMS website (www.LemtradaREMS.com).

3. Genzyme will maintain a LEMTRADA REMS Program Call Center to support healthcare providers, pharmacies, infusion sites, and patients interfacing with the LEMTRADA REMS Program.

4. Genzyme will send monthly reminders to patients enrolled and authorized in the LEMTRADA REMS Program and who have received at least one LEMTRADA treatment, reminding them of the requirement for ongoing monitoring.

5. Genzyme will ensure that all materials listed in or appended to the LEMTRADA REMS document are available through the LEMTRADA REMS Program Website (www.LemtradaREMS.com) or can be accessed by calling the REMS call center (1-855-676-6326).

6. Genzyme will monitor and audit the certified pharmacies and infusion sites within 180 days after certification and after it has dispensed at least one LEMTRADA prescription, to ensure that all processes and procedures are in place and functioning to support the requirements of the LEMTRADA REMS Program. Corrective action will be instituted by Genzyme if noncompliance is identified.

7. Genzyme will maintain a validated, secure database of patients who are enrolled in the LEMTRADA REMS Program.

8. Genzyme will take reasonable steps to improve implementation of and compliance with the requirements in the LEMTRADA REMS Program based on monitoring and evaluation of the LEMTRADA REMS Program.

D. Timetable for Submission of Assessments

Genzyme will submit REMS Assessments to FDA at 6 and 12 months from the date of the approval of the LEMTRADA REMS, and then annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Genzyme will submit each assessment so that it will be received by FDA on or before the due date.

[Month] 20[Year]

IMPORTANT DRUG WARNING

SUBJECT: Serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA® (alemtuzumab); FDA-Required REMS Program

IMPORTANT SAFETY NOTICE

Dear Healthcare Provider:

The purpose of this letter is to inform you of the approval of LEMTRADA® (alemtuzumab); a CD52-directed cytolytic monoclonal antibody for intravenous infusion indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The LEMTRADA REMS Program was developed by Genzyme in collaboration with the FDA to ensure that the benefits of LEMTRADA outweigh the serious risks. Under the LEMTRADA REMS Program, only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA.

SERIOUS RISKS OF LEMTRADA

AUTOIMMUNE CONDITIONS

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA.

INFUSION REACTIONS

- LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

MALIGNANCIES

- LEMTRADA may cause an increased risk of malignancy including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams to monitor for signs of melanoma.

LEMTRADA® alemtuzumab 12mg IV

IMPORTANT SAFETY INFORMATION ON KNOWN RISKS

Treatment with LEMTRADA® (alemtuzumab) can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions, including ITP, other cytopenias, thyroid disorders and glomerular nephropathies, which may occur many years after treatment. In order to identify these risks, laboratory tests are required. Complete blood counts with differential, serum creatinine levels and urinalysis with urine cell counts should be obtained prior to initiation of treatment and at monthly intervals until 48 months after the last infusion with LEMTRADA. Thyroid function tests should be obtained prior to initiation of treatment and every 3 months until 48 months after the last infusion with LEMTRADA. Monitoring may need to continue past 48 months based on clinical findings of autoimmune conditions.

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. Some infusion reactions may be serious and life threatening. Serious reactions occurred in 3% of patients and included anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia and rash. Premedicate patients with high dose corticosteroids (1000 mg methylprednisolone or equivalent) immediately prior to the LEMTRADA infusion and for the first 3 days of any treatment course. Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Longer periods of observation may be required if clinically indicated.

LEMTRADA may cause an increased risk of malignancy including thyroid cancer, melanoma, and lymphoproliferative disorders. Baseline and yearly skin examinations should be performed in LEMTRADA patients to monitor for signs of melanoma. Caution should be exercised in initiating LEMTRADA therapy in patients with pre-existing or ongoing malignancies.

The LEMTRADA REMS Program Requirements:

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

LEMTRADA® alemtuzumab 12mg IV

Reporting Adverse Events

It is important that you promptly report all suspected adverse events with the use of LEMTRADA. Please contact Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch.

This letter is not a comprehensive description of the risks associated with the use of LEMTRADA. Please see the enclosed Prescribing Information for a complete description of these risks.

If you have any questions about the LEMTRADA REMS Program, please call 1-855-676-6326 for more information or visit www.LemtradaREMS.com.

Sincerely,

(Name)
(Title)
Genzyme Corporation

Enclosures: LEMTRADA Prescribing Information

LEMTRADA® alemtuzumab 12mg IV

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For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS HEALTHCARE FACILITY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the healthcare facility must enroll the facility in the LEMTRADA REMS Program.

☐ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

Please complete a separate Healthcare Facility Enrollment Form for each facility site, if applicable.

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Name of Institution or Healthcare Facility*		NPI Number*	
Infusion Facility Address*			
City*		State*	ZIP Code*
Ship-to Street Address (if different)*			
City*		State*	ZIP Code*
Phone Number*	Fax Number*	Email Address	
Name of Authorized Healthcare Facility Representative*		Title*	

Site Affiliation

☐ Academic ☐ Government ☐ Ambulatory/Freestanding ☐ Hospital Based ☐ Private Practice (in office)

HEALTHCARE FACILITY AGREEMENT

I am the authorized representative designated by my healthcare facility to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following Program requirements:

- I understand that my healthcare facility must be certified with the LEMTRADA REMS Program to receive or administer LEMTRADA.
- I have completed the review of the *LEMTRADA REMS Education Program for Healthcare Facilities* and the LEMTRADA REMS Program Overview.
- I understand that my healthcare facility must confirm that the patient is authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program or verifying online at www.LemtradaREMS.com prior to initiation of each treatment course.
- I understand the risk of serious infusion reactions during and following the administration of LEMTRADA.
- I understand the need to monitor patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
  - To include the monitoring of patient vital signs before the infusion and periodically during the infusion.
- I understand that my healthcare facility must be equipped with the necessary on-site equipment and personnel to manage anaphylaxis or serious infusion reactions.
- I understand that my healthcare facility must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

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HEALTHCARE FACILITY AGREEMENT (CONTINUED)

- This healthcare facility will establish procedures and protocols that are subject to audit, to help ensure compliance with the safe use conditions required in the LEMTRADA REMS Program, including the following:
  - Ensure that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - Ensure that the prescriber is certified and the patient is enrolled and authorized by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website prior to dispensing and administering LEMTRADA.
  - Ensure that the infusion site is equipped to manage infusion reactions.
  - Ensure that LEMTRADA is not dispensed outside of the authorized representative's certified healthcare facility.
  - Prior to the first day of each treatment course, counsel and provide a copy of *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* to each patient to inform them about the risk of serious infusion reactions.
  - Observe each patient administered LEMTRADA at my healthcare facility during and for at least 2 hours after each LEMTRADA infusion, in order to provide appropriate medical treatment in the event of serious infusion reactions following LEMTRADA infusion.
  - For each patient, complete and return the LEMTRADA REMS Infusion Checklist to the LEMTRADA REMS Program within 5 business days from the patient's last infusion of LEMTRADA within a specific treatment course.
  - Renew enrollment into the LEMTRADA REMS Program every 2 years from the initial enrollment.
- To make available to Genzyme documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.
- To return to Genzyme any unused vials of LEMTRADA within 50 days from the date of receipt of the LEMTRADA REMS Patient Authorization Baseline Lab Form.
- To ensure that a LEMTRADA REMS Patient Authorization and Baseline Lab Form is received for each prescription by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website.
- To ensure that all non-prescribing HCPs who administer LEMTRADA in my healthcare setting are trained using the LEMTRADA REMS Program Overview and the *LEMTRADA REMS Education Program for Healthcare Facilities*, and a record regarding such training must be maintained.

SIGNATURE

Authorized Healthcare Facility Representative Signature* Date*

Print Name* Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT STATUS FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed every 6 months for each LEMTRADA® (alemtuzumab) patient under your care. Please complete this form 6 months after your patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the patient's last infusion.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* | Office Phone Number*

Address*

City* | State* | ZIP Code*

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)*

Patient LEMTRADA REMS Program Identification Number*

Date of Birth (MM/DD/YYYY)* | Date of Last LEMTRADA Infusion (MM/DD/YYYY)*

Is the above-named patient still under your care?* (Check one) ☐ **Yes** ☐ **No**

IF NO, please indicate the name of the healthcare provider now responsible for this patient's care

Healthcare Provider Name

Healthcare Provider Phone Number

Patient's Current Healthcare Provider Is Unknown ☐

IF YES, please complete the following information

The patient has completed the periodic monitoring within the last 6 months. ☐ Yes ☐ No

Since submitting the last LEMTRADA REMS Patient Status Form, has the patient been diagnosed with any of the following?

a. Autoimmune conditions ☐ Yes ☐ No

b. Infusion reactions ☐ Yes ☐ No

c. Malignancies ☐ Yes ☐ No

☐ This adverse event has already been reported to Genzyme (specify date of report):

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

In signing this form, I acknowledge that I have reviewed *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with this patient and counseled the patient about the serious risks associated with the use of LEMTRADA, and how to mitigate these risks through periodic monitoring.

PRESCRIBER'S SIGNATURE

Prescriber Signature* | Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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LEMTRADA REMS PROGRAM OVERVIEW

What is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug. It is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions, and malignancies, LEMTRADA® (alemtuzumab) is only available through a restricted program called the LEMTRADA REMS Program.

LEMTRADA REMS Program Requirements

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

PRESCRIBER ENROLLMENT INSTRUCTIONS

1. Complete the training program, which includes reviewing the following:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - *LEMTRADA REMS Education Program for Prescribers*
2. Successfully complete the 8-question LEMTRADA REMS Knowledge Assessment.
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form.
4. Submit the completed and signed forms to the LEMTRADA REMS Program.

PHARMACY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the pharmacy by reviewing the LEMTRADA REMS Program Overview and completing the LEMTRADA REMS Pharmacy Enrollment Form, which acknowledges that the pharmacy agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All relevant staff at the pharmacy who will be involved with the dispensing of LEMTRADA must be educated and trained.
   - The pharmacy will verify that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
   - The pharmacy will verify that prescribers and healthcare facilities are certified and patients are authorized to receive LEMTRADA prior to dispensing LEMTRADA.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.
2. Submit the completed and signed LEMTRADA REMS Pharmacy Enrollment Form to the LEMTRADA REMS Program.

(Continued on next page)

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HEALTHCARE FACILITY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the healthcare facility by reviewing the *LEMTRADA REMS Education Program for Healthcare Facilities* and completing the LEMTRADA REMS Healthcare Facility Enrollment Form, which acknowledges that the healthcare facility agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All staff at the facility who will be involved with the dispensing and administration of LEMTRADA must be trained.
   - The healthcare facility will verify that prescribers are certified and patients are authorized to receive LEMTRADA prior to dispensing or administering LEMTRADA.
   - The healthcare facility will provide a copy of *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* to the patient on the first day of each treatment course when LEMTRADA is dispensed.
   - The healthcare facility will complete a LEMTRADA REMS Infusion Checklist for each patient at the conclusion of each treatment course and submit it to the LEMTRADA REMS Program within 5 business days.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.
2. Submit the completed and signed LEMTRADA REMS Healthcare Facility Enrollment Form to the LEMTRADA REMS Program.

PATIENT ENROLLMENT INSTRUCTIONS

1. Complete the LEMTRADA REMS Patient Enrollment Form, which contains information to be completed by both the prescriber and the patient.
2. Provide a copy of *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and a LEMTRADA Patient Safety Information Card to each patient who will receive LEMTRADA. You must use *What You Need to Know About LEMTRADA Treatment: A Patient Guide* to counsel your patients on the serious risks and REMS requirements with the use of LEMTRADA.
3. Submit the completed and signed LEMTRADA REMS Patient Enrollment Form to the LEMTRADA REMS Program.
4. Provide the patient with a copy of the LEMTRADA REMS Patient Enrollment Form and keep a copy in the patient's medical record.

Where to Find REMS Program Information and Resources

To enroll in the LEMTRADA REMS Program, call 1-855-676-6326. For information related to enrollment in the LEMTRADA REMS Program, call 1-855-676-6326 or visit **www.LemtradaREMS.com**

Indication

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA.

Please see accompanying Prescribing Information for complete safety information, including BOXED WARNING.

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Reference ID: 3821900

LEMTRADA® alemtuzumab 12mg IV

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is available only through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA.

Instructions:

1. Review the LEMTRADA REMS Education Program for Prescribers, including the Prescribing Information
2. Successfully complete the LEMTRADA REMS Knowledge Assessment
3. Complete and submit this LEMTRADA REMS Prescriber Enrollment Form
4. Send your patient to a healthcare facility that is enrolled in the LEMTRADA REMS Program

Please complete all required fields on this form and fax it to 1-855-557-2478. You will receive enrollment confirmation via your preferred method of communication (email or fax) within 2 business days.

*Indicates a mandatory field.

LEMTRADA PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)/Degree*

Name of Institution or Healthcare Facility*

Street Address*

City*		State*	ZIP Code*
Office Phone Number*	Fax Number*	Email Address	Mobile Phone Number

National Provider Identification (NPI) Number*

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

PRESCRIBER AGREEMENT

By completing this form, I attest that:

- I understand that LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- I understand that LEMTRADA is only available through the LEMTRADA REMS Program and that I must comply with the program requirements in order to prescribe LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Prescribers*, including a review of the LEMTRADA Prescribing Information, and successfully completed the LEMTRADA REMS Knowledge Assessment.
- I understand that by completing the training program and signing this LEMTRADA REMS Prescriber Enrollment Form, I will be enrolled in the LEMTRADA REMS Program and can prescribe LEMTRADA.
- I understand that I am responsible for reviewing *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with each patient, and counseling each patient on an ongoing basis about the serious risks associated with the use of LEMTRADA and how to mitigate these risks through periodic monitoring.
- I understand that I must enroll all patients being treated with LEMTRADA into the LEMTRADA REMS Program prior to initiating the patient on treatment with LEMTRADA. I am responsible for completing a LEMTRADA REMS Patient Enrollment Form with the patient (or patient's legal representative), obtaining the patient's (or patient's legal representative's) signature on the form, and submitting the signed form to the LEMTRADA REMS Program. A completed copy should be provided to the patient and another copy should be stored in the patient's records.
- I will provide enrolled patients with a LEMTRADA Patient Safety Information Card and instruct patients to carry this card with them at all times in case of an emergency.
- I understand that I must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription. I understand that I am responsible for completing baseline lab monitoring within 30 days prior to infusion of LEMTRADA.

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PRESCRIBER AGREEMENT (CONTINUED)

- I understand that I must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form indicating completion of each patient's baseline labs within 30 days prior to the patient's infusion date.
- I understand the risks of autoimmune conditions and malignancies associated with the use of LEMTRADA, and the need for periodic monitoring in order to identify and mitigate these risks:
  - Complete blood counts with differential obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Serum creatinine levels obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Urinalysis with urine cell counts obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Thyroid function tests, such as thyroid stimulating hormone (TSH) level, obtained within 30 days prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion.
  - Baseline and yearly skin examinations.
- I will report any adverse events of autoimmune conditions, infusion reactions, or malignancies to Genzyme.
- I will complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the Program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

WEBSITE CONSENT

I understand that the LEMTRADA REMS Program will publish my name, business address, and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-855-676-6326.

☐ Yes ☐ No

SIGNATURE

Prescriber Signature* Date*

Print Name*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS INFUSION CHECKLIST

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must be completed for each patient by the last day of each patient's treatment course and submitted within 5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

All fields on this form are mandatory.

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First) | DOB (MM/DD/YYYY)

Patient LEMTRADA REMS Program Identification Number

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (Last, First)

Prescriber LEMTRADA REMS Program Identification Number

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Healthcare Facility Name

Healthcare Facility LEMTRADA REMS Program Identification Number

STEP 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course.

Is the patient authorized to receive LEMTRADA? ☐ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE.** Refer patient back to the LEMTRADA prescriber.

STEP 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide"*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course. Has the patient been counseled and received the guide?

☐ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP** — provide the patient guide. Proceed to the next question after the patient has received this guide and has been counseled.

STEP 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:

1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available? ☐ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE** until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information.

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First)	DOB (MM/DD/YYYY)

STEP 4: RECORD infusion information

Was patient infused with LEMTRADA? ☐ **Yes** ☐ **No**

Yes Fill in Dates of Infusion below and then proceed to Step 5.

No Proceed to Step 5.

LEMTRADA Infusions

Dates of Infusion:

Date: _____ Date: _____

Date: _____ Date: _____

Date: _____

STEP 5: RETURN unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Baseline Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

STEP 6: SIGNATURE

_____ _____

Signature of staff completing checklist Date

_____

Name of staff completing checklist (Please Print)

STEP 7: Fax the Infusion Checklist to the LEMTRADA REMS Program at 1 855 557 2478 or submit online at *www.LemtradaREMS.com* within 5 business days.

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326.

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For Patients to Complete

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LEMTRADA REMS PATIENT ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

This form must be completed before you can receive LEMTRADA® (alemtuzumab). LEMTRADA is available only through a restricted distribution program called the LEMTRADA REMS Program. Your prescriber will help you complete this form and will give you a copy.

*Indicates a mandatory field.

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)*

Date of Birth (MM/DD/YYYY)*

Street Address*

City*

State*

ZIP Code*

Phone Number*

Gender* ☐ Male ☐ Female

Secondary Contact (Last, First)

Phone Number

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (Last, First)*

NPI Number*

Phone Number*

PATIENT AGREEMENT

By signing this form, I acknowledge that:

- I have received, read, and understand *What You Need to Know About LEMTRADA Treatment: A Patient Guide* that my doctor has given to me.
- My doctor has reviewed with me the benefits and risks of treatment with LEMTRADA.
- I am aware that LEMTRADA is associated with serious risks, including autoimmune conditions, infusion reactions, and malignancies, and that these complications can be identified through periodic monitoring and awareness of the initial signs and symptoms.
- I understand the need to have blood and urine tests within 30 days prior to my first LEMTRADA treatment, then each month for 4 years following my last treatment with LEMTRADA.
- I understand the need to have thyroid testing within 30 days prior to my first LEMTRADA treatment, then every 3 months for 4 years following my last treatment with LEMTRADA.
- I understand the need to have yearly skin exams prior to my first LEMTRADA treatment, and continuing for 4 years following my last treatment with LEMTRADA.
- I will tell my doctor if I have any reactions or symptoms after receiving LEMTRADA.
- I understand that I must tell all of my doctors that I have received LEMTRADA.
- I understand that in order to receive LEMTRADA, I am required to enroll in the LEMTRADA REMS Program and my information will be stored in a secure and confidential database of all patients who receive LEMTRADA in the United States. After enrolling, my doctor will provide me with a signed copy of the enrollment form.
- My doctor has counseled and provided me with a LEMTRADA Patient Safety Information Card, which I should carry with me at all times in case of an emergency.
- I understand that I must tell Genzyme if I change my doctor.
- I understand that I must tell Genzyme if my contact information changes.
- I give permission to Genzyme and its agents to use and share my personal health information for the purposes of enrolling me into the LEMTRADA REMS Program, coordinating the dispensing of receiving LEMTRADA, administering the LEMTRADA REMS Program, and releasing my personal health information to the Food and Drug Administration (FDA) as necessary.
- By completing the information below, I understand Genzyme and its agents will contact me via phone, mail, or email to support administration of the LEMTRADA REMS Program.

I prefer to be contacted:

☐ By mail ☐ By phone

☐ By email (please provide email address)

_____

PATIENT SIGNATURE

_____

Patient/Legal Representative Signature*

Relationship to Patient*

_____

Print Name*

Date*

PRESCRIBER SIGNATURE

I acknowledge that I have explained the LEMTRADA REMS Program to this patient.

_____

Prescriber Signature*

Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

	Healthcare Provider's Name (e.g., neurologist)	Healthcare Provider's Name (e.g., primary care provider)
Name:		
Phone Number:		
Fax Number: (for medical records or lab tests)		

Reference ID: 3821900

For more information on LEMTRADA, including important risks, please refer to the Prescribing Information and/or **www.LEMTRADA.com**

For information on LEMTRADA or the LEMTRADA REMS Program, call **1-855-676-6326**

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LEMTRADA® alemtuzumab 12mg IV

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LEMTRADA® alemtuzumab 12mg IV

Patient Safety Information Card

Please show this card to all emergency workers and healthcare providers.

Important information to know about LEMTRADA

<<insert your name>>

has been treated with LEMTRADA, a treatment for multiple sclerosis (MS), which lowers the number of circulating white blood cells for a period of time after treatment and also affects the immune system. Therefore, the patient is part of a laboratory monitoring program that continues for 4 years after his/her last treatment.

Reference ID: 3821900

LEMTRADA alemtuzumab 12mg IV

LEMTRADA treatment can increase the risk of:

Autoimmune conditions such as:

- A bleeding problem called immune thrombocytopenia (ITP)
- Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)
- Disorders of the thyroid gland (hypo/hyperthyroidism)
- Kidney disorders (nephropathies, including anti-glomerular basement membrane [anti-GBM] disease)

Infusion reactions (may occur more than 24 hours after the infusions), such as:

- Hypersensitivity reactions (including anaphylaxis)
- Fever
- Hives
- Irregular heartbeat
- Nausea
- Chest pain
- Low blood pressure

Malignancies such as:

- Thyroid cancer
- Melanoma
- Lymphoproliferative disorders and lymphoma

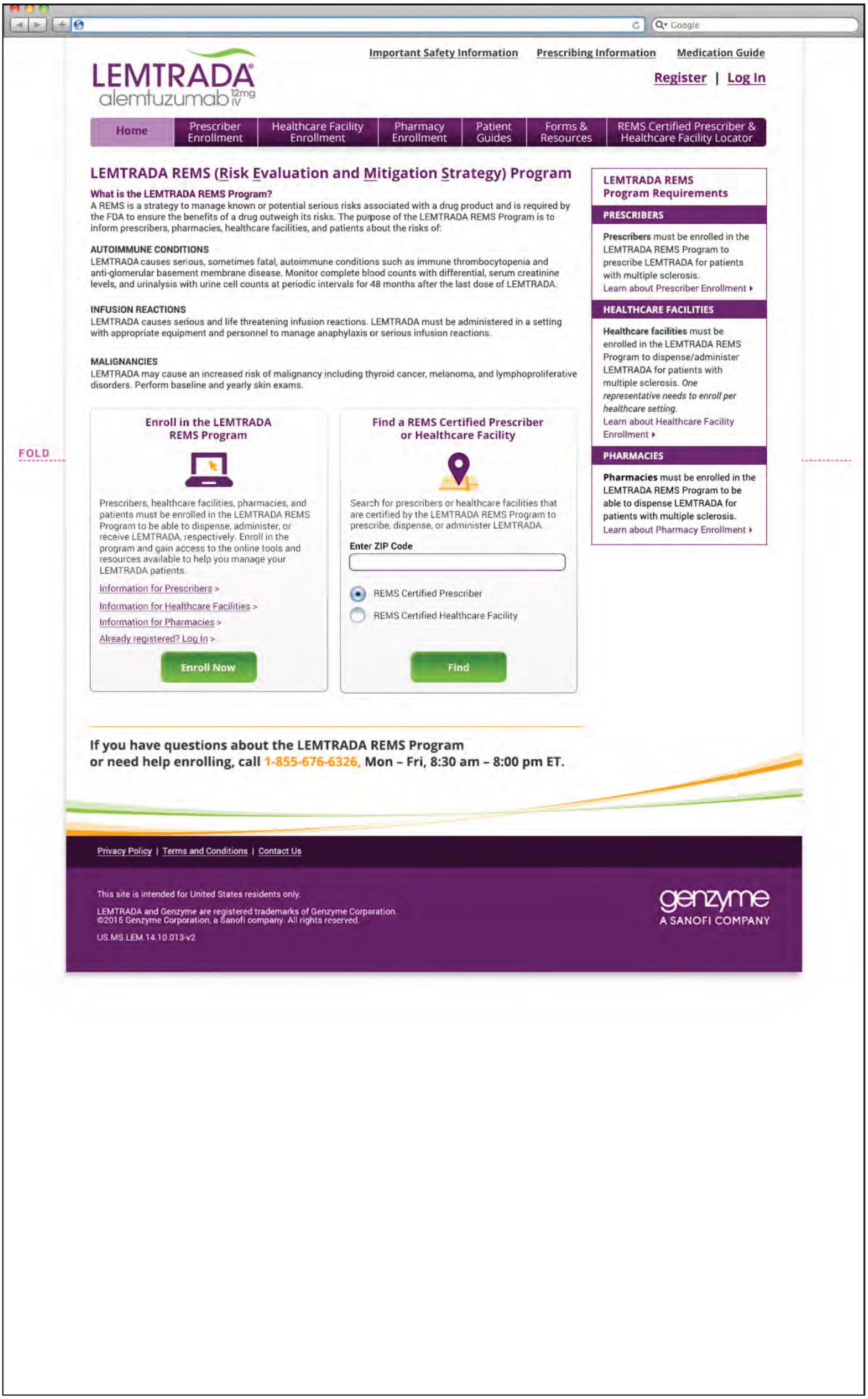
LEMTRADA alemtuzumab 12mg IV

LEMTRADA REMS DESKTOP

PUBLIC and Prescriber Desktop Pages Only

PUBLIC FACING PAGES

LEMTRADA REMS Desktop - Public Home



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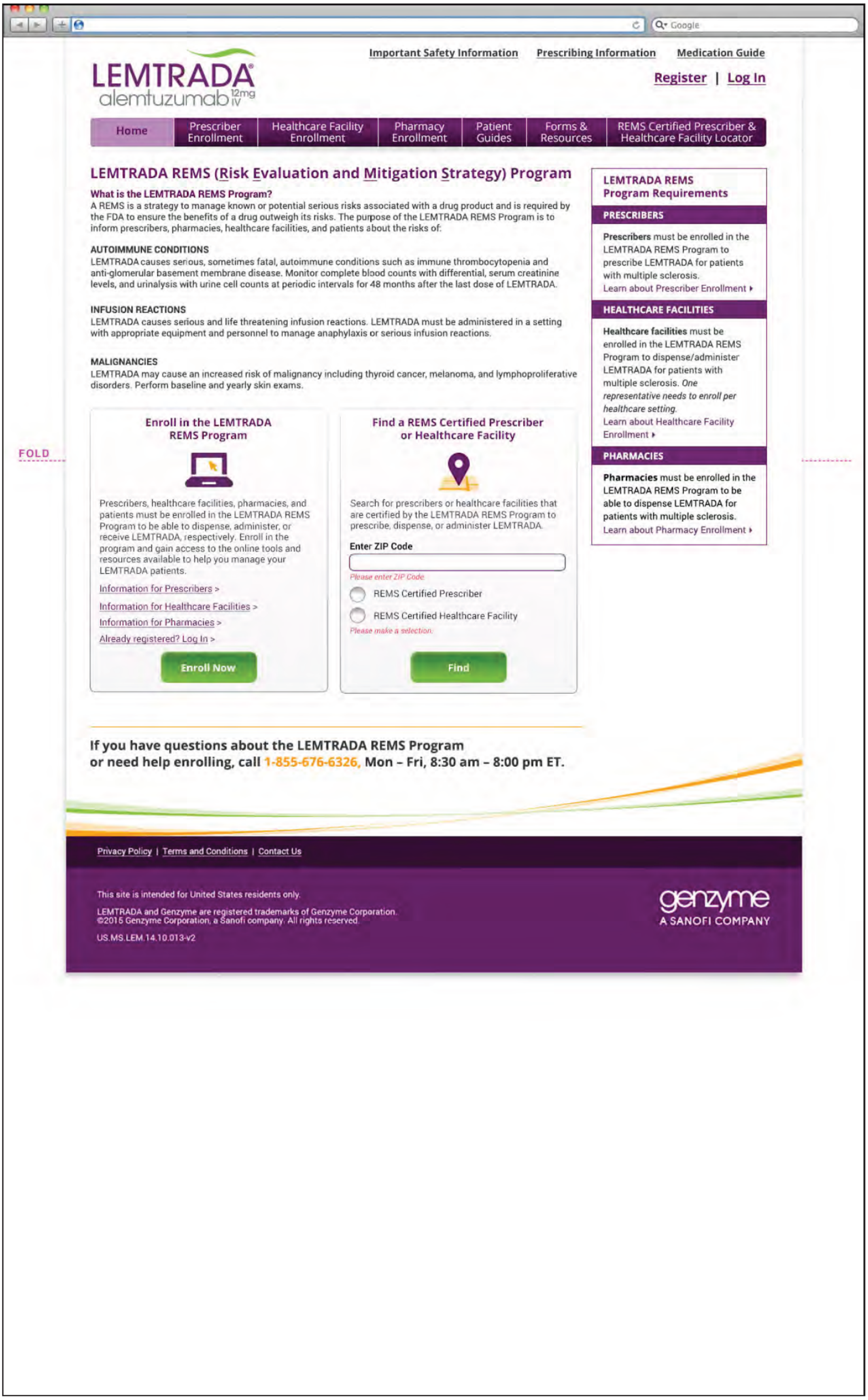
Reference ID: 3821900

LEMTRADA REMS Desktop - Public Home, Error



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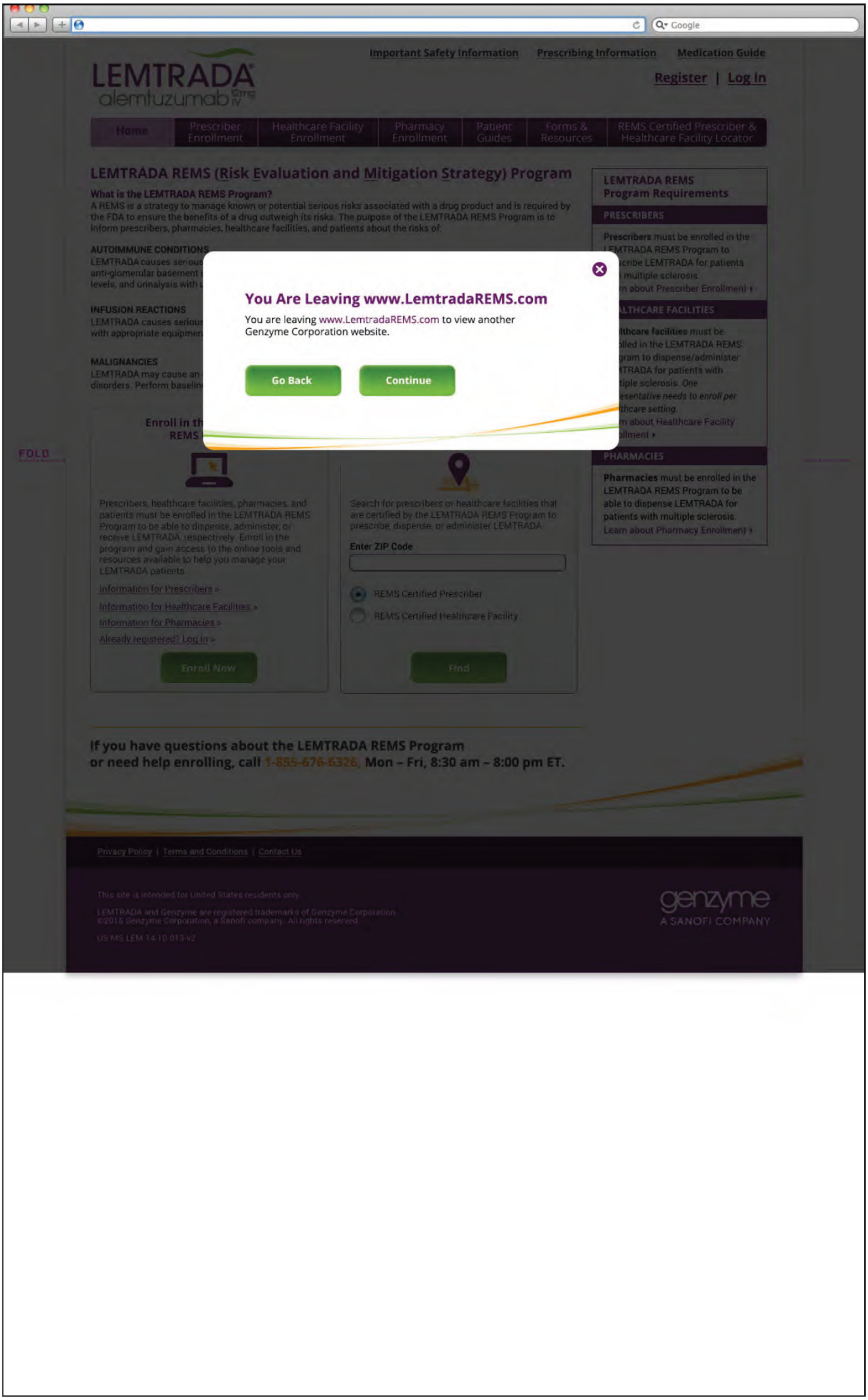
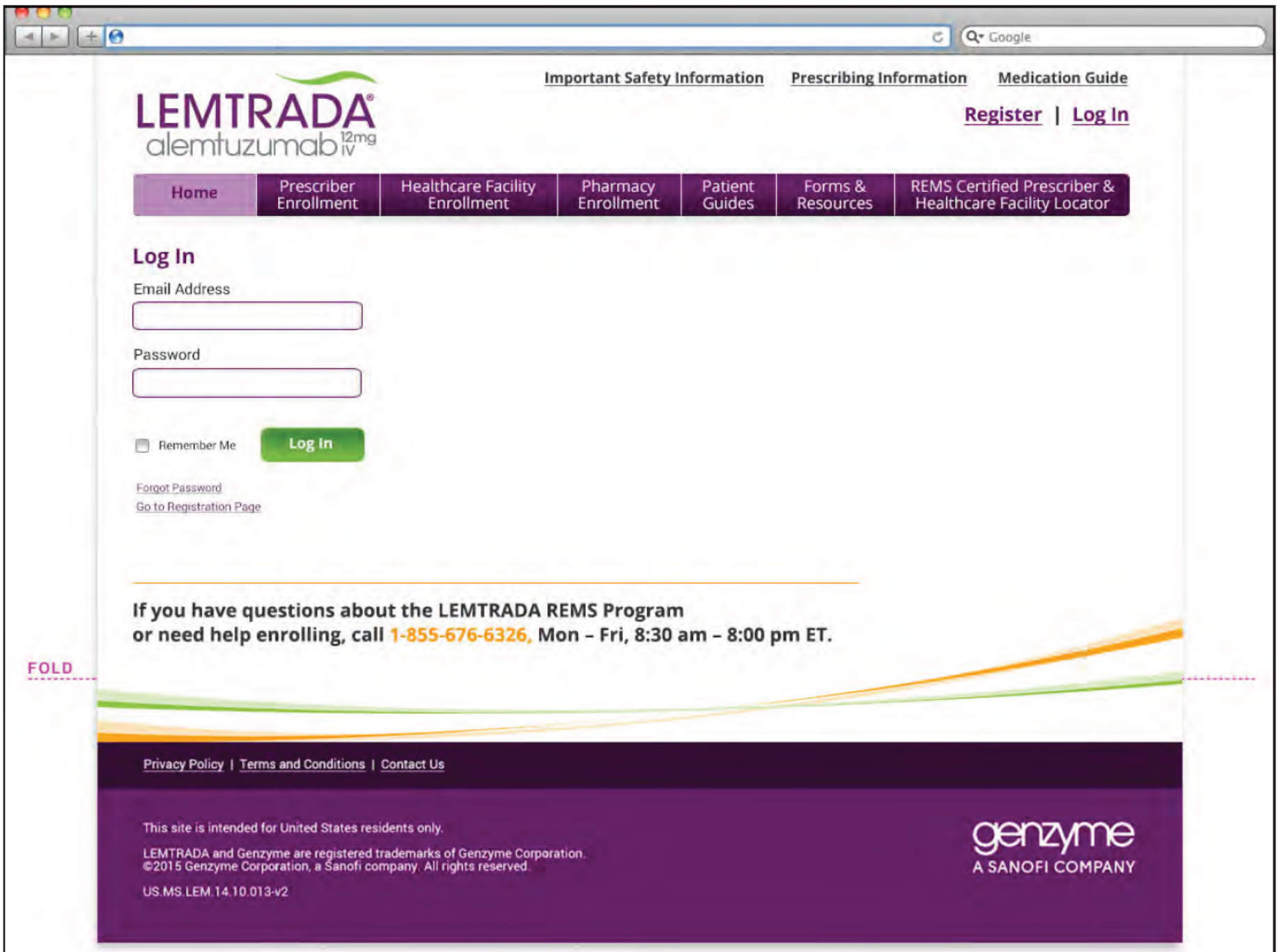
LEMTRADA REMS Desktop - Public Home, 3rd Party Interstitial Page



Reference ID: 3821900

LEMTRADA REMS Desktop - Public Home, Log In



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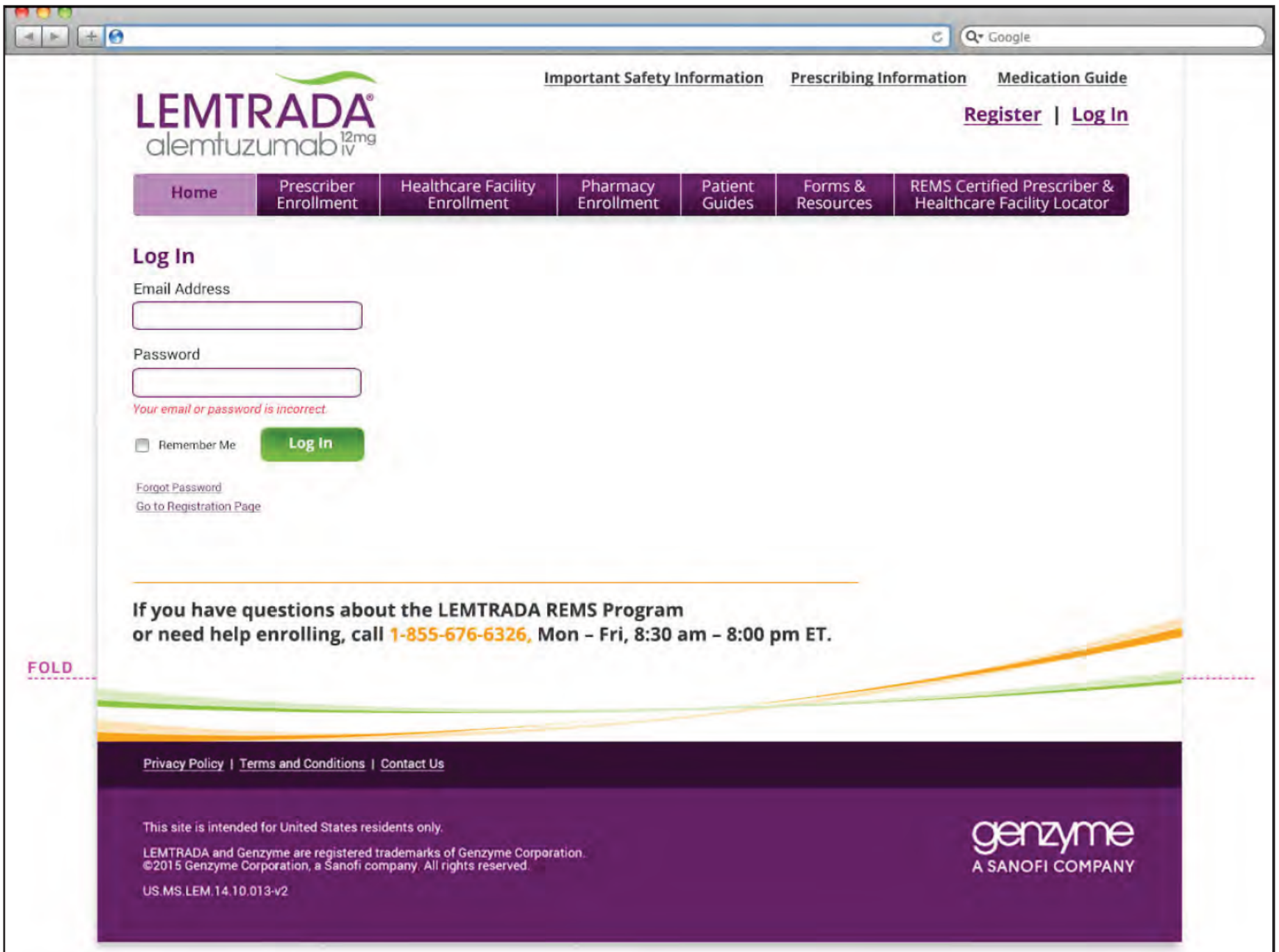

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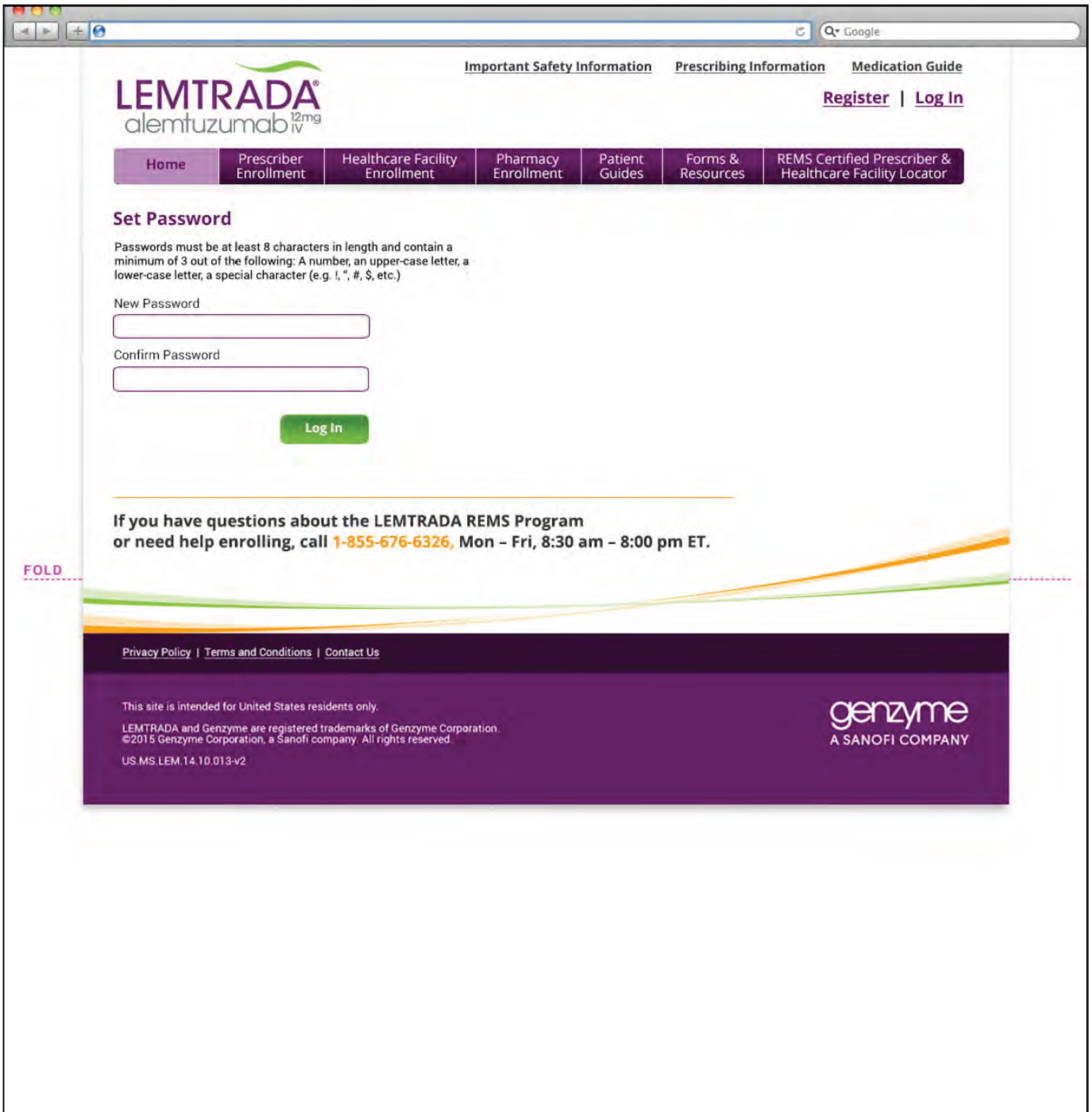

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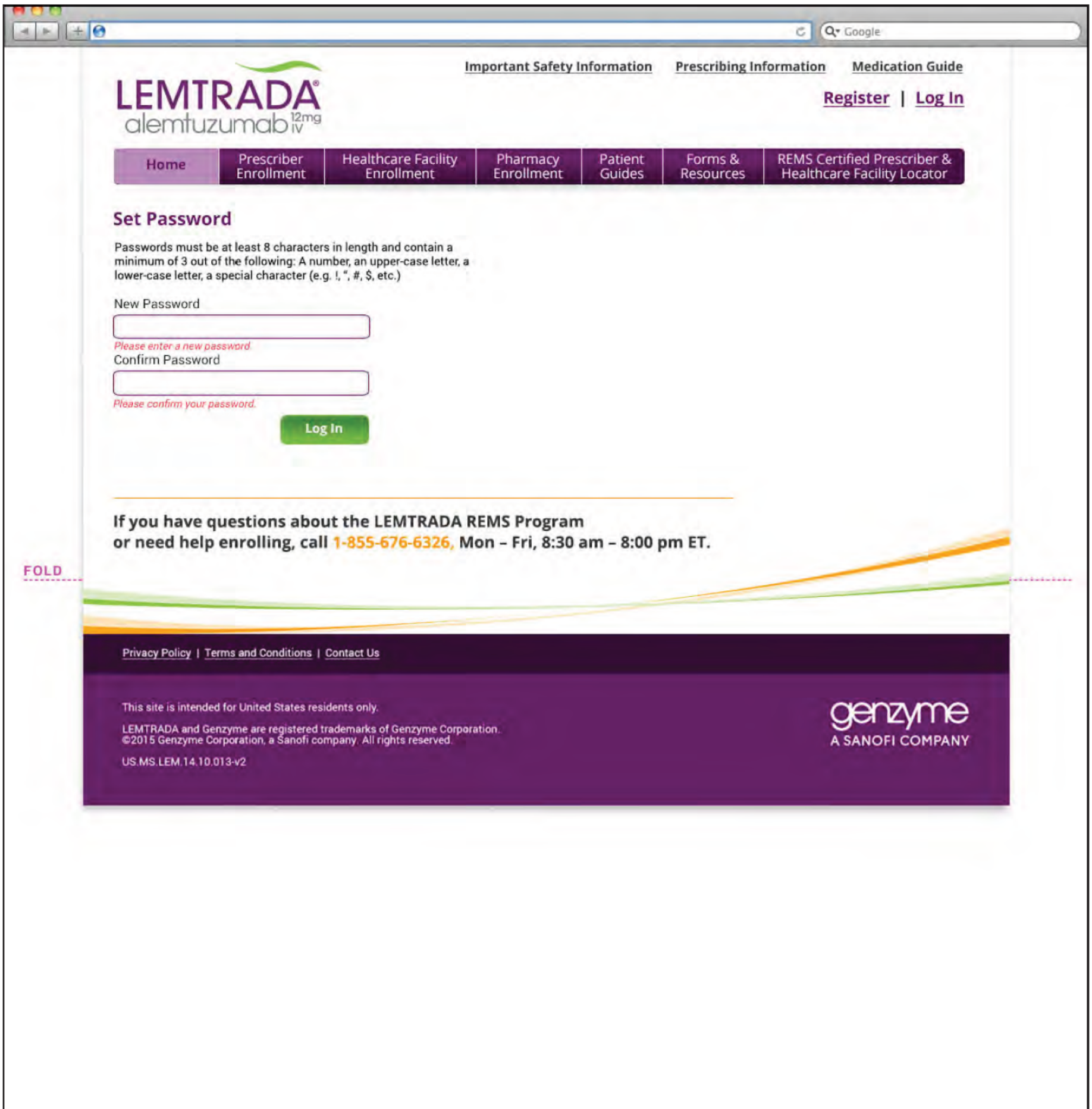

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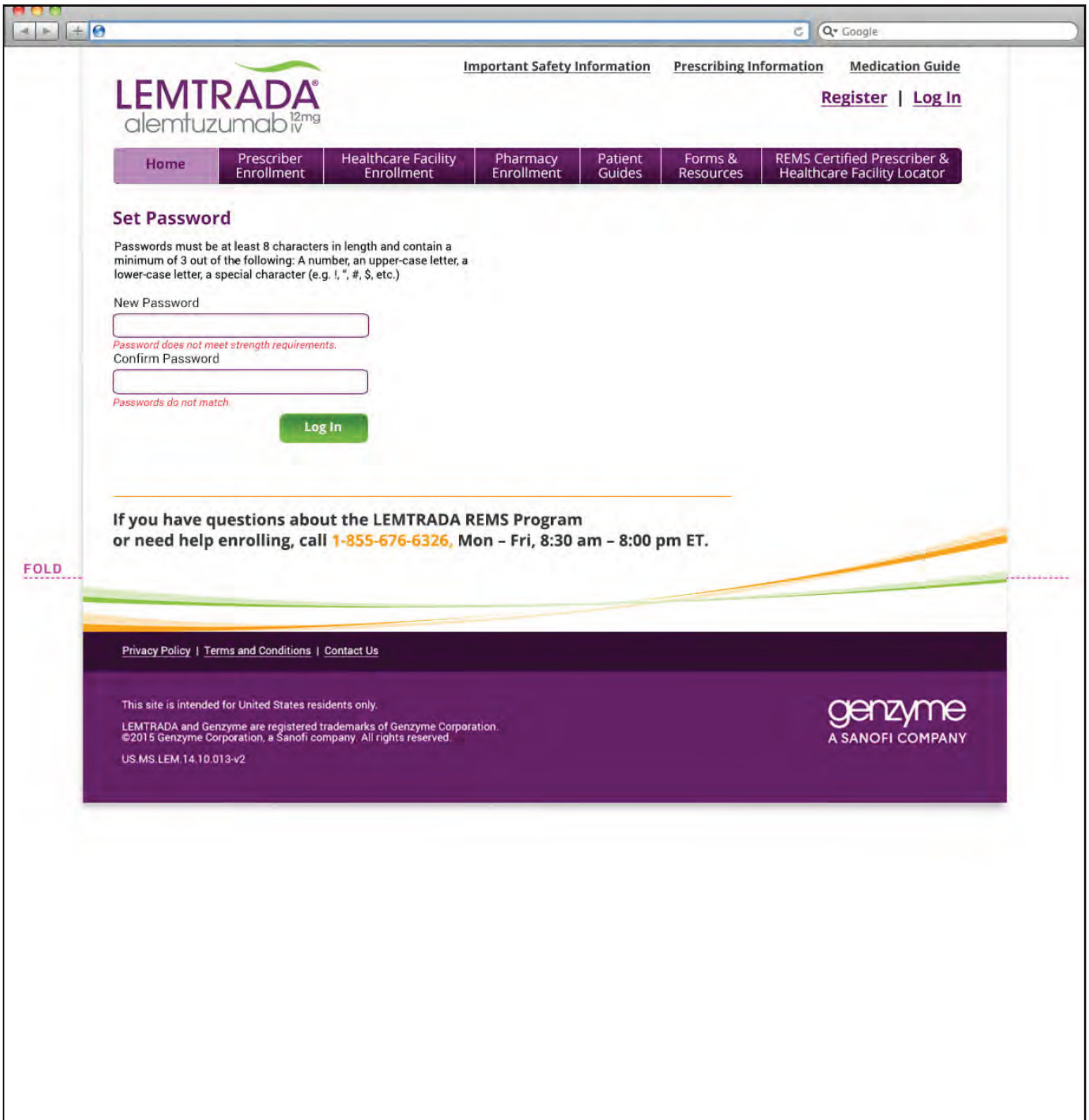

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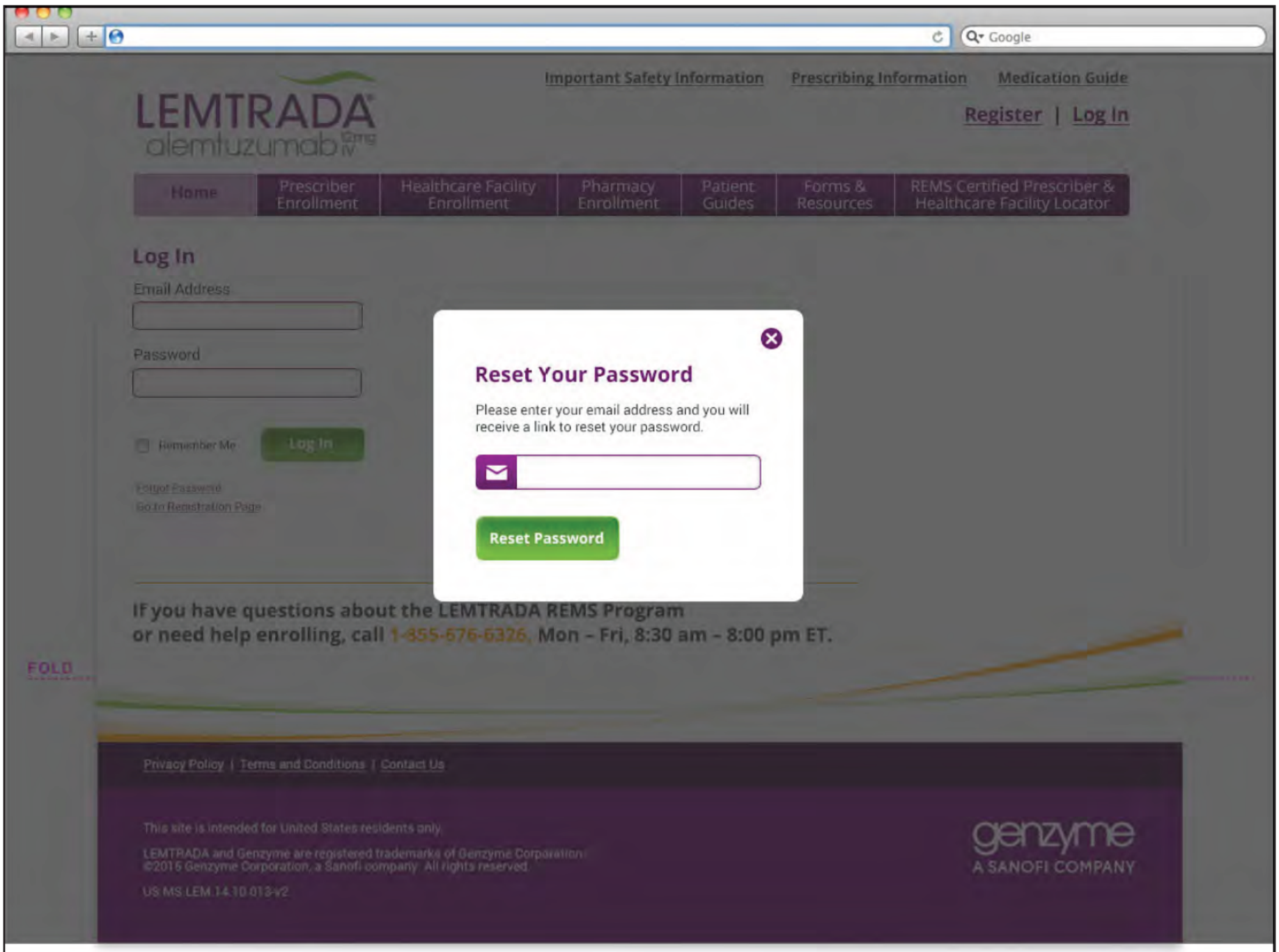

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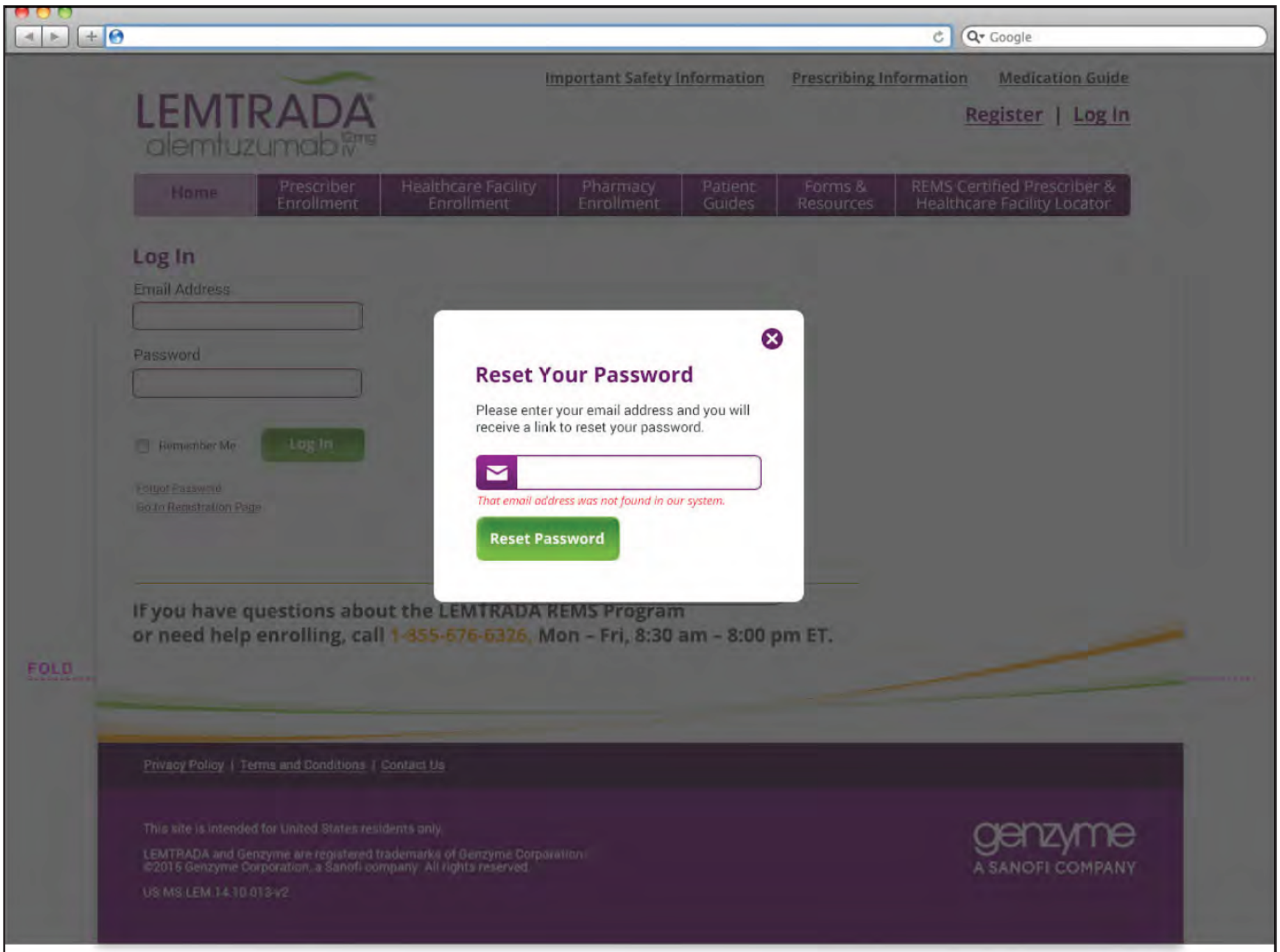
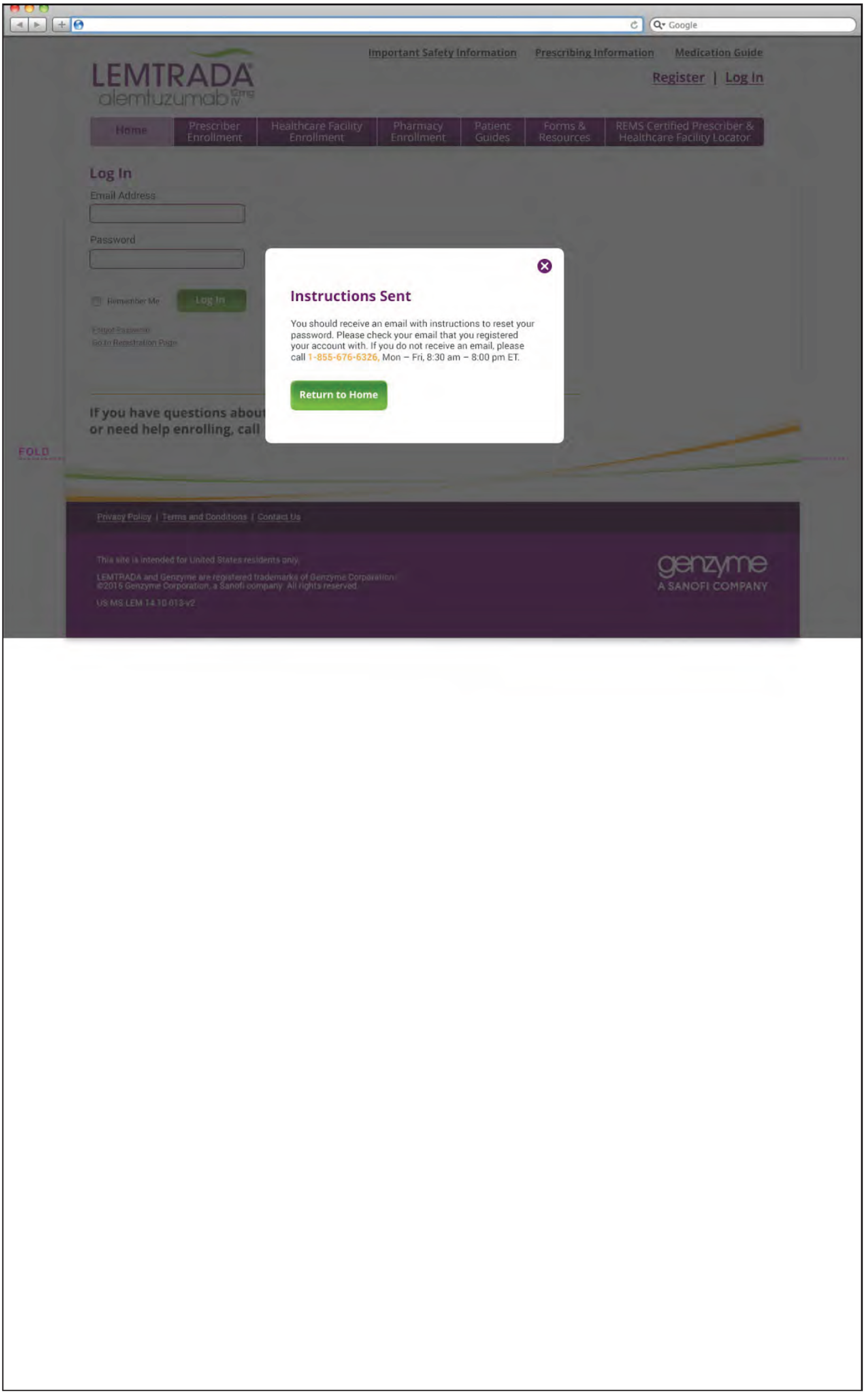


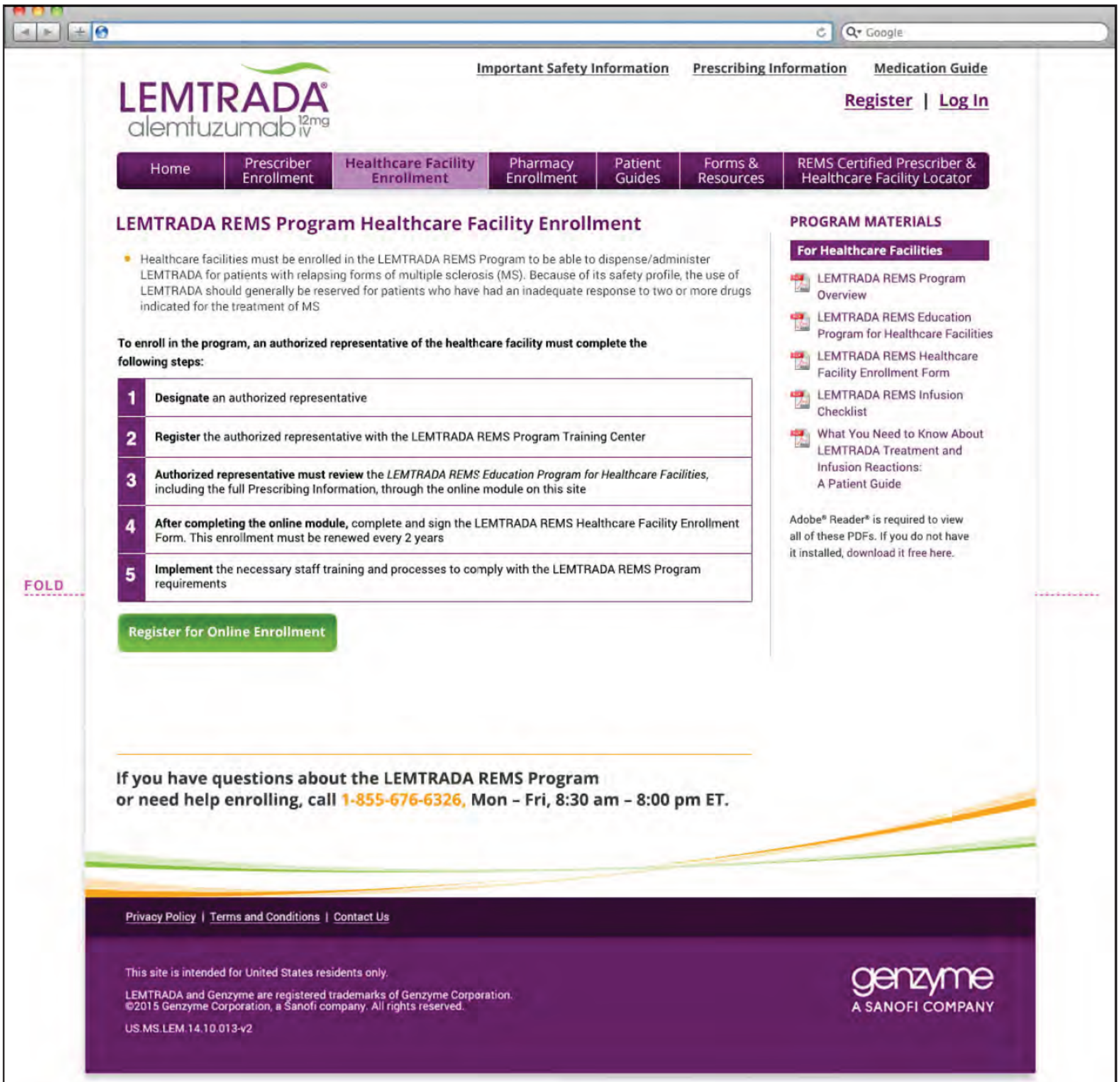
LEMTRADA REMS Desktop - Public Home, Instructions Sent



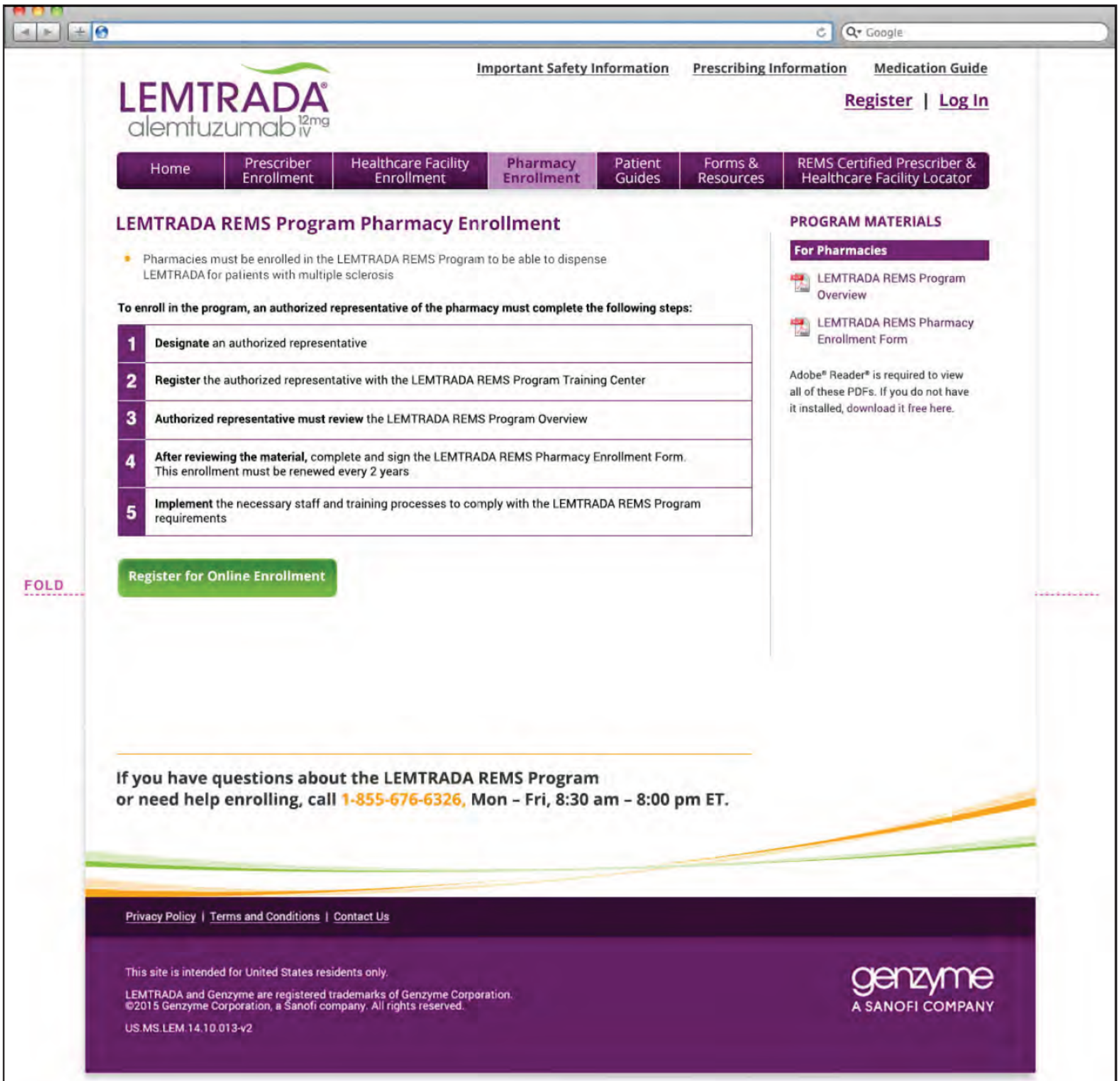
LEMTRADA REMS Desktop - Public Home, Prescriber Enrollment



LEMTRADA REMS Desktop - Public Home, Healthcare Facility Enrollment



LEMTRADA REMS Desktop - Public Home, Pharmacy Enrollment



LEMTRADA REMS Desktop - Public Home, Patient Guides



LEMTRADA REMS Desktop - Public Home, Forms and Resources



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LEMTRADA REMS Desktop - Public Home, REMS Certified Prescriber and Healthcare Facility Locator

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REMS Certified Prescriber & Healthcare Facility

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Please enter street address, city, state, or ZIP Code you would like to search for.

New Search: Street address, city, state, or ZIP Code

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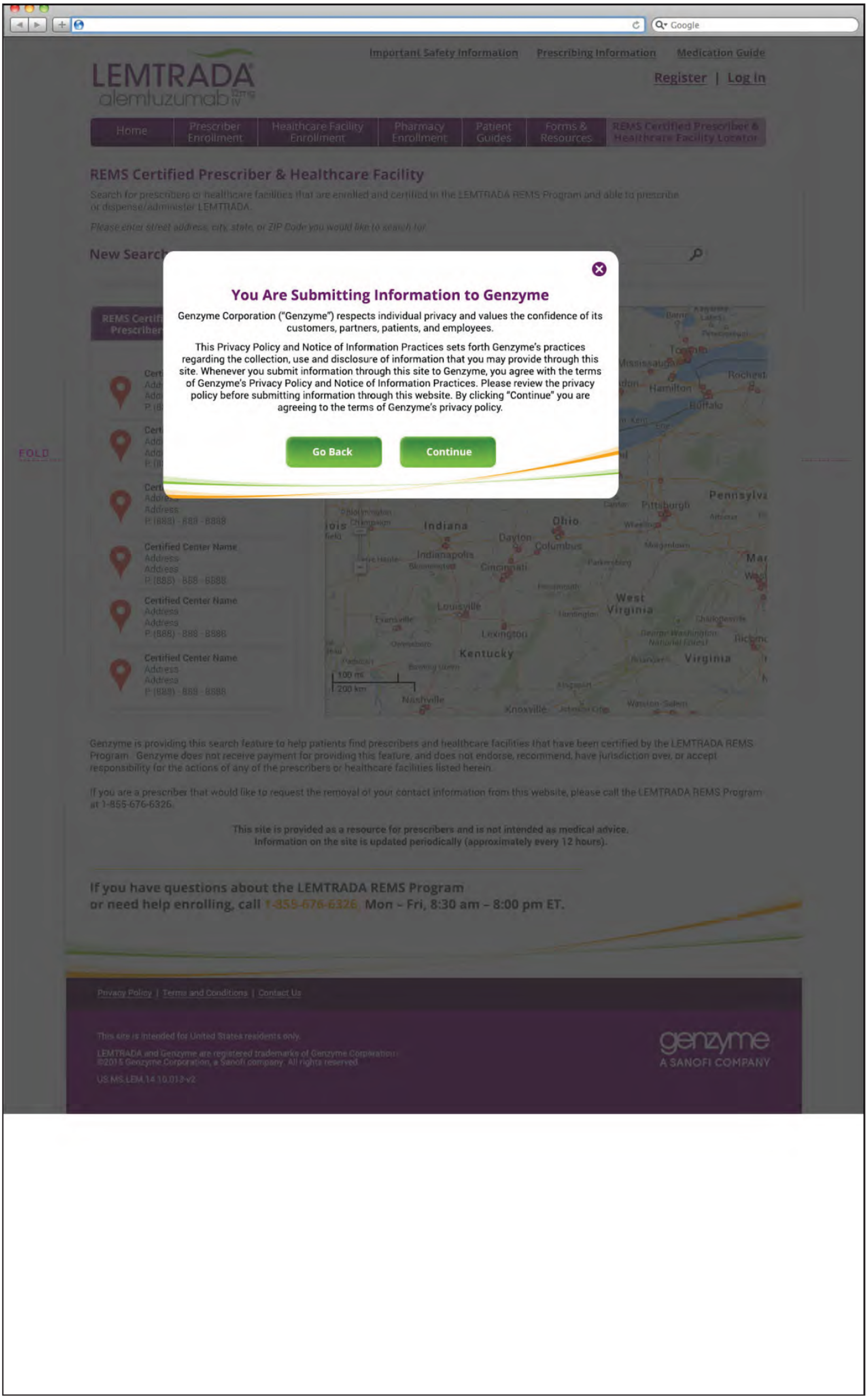

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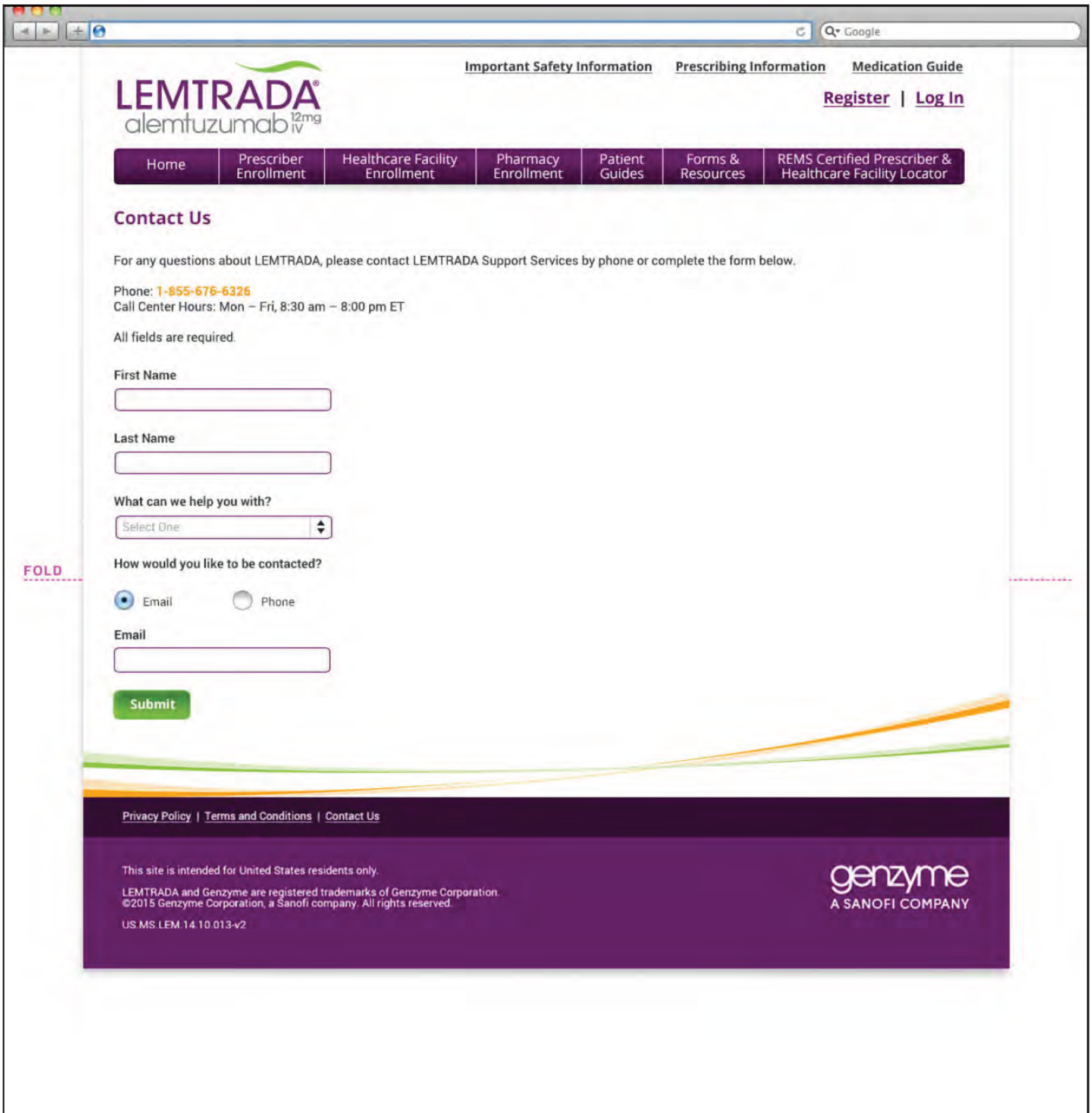
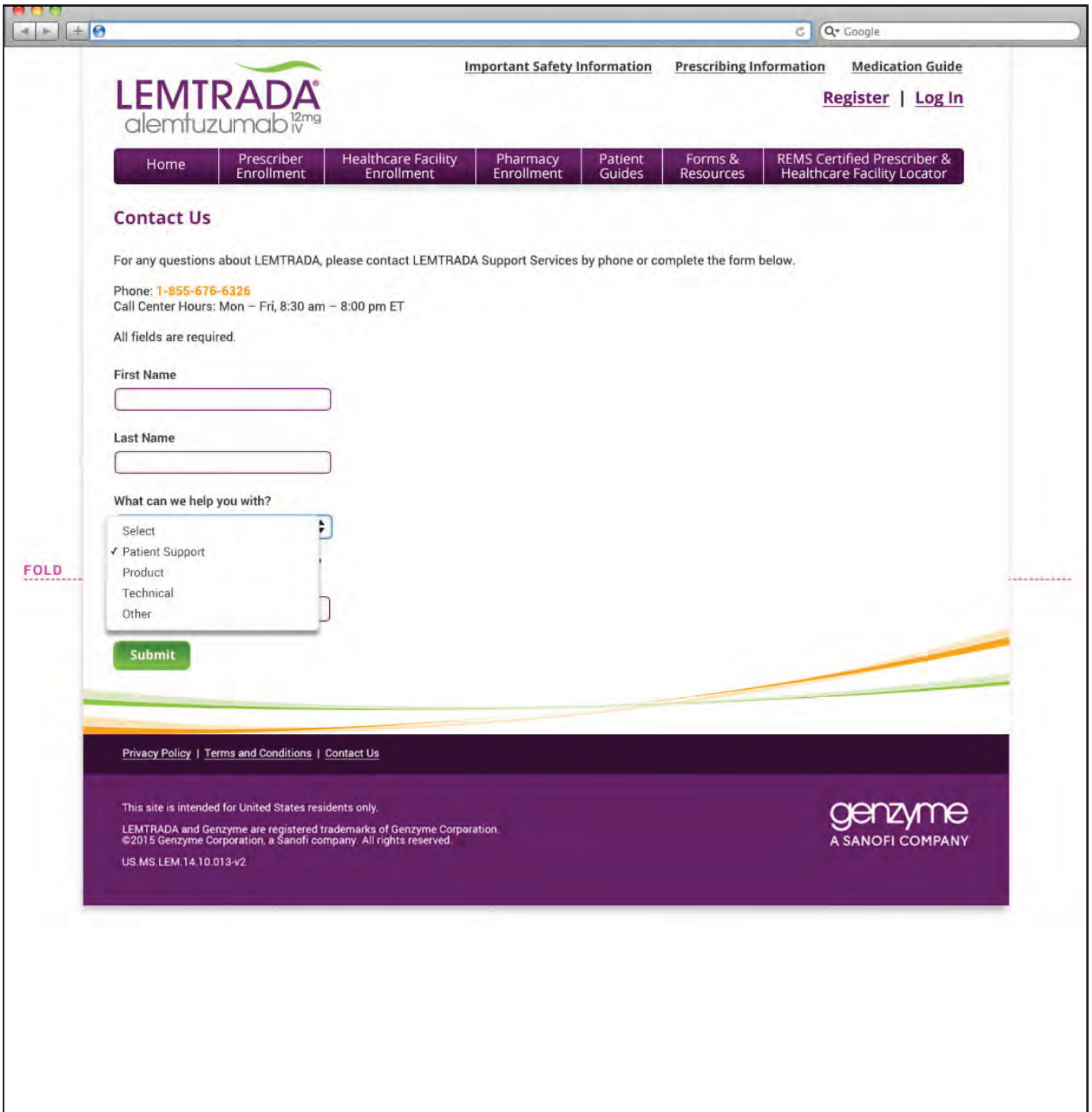
LEMTRADA REMS Desktop - Public Home, Contact Us



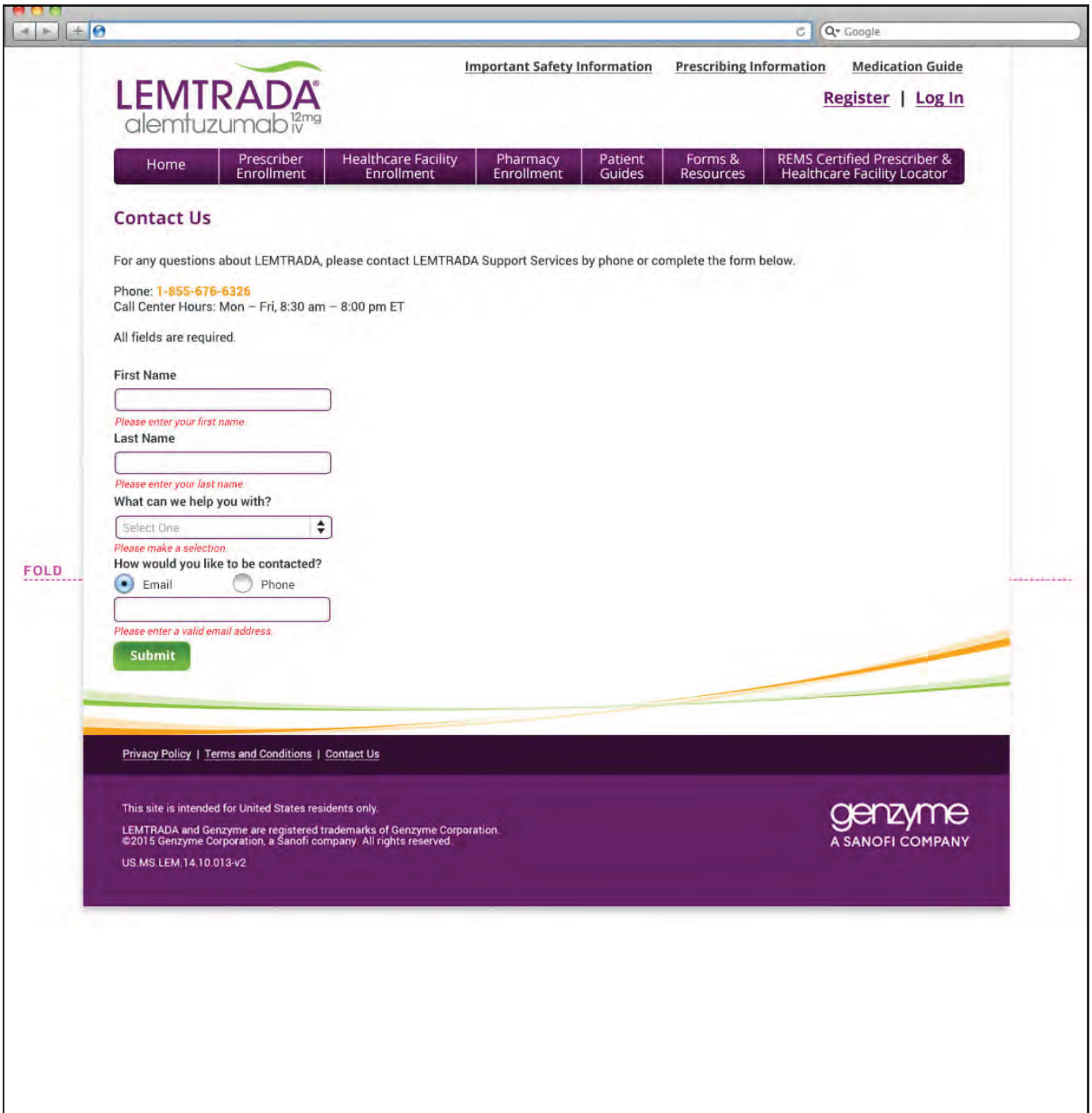
LEMTRADA REMS Desktop - Public Home, Contact Us - Email Selected



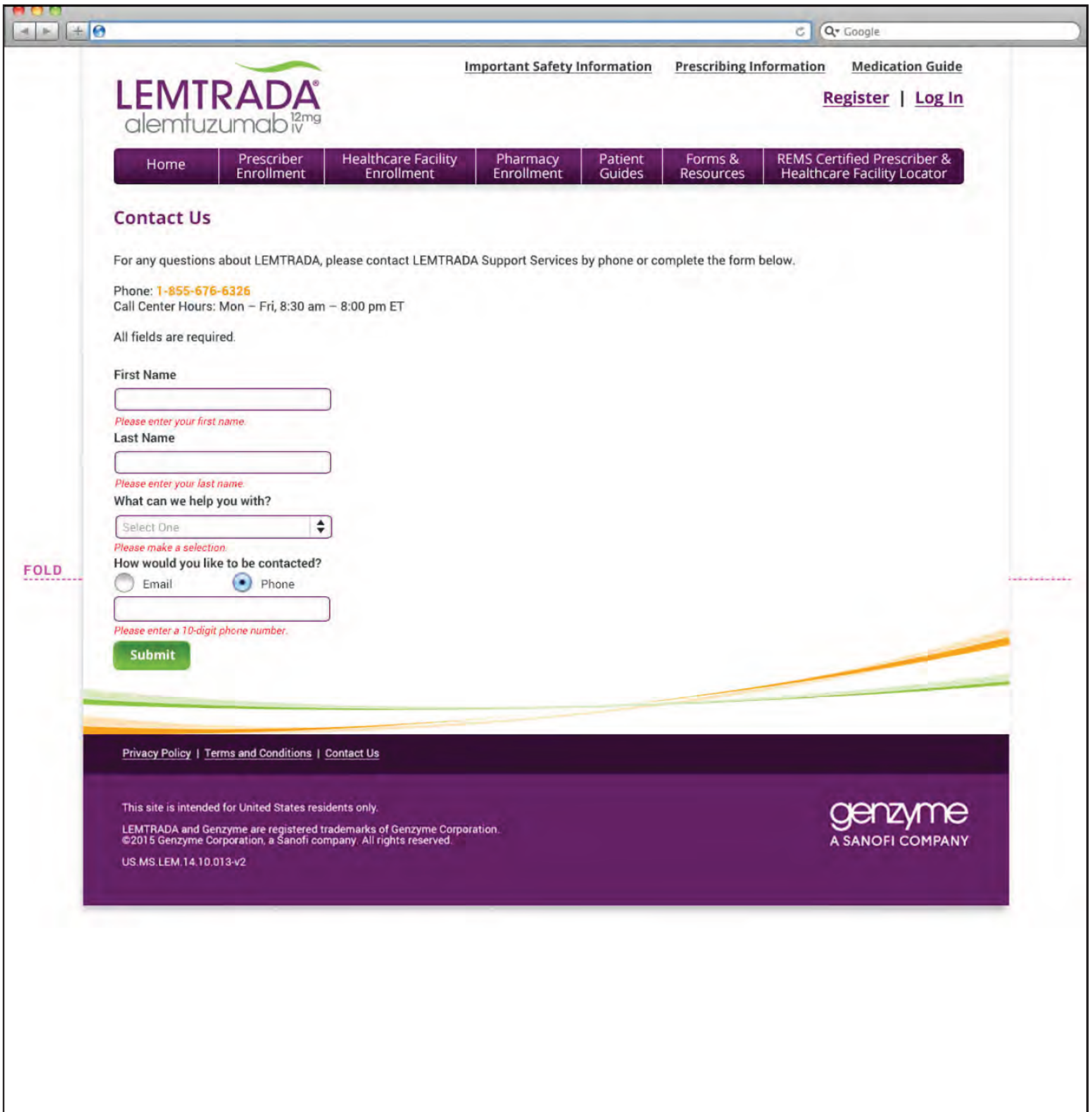
LEMTRADA REMS Desktop - Public Home, Contact Us - Dropdown



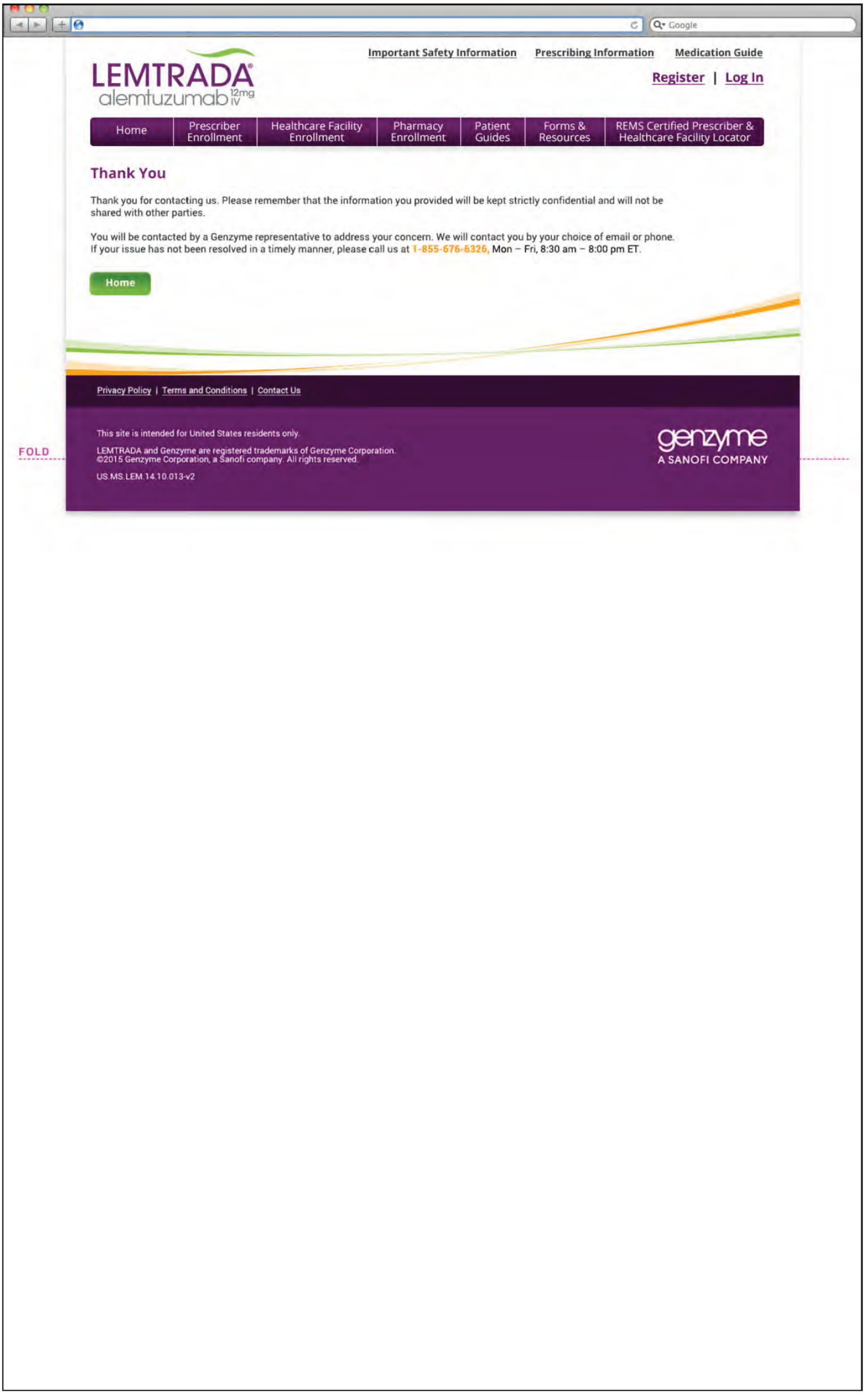
LEMTRADA REMS Desktop - Public Home, Contact Us - Email Error Selected Error



LEMTRADA REMS Desktop - Public Home, Contact Us - Phone Selected Error

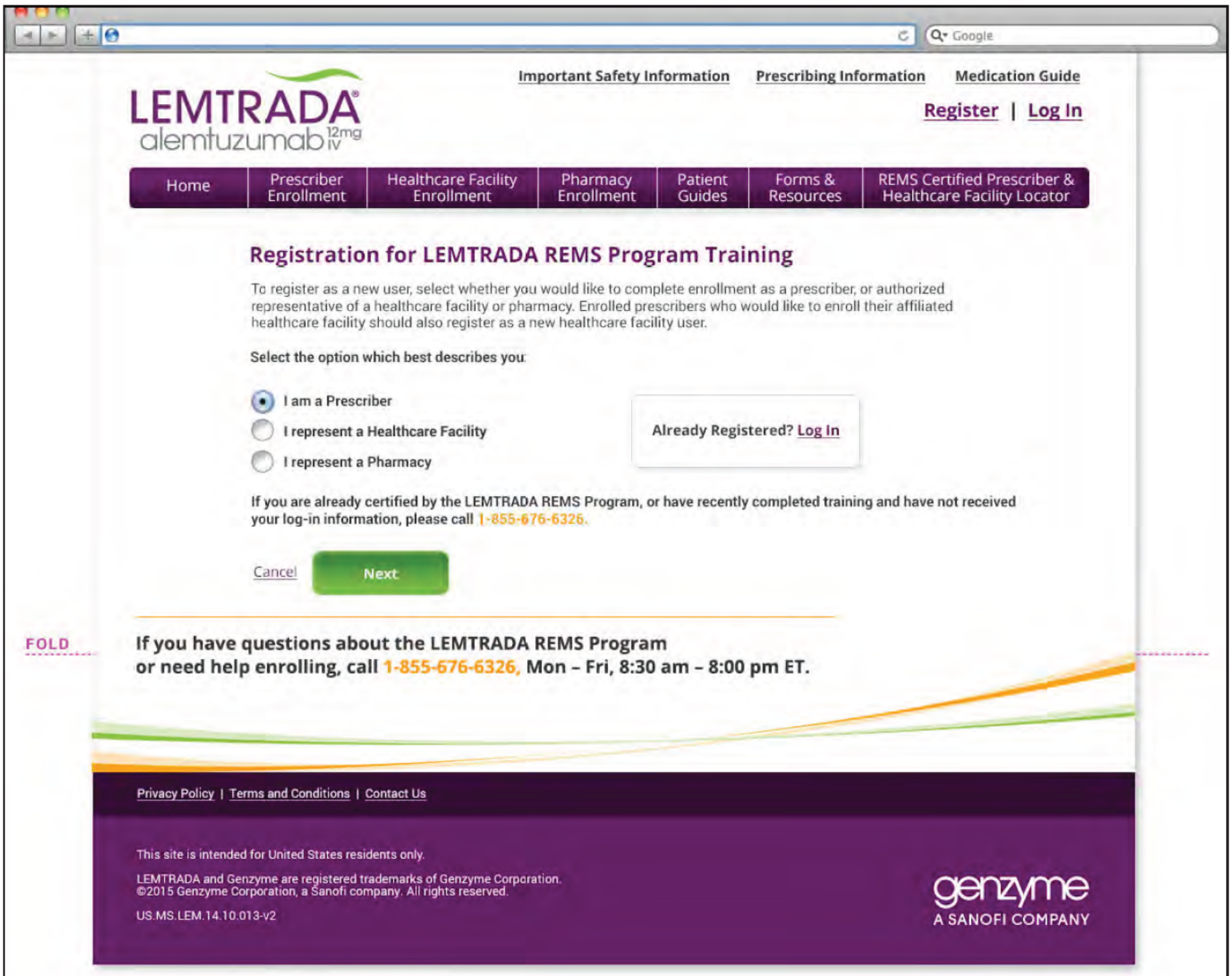


LEMTRADA REMS Desktop - Public Home, Contact Us Confirmation

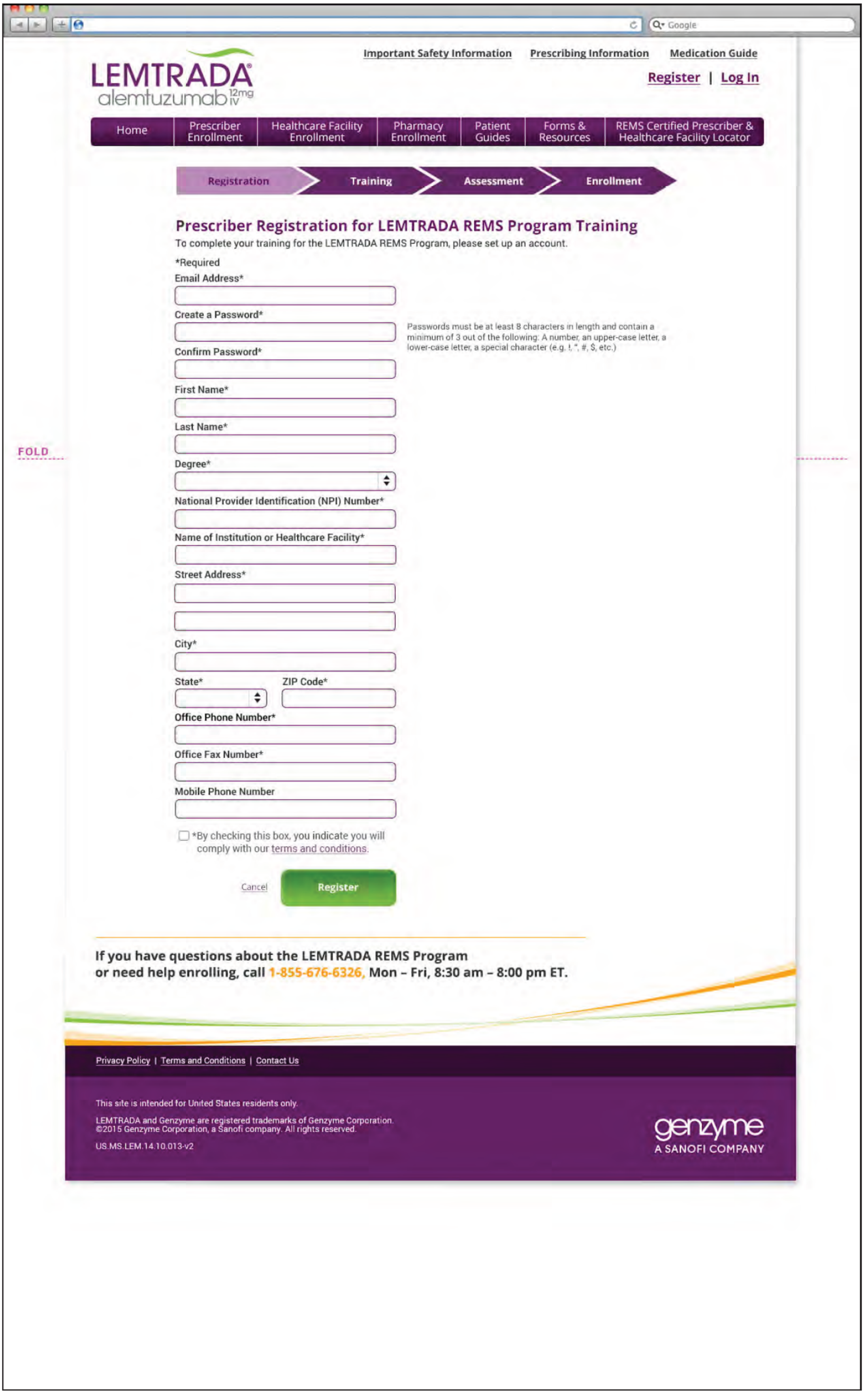


PRESCRIBER TRAINING PAGES

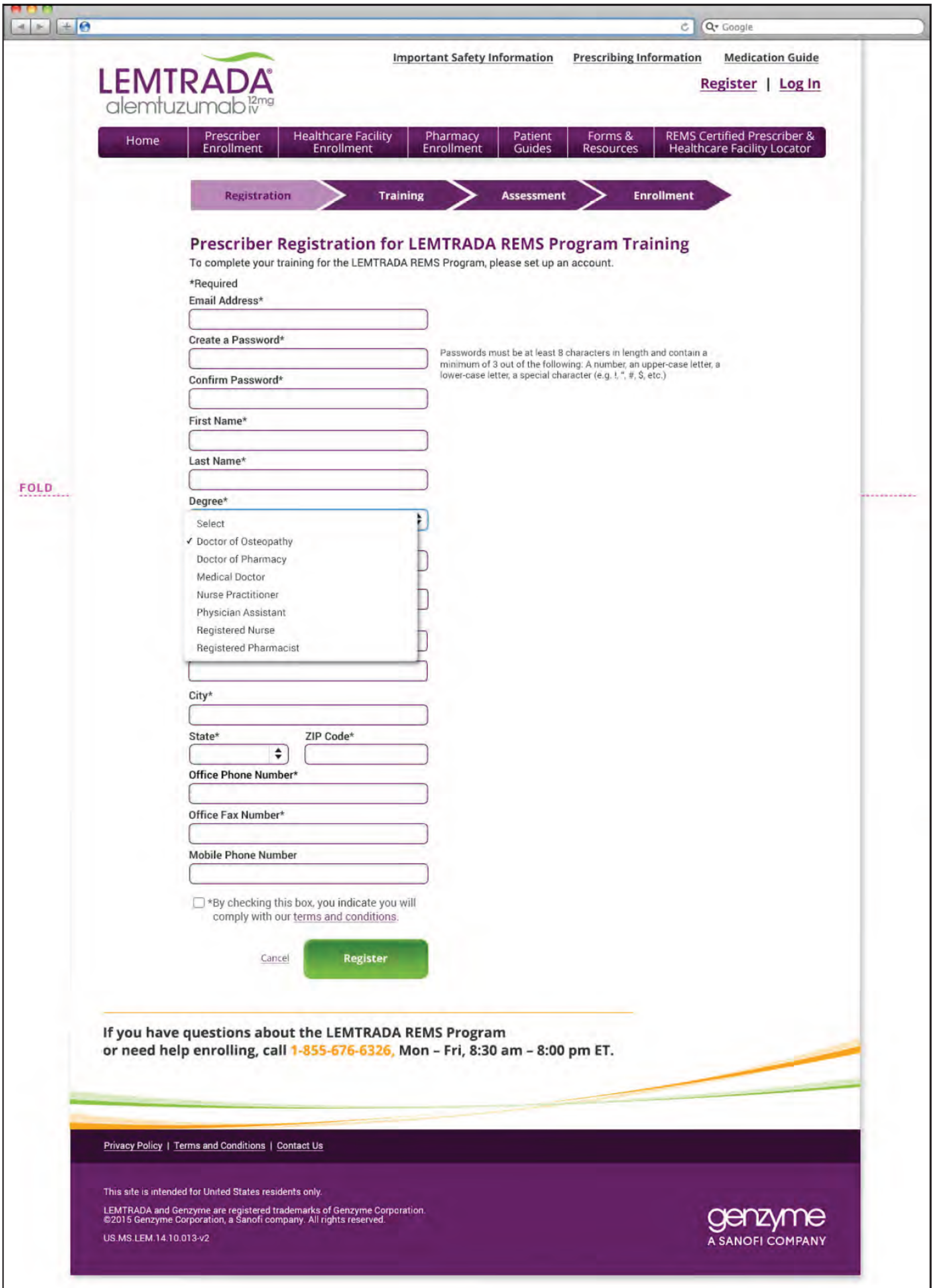
LEMTRADA REMS Desktop - Prescriber Training, Registration - HCP Selection



LEMTRADA REMS Desktop - Prescriber Training, Registration



LEMTRADA REMS Desktop - Prescriber Training, Registration, Degree Dropdown



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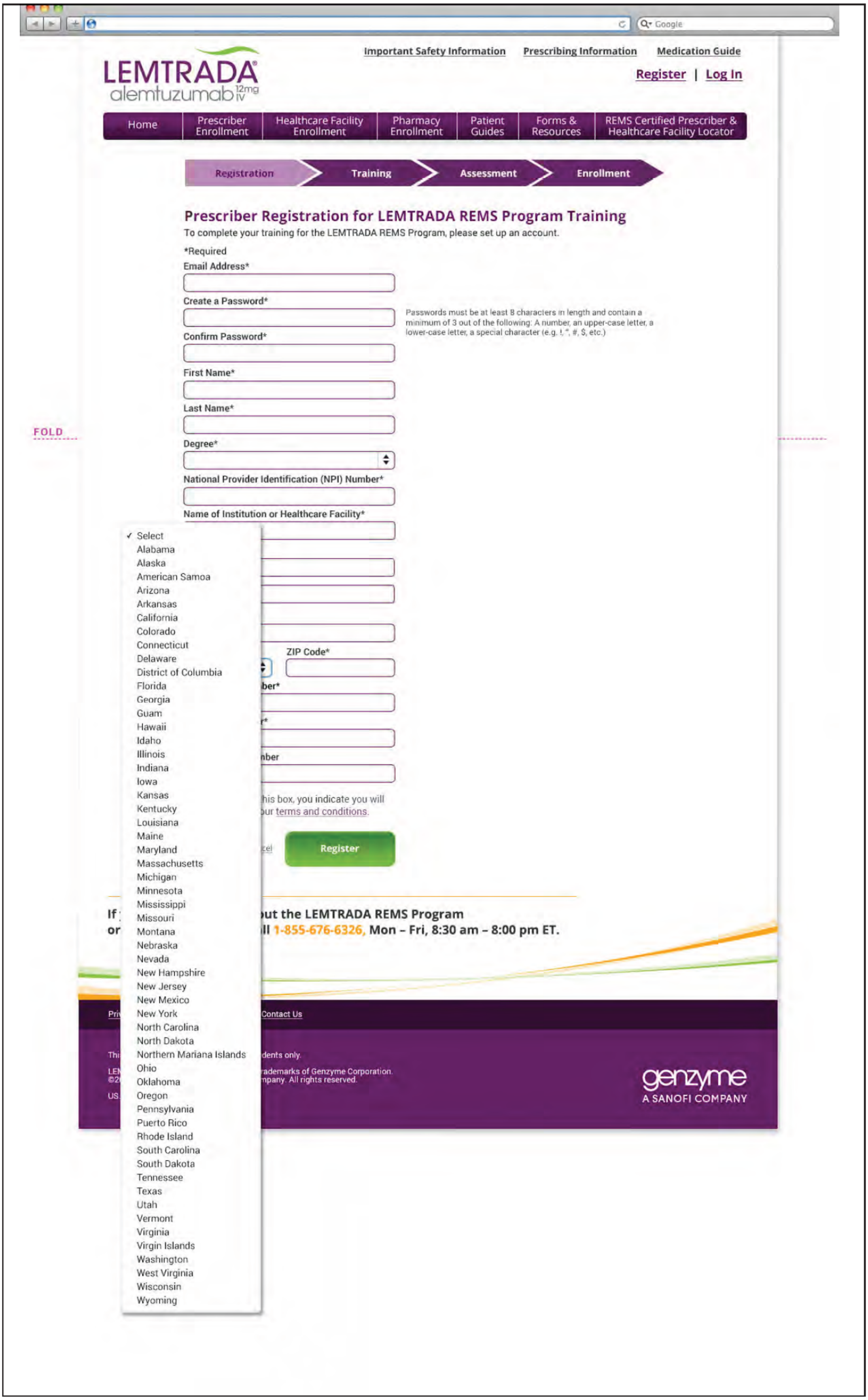
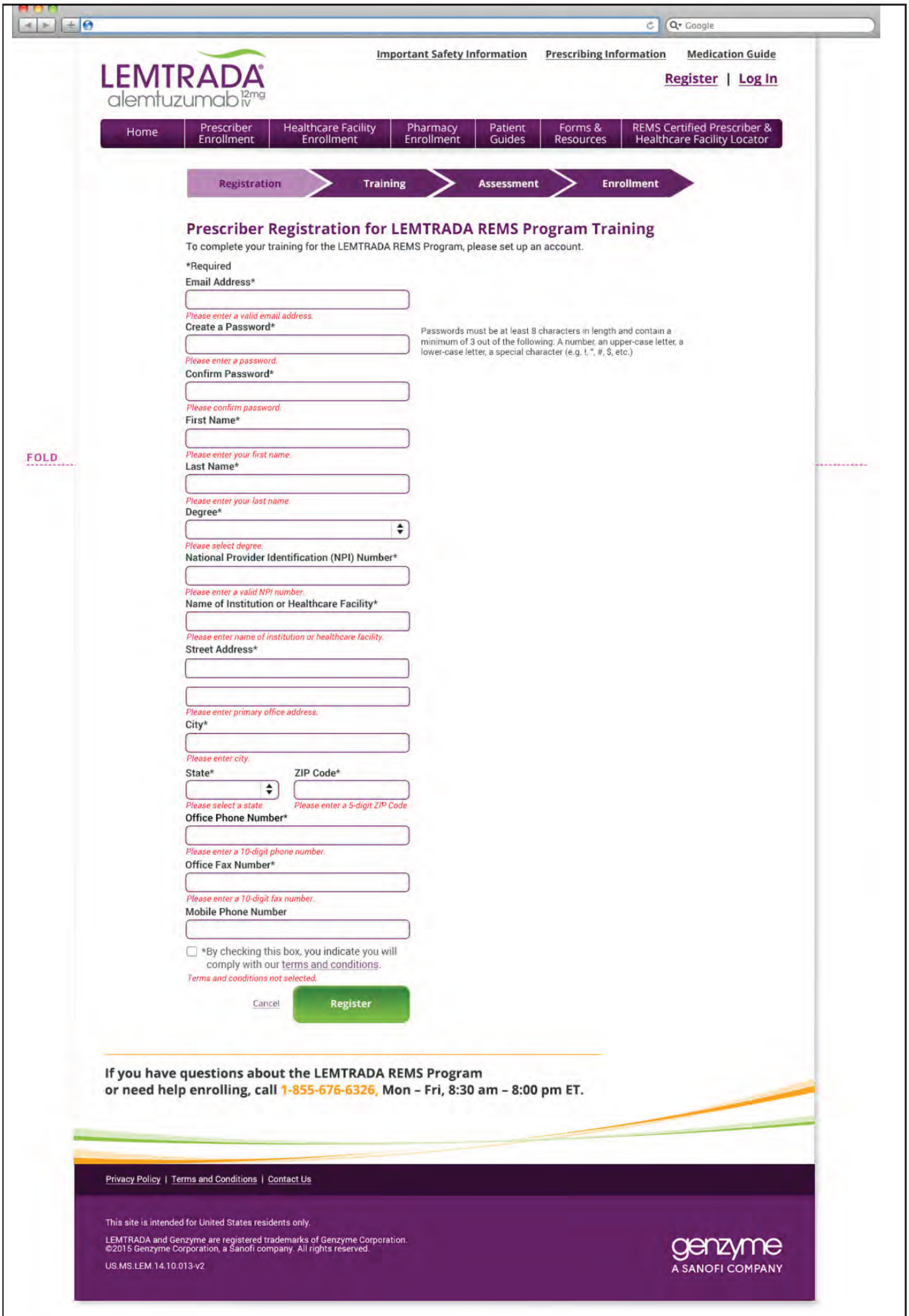


LEMTRADA REMS Desktop - Prescriber Training, Registration, Error



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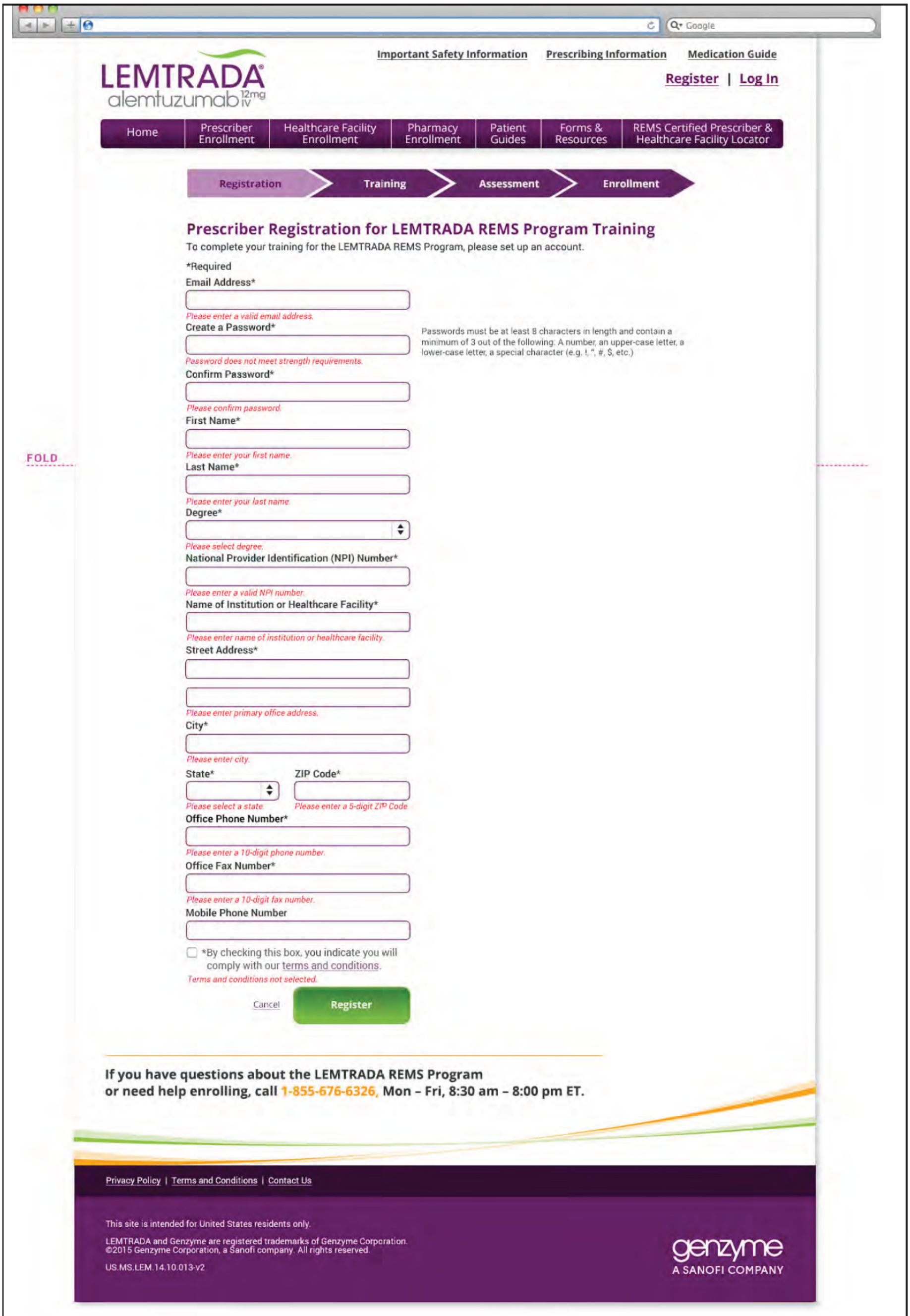

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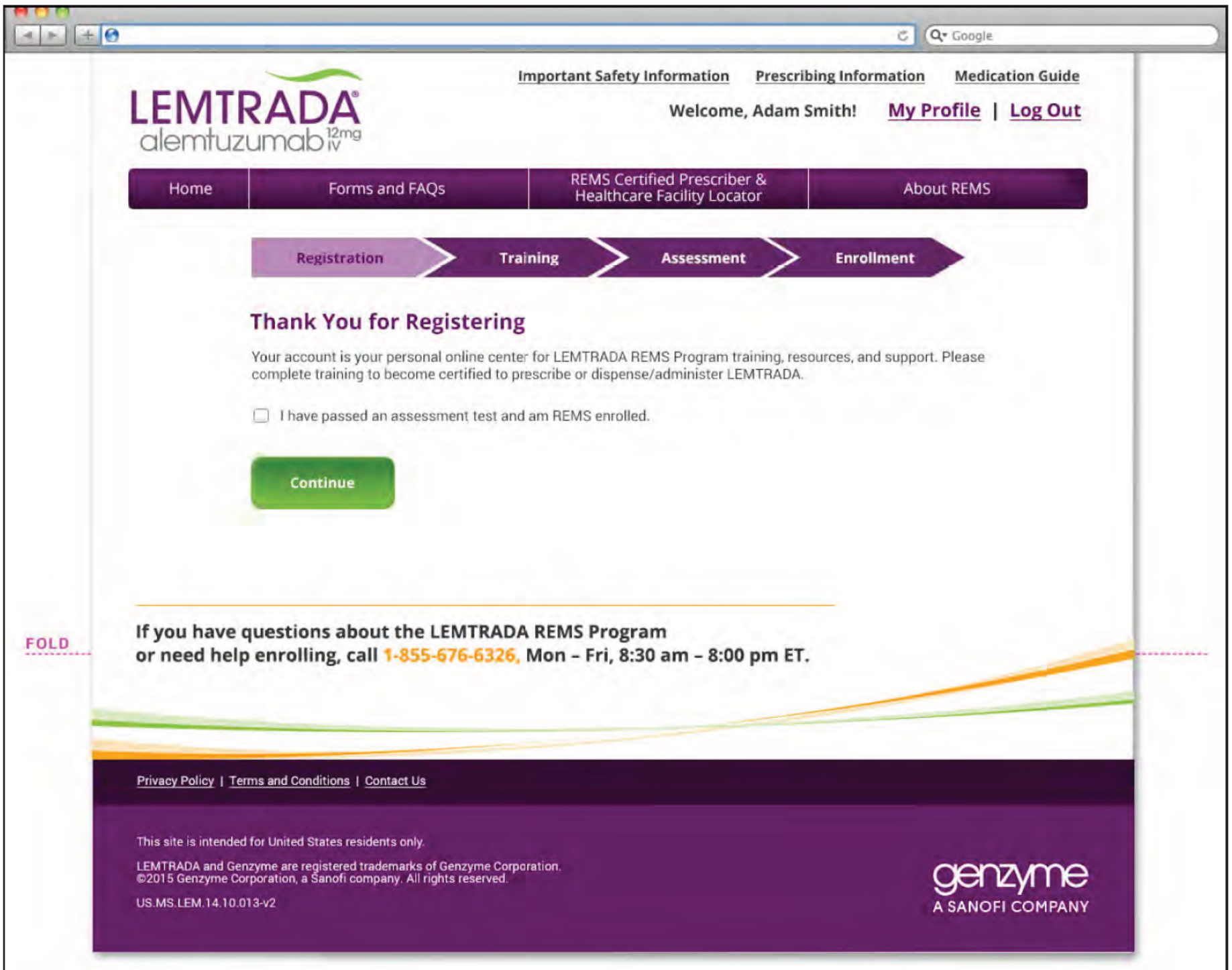
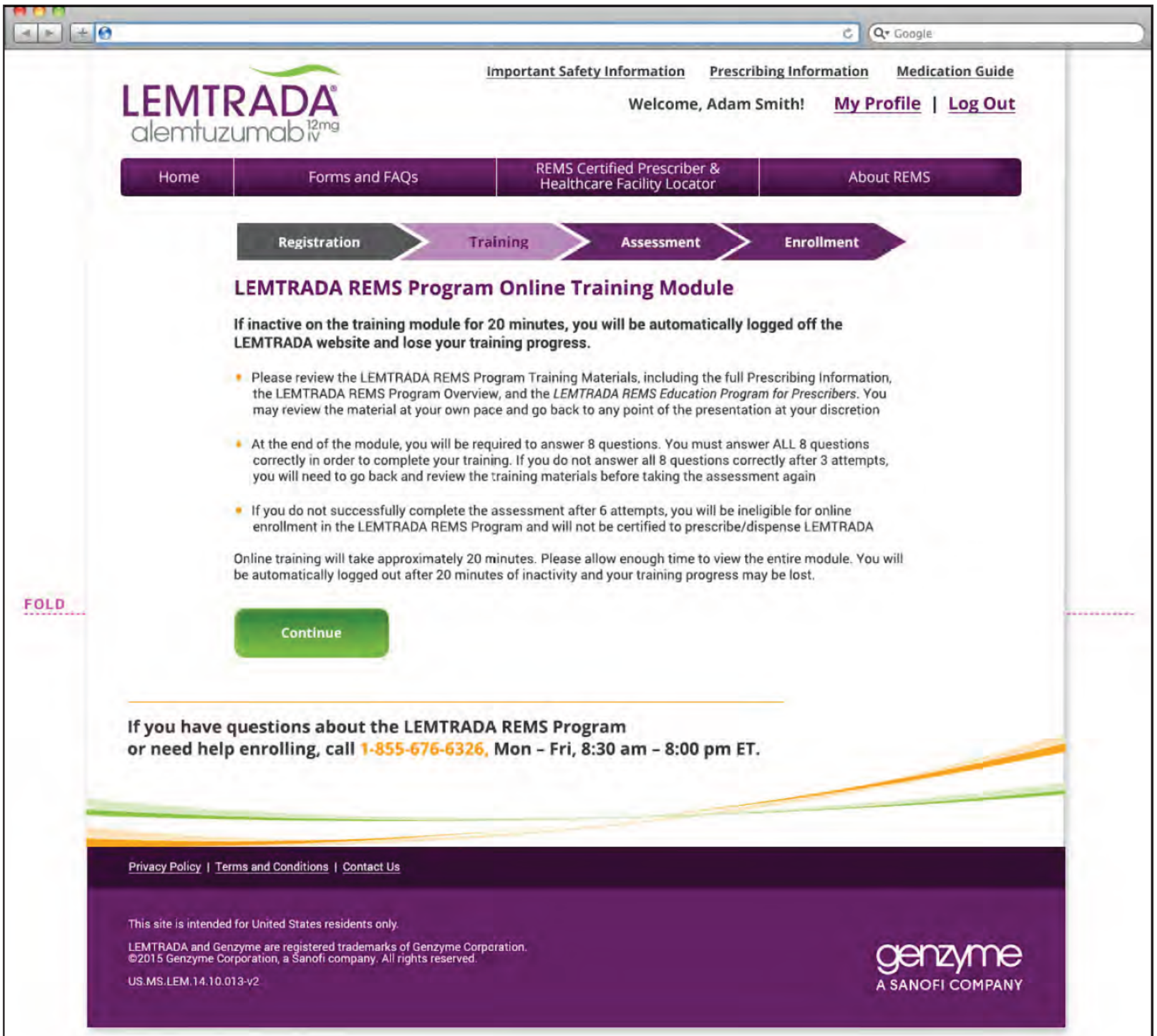
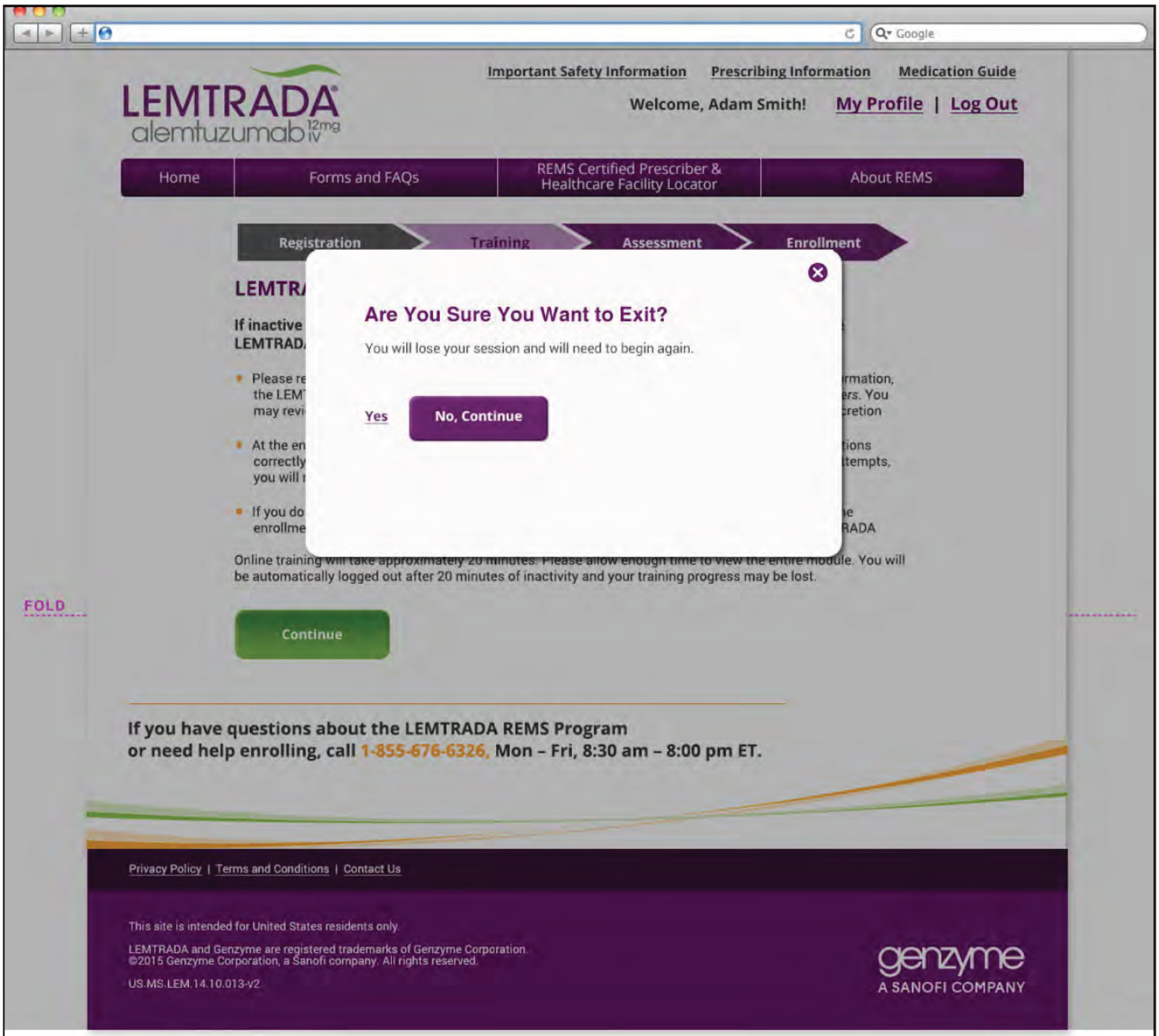


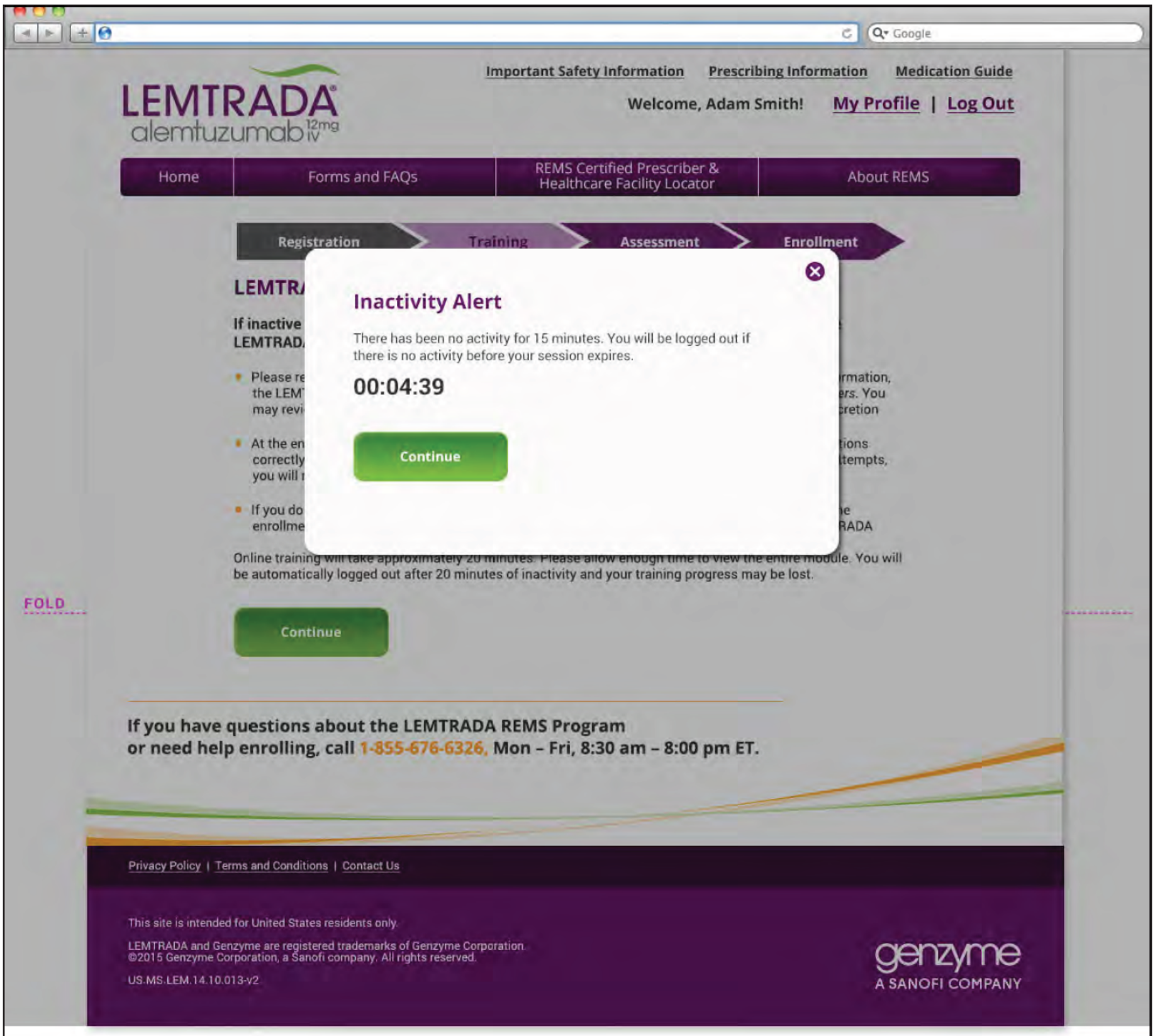
LEMTRADA REMS Desktop - Prescriber Training, Registration, Training Introduction



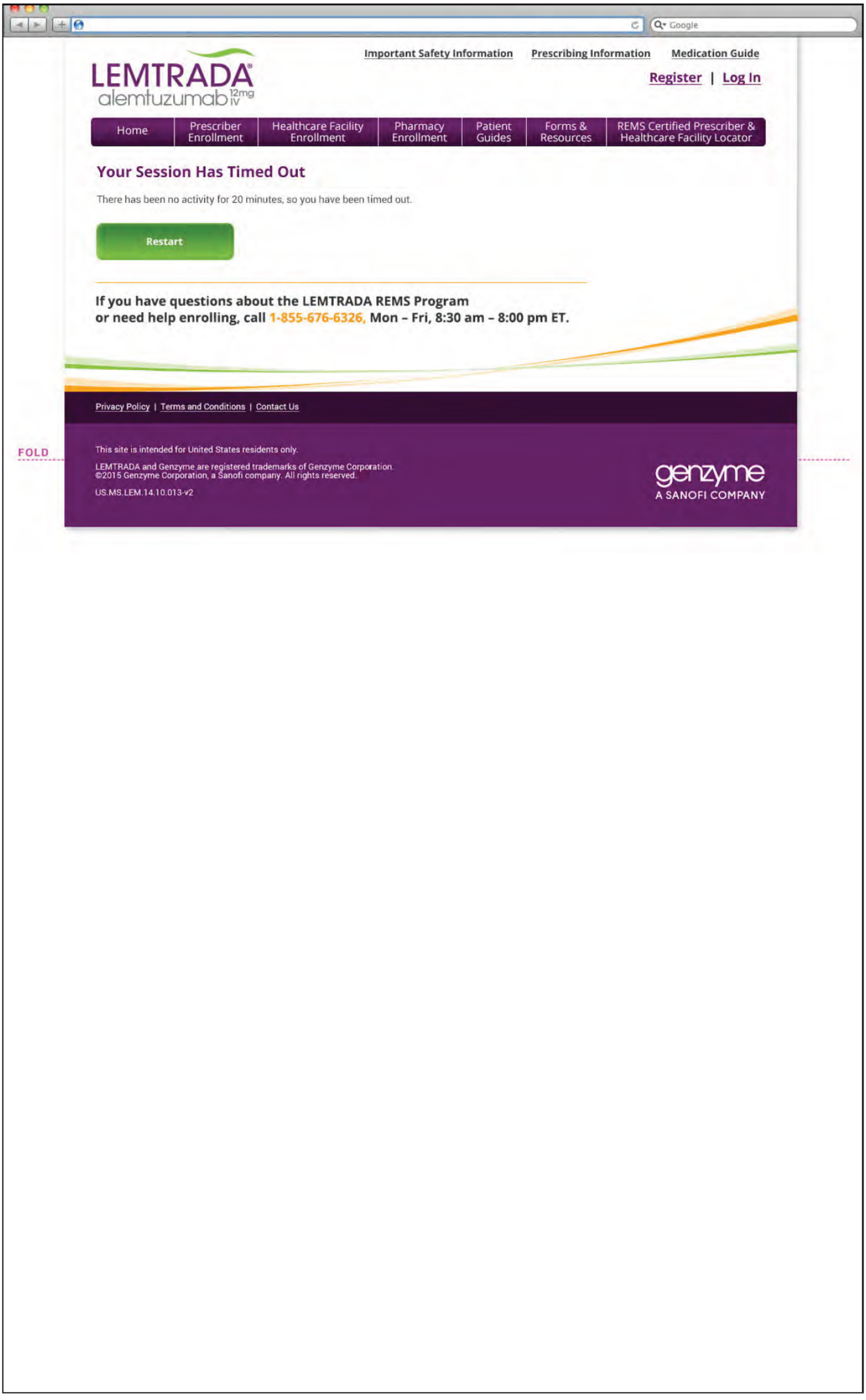
LEMTRADA REMS Desktop - Prescriber Training, Registration, Training Exit



LEMTRADA REMS Desktop - Prescriber Training, Training Timer



LEMTRADA REMS Desktop - Prescriber Training, Training Time Out



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Registration → Training → Assessment → Enrollment

LEMTRADA REMS Program Training

Full Prescribing Information (1 of 8)

Total Training Screens: 1 of 22

FOLD

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- **LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as** immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- **LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA** must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- **LEMTRADA may cause an increased risk of malignancies, including thyroid cancer,** melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- **LEMTRADA is available only through a restricted distribution program. (5.4)**

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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2.2 Vaccinations
2.3 Recommended Premedication and Concomitant Medication
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*Sections or subsections omitted from the full prescribing information are not listed

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

Full Prescribing Information (2 of 8)

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FULL PRESCRIBING INFORMATION

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA *[see Warnings and Precautions (5.1)]*.
- LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period *[see Warnings and Precautions (5.2)]*.
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams *[see Warnings and Precautions (5.3)]*.
- Because of the risk of autoimmunity, infusion reactions, and malignancies, LEMTRADA is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS program *[see Warnings and Precautions (5.4)]*.

1 INDICATIONS AND USAGE

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Information

The recommended dosage of LEMTRADA is 12 mg/day administered by intravenous infusion for 2 treatment courses:

- First Treatment Course: 12 mg/day on 5 consecutive days (60 mg total dose)
- Second Treatment Course: 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course.

2.2 Vaccinations

Patients should complete any necessary immunizations at least 6 weeks prior to treatment with LEMTRADA *[see Warnings and Precautions (5.9)]*.

Prior to LEMTRADA treatment determine whether patients have a history of varicella or have been vaccinated for varicella zoster virus (VZV). If not, test the patient for antibodies to VZV and consider vaccination for those who are antibody-negative. Postpone treatment with LEMTRADA until 6 weeks after VZV vaccination.

2.3 Recommended Premedication and Concomitant Medication

Corticosteroids

Premedicate patients with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course *[see Warnings and Precautions (5.2)]*.

Herpes Prophylaxis

Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later *[see Warnings and Precautions (5.9)]*.

2.4 Preparation Instructions

Follow the steps below to prepare the diluted solution of LEMTRADA for intravenous infusion:

- Inspect LEMTRADA visually for particulate matter and discoloration prior to administration. Do not use if particulate matter is present or the solution is discolored. Do not freeze or shake vials prior to use.
- Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique and inject into a 100 mL bag of sterile 0.9% Sodium Chloride, USP or 5% Dextrose in Water, USP.
- Gently invert the bag to mix the solution. Ensure the sterility of the prepared solution, because it contains no antimicrobial preservatives. Each vial is for single use only.

Prior to administration, protect diluted LEMTRADA solution from light and store for as long as 8 hours either at room temperature 15°C to 25°C (59°F to 77°F) or keep refrigerated at conditions 2°C to 8°C (36°F to 46°F).

2.5 Infusion Instructions

Infuse LEMTRADA over 4 hours starting within 8 hours after dilution. Extend the duration of the infusion if clinically indicated.

Administer LEMTRADA in a setting in which equipment and personnel to appropriately manage anaphylaxis or serious infusion reactions are available *[see Warnings and Precautions (5.4)]*.

Do not add or simultaneously infuse other drug substances through the same intravenous line. Do not administer as an intravenous push or bolus.

Monitor vital signs before the infusion and periodically during the infusion. Provide appropriate symptomatic treatment for infusion reactions as needed. Consider immediate discontinuation of the intravenous infusion if severe infusion reactions occur.

Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Inform patients that they should report symptoms that occur during and after each infusion because they may indicate a need for prompt medical intervention *[see Warnings and Precautions (5.2)]*.

2.6 Laboratory Testing and Monitoring to Assess Safety

Conduct the following laboratory tests at baseline and at periodic intervals for 48 months following the last treatment course of LEMTRADA in order to monitor for early signs of potentially serious adverse effects:

- Complete blood count (CBC) with differential (prior to treatment initiation and at monthly intervals thereafter)
- Serum creatinine levels (prior to treatment initiation and at monthly intervals thereafter)
- Urinalysis with urine cell counts (prior to treatment initiation and at monthly intervals thereafter)
- A test of thyroid function, such as thyroid stimulating hormone (TSH) level (prior to treatment initiation and every 3 months thereafter)

Conduct baseline and yearly skin exams to monitor for melanoma *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. LEMTRADA is a clear and colorless to slightly yellow solution that requires dilution prior to intravenous infusion.

4 CONTRAINDICATIONS

LEMTRADA is contraindicated in patients who are infected with Human Immunodeficiency Virus (HIV) because LEMTRADA causes prolonged reductions of CD4+ lymphocyte counts.

5 WARNINGS AND PRECAUTIONS

5.1 Autoimmunity

Treatment with LEMTRADA can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions. In clinical studies LEMTRADA-treated patients experienced thyroid disorders (34%), immune thrombocytopenia (2%), and glomerular nephropathies (0.3%) *[see Warnings and Precautions (5.5, 5.6, 5.7)]*. Autoimmune hemolytic anemia and autoimmune pancytopenia *[see Warnings and Precautions (5.8)]*, undifferentiated connective tissue disorders, and acquired hemophilia A (anti-Factor VIII antibodies) each occurred in 0.2% of patients. Rheumatoid arthritis, type I diabetes, vitiligo, and retinal pigment epitheliopathy occurred in 0.1% of patients.

During postmarketing use, additional autoimmune events including Guillain-Barre syndrome and chronic inflammatory demyelinating polyradiculoneuropathy have been reported in the treatment of patients with B-cell chronic lymphocytic leukemia (B-CLL), as well as other disorders, generally at higher and more frequent doses than recommended in MS. An oncology patient treated with alemtuzumab had fatal transfusion-associated graft-versus-host disease.

Autoantibodies may be transferred from the mother to the fetus during pregnancy. A case of transplacental transfer of anti-thyrotropin receptor antibodies resulting in neonatal Graves' disease occurred after alemtuzumab treatment in the mother *[see Use in Specific Populations (8.1)]*.

LEMTRADA may increase the risk of other autoimmune conditions because of the broad range of autoantibody formation with LEMTRADA.

Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts before starting treatment and then at monthly intervals for 48 months after the last dose of LEMTRADA to allow for early detection and treatment of autoimmune adverse reactions *[see Dosage and Administration (2.6)]*. After 48 months, testing should be performed based on clinical findings suggestive of autoimmunity.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.2 Infusion Reactions

LEMTRADA causes cytokine release syndrome resulting in infusion reactions, some of which may be serious and life threatening. In clinical studies, 92% of LEMTRADA-treated patients experienced infusion reactions. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients and included anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

During postmarketing use, other serious and sometimes fatal infusion reactions included hypotension, syncope, acute respiratory distress syndrome, respiratory arrest, myocardial infarction, acute cardiac insufficiency, and cardiac arrest have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Premedicate patients with corticosteroids immediately prior to LEMTRADA infusion for the first 3 days of each treatment course. In clinical trials, patients received 1,000 mg of methylprednisolone for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment. Consider additional monitoring in patients with medical conditions which predispose them to cardiovascular or pulmonary compromise.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.3 Malignancies

Thyroid cancer

LEMTRADA may increase the risk of thyroid cancer. In controlled clinical studies, 3 of 918 (0.3%) LEMTRADA-treated patients developed thyroid cancer, compared to none in the interferon beta-1a-treated group. However, screening for thyroid cancer was performed more frequently in the LEMTRADA-treated group, because of the higher incidence of autoimmune thyroid disorders in those patients. Two additional cases of thyroid cancer in LEMTRADA-treated patients occurred in uncontrolled studies.

Patients and healthcare providers should monitor for symptoms of thyroid cancer including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

Melanoma

LEMTRADA may increase the risk of melanoma. In uncontrolled studies, 4 of 1486 (0.3%) LEMTRADA-treated patients developed melanoma or melanoma *in situ*. One of those patients had evidence of locally advanced disease.

Perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.

Lymphoproliferative disorders and lymphoma

Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS, including a MALT lymphoma, Castleman's Disease, and a fatality following treatment of non-Epstein Barr Virus-associated Burkitt's lymphoma. There are postmarketing reports of Epstein Barr Virus-associated lymphoproliferative disorders in non-MS patients.

Because LEMTRADA is an immunomodulatory therapy, caution should also be exercised in initiating LEMTRADA in patients with pre-existing or ongoing malignancies.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.4 LEMTRADA REMS Program

LEMTRADA is available only through a restricted program under a REMS called the LEMTRADA REMS Program, because of the risks of autoimmunity, infusion reactions, and malignancies *[see Warnings and Precautions (5.1, 5.2, 5.3)]*.

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Notable requirements of the LEMTRADA REMS Program include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Patients must enroll in the program and comply with ongoing monitoring requirements [see Dosage and Administration (2.6)].
- Pharmacies must be certified with the program and must only dispense to certified healthcare facilities that are authorized to receive LEMTRADA.
- Healthcare facilities must enroll in the program and verify that patients are authorized before infusing LEMTRADA. Healthcare facilities must have on-site access to equipment and personnel trained to manage infusion reactions.

Further information, including a list of qualified healthcare facilities, is available at 1-855-676-6326.

5.5 Immune Thrombocytopenia

Immune thrombocytopenia (ITP) occurred in 2% of LEMTRADA-treated patients in clinical studies in MS.

In a controlled clinical trial in patients with MS, one LEMTRADA-treated patient developed ITP that went unrecognized prior to the implementation of monthly blood monitoring requirements, and died from intracerebral hemorrhage. Nadir platelet counts ≤20,000 cells per microliter as a result of ITP occurred in 2% of all LEMTRADA-treated patients in clinical studies in MS. Anti-platelet antibodies did not precede ITP onset. ITP has been diagnosed more than 3 years after the last LEMTRADA dose.

Symptoms of ITP include easy bruising, petechiae, spontaneous mucocutaneous bleeding (e.g., epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. Hemoptysis may also be indicative of anti-glomerular basement membrane (GBM) disease [see Warnings and Precautions (5.6)], and an appropriate differential diagnosis has to be undertaken. Remind the patient to remain vigilant for symptoms they may experience and to seek immediate medical help if they have any concerns.

Obtain complete blood counts (CBCs) with differential prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion [see Dosage and Administration (2.6)]. After this period of time, testing should be performed based on clinical findings suggestive of ITP. If ITP is suspected, a complete blood count should be obtained immediately. If ITP onset is confirmed, promptly initiate appropriate medical intervention.

5.6 Glomerular Nephropathies

Glomerular nephropathies occurred in 0.3% of LEMTRADA-treated patients in MS clinical trials. There were 3 cases of membranous glomerulonephritis and 2 cases of anti-glomerular basement membrane (anti-GBM) disease. There are published and post-marketing cases of MS patients treated with alemtuzumab who developed anti-GBM disease and subsequently developed end stage renal disease requiring renal transplantation. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA. Urgent evaluation and treatment is required because anti-GBM disease can lead to renal failure requiring dialysis or transplantation and can be life-threatening if left untreated. Clinical manifestations of nephropathy may include elevated serum creatinine levels, hematuria, or proteinuria. Alveolar hemorrhage manifested as hemoptysis is a common component of anti-GBM disease but did not occur in clinical trials.

Obtain serum creatinine levels and urinalysis with cell counts prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

If clinically significant changes from baseline in serum creatinine, unexplained hematuria, or proteinuria are observed, perform further evaluation for nephropathies. Early detection and treatment of nephropathies may decrease the risk of poor outcomes.

5.7 Thyroid Disorders

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Autoimmune thyroid disorders included Graves' disease, hyperthyroidism and hypothyroidism. Graves' ophthalmopathy with decreased vision, eye pain, and exophthalmos occurred in 1% of LEMTRADA-treated patients. Two patients required surgical orbital decompression. Serious thyroid events occurred in about 2% of LEMTRADA-treated patients in clinical studies and included cardiac and psychiatric events associated with thyroid disease. Of all LEMTRADA-treated patients, 3% underwent thyroidectomy.

Thyroid disease poses special risks in women who are pregnant [see Use in Specific Populations (8.1)].

Obtain thyroid function tests, such as TSH levels, prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

In patients with ongoing thyroid disorder, LEMTRADA should be administered only if the potential benefit justifies the potential risks.

5.8 Other Autoimmune Cytopenias

Autoimmune cytopenias such as neutropenia (0.1%), hemolytic anemia (0.2%), and pancytopenia (0.2%) occurred in LEMTRADA-treated patients in clinical studies in MS. In cases of autoimmune hemolytic anemia, patients tested positive for direct antiglobulin antibodies, and nadir hemoglobin levels ranged from 2.9-8.6 g/dL. Symptoms of autoimmune hemolytic anemia include weakness, chest pain, jaundice, dark urine, and tachycardia. One LEMTRADA-treated patient with autoimmune pancytopenia died from sepsis.

During postmarketing use, additional autoimmune cytopenias including fatal autoimmune hemolytic anemia and aplastic anemia have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Use CBC results to monitor for cytopenias. Prompt medical intervention is indicated if a cytopenia is confirmed.

5.9 Infections

Infections occurred in 71% of LEMTRADA-treated patients compared to 53% of patients treated with interferon beta-1a in controlled clinical trials in MS up to 2 years in duration. Infections that occurred more often in LEMTRADA-treated patients than interferon beta-1a patients included nasopharyngitis, urinary tract infection, upper respiratory tract infection, sinusitis, herpetic infections, influenza, and bronchitis. Serious infections occurred in 3% of patients treated with LEMTRADA as compared to 1% of patients treated with interferon beta-1a. Serious infections in the LEMTRADA group included appendicitis, gastroenteritis, pneumonia, herpes zoster, and tooth infection.

Do not administer live viral vaccines following a course of LEMTRADA. Patients treated with LEMTRADA have altered immunity and may be at increased risk of infection following administration of live viral vaccines.

Consider delaying LEMTRADA administration in patients with active infection until the infection is fully controlled.

Concomitant use of LEMTRADA with antineoplastic or immunosuppressive therapies could increase the risk of immunosuppression.

Herpes Viral Infections

In controlled clinical trials, 16% of LEMTRADA-treated patients developed a herpes viral infection compared to 3% of interferon beta-1a patients. These events included oral herpes (8.8%), herpes zoster (4.2%), herpes simplex (1.8%), and genital herpes (1.3%). Serious herpetic infections in LEMTRADA-treated patients included primary varicella (0.1%), herpes zoster (0.2%), and herpes meningitis (0.1%). Administer antiviral agents for herpetic prophylaxis at appropriate suppressive dosing regimens. Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later [see Dosage and Administration (2.3)].

Human Papilloma Virus

Cervical human papilloma virus (HPV) infection, including cervical dysplasia, occurred in 2% of LEMTRADA-treated patients. Annual HPV screening is recommended for female patients.

Tuberculosis

Tuberculosis occurred in patients treated with LEMTRADA and interferon beta-1a in controlled clinical trials. Active and latent tuberculosis cases occurred in 0.3% of LEMTRADA-treated patients, most often in endemic regions. Perform tuberculosis screening according to local guidelines prior to initiation of LEMTRADA. For patients testing positive in tuberculosis screening, treat by standard medical practice prior to therapy with LEMTRADA.

Fungal Infections

Fungal infections, especially oral and vaginal candidiasis, occurred more commonly in LEMTRADA-treated patients (12%) than in patients treated with interferon beta-1a (3%) in controlled clinical trials in MS.

Listeria Infections

Listeria meningitis has been reported in LEMTRADA-treated patients. Cases of listeria meningitis occurred within 1 month of alemtuzumab dosing. The duration of increased risk for listeria meningitis is unclear. Patients should avoid or adequately heat foods that are potential sources of *Listeria monocytogenes*.

Infections in non-MS patients

During postmarketing use, serious and sometimes fatal viral, bacterial, protozoan, and fungal infections, including some due to reactivation of latent infections, have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Hepatitis

No data are available on the association of LEMTRADA with Hepatitis B virus (HBV) or Hepatitis C virus (HCV) reactivation because patients with evidence of active or chronic infections were excluded from the clinical trials. Consider screening patients at high risk of HBV and/or HCV infection before initiation of LEMTRADA and exercise caution in prescribing LEMTRADA to patients identified as carriers of HBV and/or HCV as these patients may be at risk of irreversible liver damage relative to a potential virus reactivation as a consequence of their pre-existing status.

5.10 Pneumonitis

In clinical studies, 6 of 1217 (0.5%) LEMTRADA-treated patients had pneumonitis of varying severity. Cases of hypersensitivity pneumonitis and pneumonitis with fibrosis occurred in clinical studies. Patients should be advised to report symptoms of pneumonitis, which include shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

5.11 Drug Products with Same Active Ingredient

LEMTRADA contains the same active ingredient (alemtuzumab) found in CAMPATH®. If LEMTRADA is considered for use in a patient who has previously received CAMPATH, exercise increased vigilance for additive and long-lasting effects on the immune system.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling:

- Autoimmunity [see Boxed Warning and Warnings and Precautions (5.1)]
- Infusion reactions [see Boxed Warning and Warnings and Precautions (5.2)]
- Malignancies [see Warnings and Precautions (5.3)]
- Immune Thrombocytopenia [see Warnings and Precautions (5.5)]
- Glomerular Nephropathies [see Warnings and Precautions (5.6)]
- Thyroid Disorder [see Warnings and Precautions (5.7)]
- Other Autoimmune Cytopenias [see Warnings and Precautions (5.8)]
- Infections [see Warnings and Precautions (5.9)]
- Pneumonitis [see Warnings and Precautions (5.10)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In controlled clinical trials (Study 1 and Study 2), a total of 811 patients with relapsing forms of MS received LEMTRADA. A total of 811 patients received 1 course of therapy, and 789 patients received a second course of therapy at 12 months. The overall follow-up in the controlled trials was equivalent to 1822 patient years, with an additional 3411 person-years of follow-up in an open label extension study. The population was 18-55 years of age, 65% were female, and 92% were Caucasian.

Most Common Adverse Reactions

In clinical trials, the most common adverse reactions with LEMTRADA (in at least 10% of patients and more frequently than in interferon beta-1a) were rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting.

Table 1 lists adverse reactions occurring in ≥5% of LEMTRADA-treated patients in Study 1 and 2 and at the same or at a higher rate than interferon beta-1a.

Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=389) %
Rash	53	6
Headache	52	29
Pyrexia	29	9

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Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis (continued)

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=389) %
Nasopharyngitis	25	19
Nausea	21	9
Urinary tract infection	19	8
Fatigue	18	13
Insomnia	16	15
Upper respiratory tract infection	16	13
Herpes viral infection	16	3
Urticaria	16	2
Pruritus	14	2
Thyroid gland disorders	13	3
Fungal infection	13	4
Arthralgia	12	9
Pain in extremity	12	9
Back pain	12	8
Diarrhea	12	6
Sinusitis	11	8
Oropharyngeal pain	11	5
Paresthesia	10	8
Dizziness	10	5
Abdominal pain	10	5
Flushing	10	4
Vomiting	10	3
Cough	9	4
Chills	9	3
Dysgeusia	8	7
Influenza	8	6
Dermatitis	8	5
Dyspepsia	8	4
Blood in urine	8	3
Dyspnea	8	1
Tachycardia	8	1
Anxiety	7	6
Muscular weakness	7	5
Bronchitis	7	4
Chest discomfort	7	2
Muscle spasms	6	5
Myalgia	6	5
Decrease in CD4 lymphocytes	6	2
Decrease in CD8 lymphocytes	6	2
Asthenia	5	4
Decrease in T-lymphocyte count	5	3
Erythema	5	2
Peripheral edema	5	2
Epistaxis	5	2
Neck Pain	5	2
Abnormal uterine bleeding	5	1

6.2 Lymphopenia

Nearly all (99.9%) patients treated with LEMTRADA in MS clinical trials experienced lymphopenia. The lowest lymphocyte counts occurred approximately by 1 month after each course of treatment. The mean lymphocyte count at 1 month after LEMTRADA treatment was 0.25 x 10^9/L (range: 0.02-0.30 x 10^9/L) and 0.32 (0.02-1.81 x 10^9/L) for treatment courses 1 and 2, respectively. Total lymphocyte counts increased to reach the lower limit of normal in approximately 40% of patients by 6 months after each LEMTRADA treatment course and approximately 80% of patients by 12 months after each course *[see Clinical Pharmacology (12.2)]*.

6.3 Suicidal Behavior or Ideation

In clinical studies, 0.6% of patients in both the LEMTRADA and interferon beta-1a groups had events of attempted suicide or suicidal ideation. There were no completed suicides in either clinical study treatment group. Suicidal behavior or ideation occurred in patients with or without a history of a psychiatric or thyroid disorder. Advise patients to report immediately any symptoms of depression or suicidal ideation to the prescribing physician.

6.4 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Using an enzyme-linked immunosorbent assay (ELISA) and a competitive binding assay, anti-alemtuzumab binding antibodies were detected in 62%, 67%, and 29% of LEMTRADA-treated patients, at months 1, 3, 12 (Course 1) as well as 83%, 83%, and 75% of LEMTRADA-treated patients at months 13, 15, and 24 (Course 2). Samples that tested positive for binding antibodies were further evaluated for evidence of *in vitro* inhibition using a flow cytometry assay. Neutralizing antibodies were detected in 87%, 46%, and 5% of positive binding antibody patients at months 1, 3, 12 (Course 1) as well as 94%, 88%, and 42% of positive binding antibody patients at months 13, 15, and 24 (Course 2). Anti-alemtuzumab antibodies were associated with decreased alemtuzumab concentration during Course 2 but not Course 1. There was no evidence from clinical trials that the presence of binding or inhibitory anti-alemtuzumab antibodies had a significant effect on clinical outcomes, total lymphocyte count, or adverse events. The incidence of antibodies is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including inhibitory antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to LEMTRADA with the incidence of antibodies to other products may be misleading.

6.5 Postmarketing Experience

The following adverse reactions, not described elsewhere, were identified during post-approval use of alemtuzumab (CAMPATH) for the treatment of B-cell chronic lymphocytic leukemia (B-CLL), as well as for the treatment of other disorders, generally at higher and more frequent doses (e.g., 30 mg) than that recommended in the treatment of MS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac Disorders

Congestive heart failure, cardiomyopathy, and decreased ejection fraction in non-MS patients previously treated with potentially cardiotoxic agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. LEMTRADA was embryolethal in pregnant huCD52 transgenic mice when administered during organogenesis. Auto-antibodies may develop after administration of LEMTRADA. Placental transfer of anti-thyroid antibodies resulting in neonatal Graves' disease has been reported. LEMTRADA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

When LEMTRADA was administered to pregnant huCD52 transgenic mice during organogenesis (gestation days [GD] 6-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, no teratogenic effects were observed. However, there was an increase in embryolethality (increased post-implantation loss and the number of dams with all fetuses dead or resorbed) in pregnant animals dosed during GD 11-15.

In a separate study in pregnant huCD52 transgenic mice, administration of LEMTRADA during organogenesis (GD 6-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, decreases in B lymphocytes and T-lymphocyte populations were observed in the offspring at both doses tested. The effects of LEMTRADA, administered during organogenesis, on postnatal development have not been adequately assessed.

Clinical Considerations

To avoid in utero exposure to LEMTRADA, women of child bearing potential should use effective contraceptive measures when receiving a course of treatment with LEMTRADA and for 4 months following that course of treatment.

LEMTRADA induces persistent thyroid disorders *[see Warnings and Precautions (5.7)]*. Untreated hypothyroidism in pregnant women increases the risk for miscarriage and may have effects on the fetus including mental retardation and dwarfism. In mothers with Graves' disease, maternal thyroid stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause neonatal Graves' disease. In a patient who developed Graves' disease after treatment with alemtuzumab, placental transfer of anti-thyrotropin receptor antibodies resulted in neonatal Graves' Disease with thyroid storm in her infant who was born 1 year after alemtuzumab dosing *[see Warnings and Precautions (5.1)]*.

8.3 Nursing Mothers

Alemtuzumab was detected in the milk of lactating mice administered 10 mg/kg LEMTRADA on Days 8 through 12 postpartum. Serum levels of alemtuzumab were similar in lactating mice and offspring on Day 13 postpartum, and were associated with evidence of pharmacological activity (decrease in lymphocyte counts) in the offspring.

It is not known whether alemtuzumab is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from LEMTRADA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients less than 17 years of age have not been established. Use of LEMTRADA is not recommended in pediatric patients due to the risks of autoimmunity, infusion reactions, and because it may increase the risk of malignancies (thyroid, melanoma, lymphoproliferative disorders, and lymphoma) *[see Warnings and Precautions (5.1, 5.2, 5.3)]*.

8.5 Geriatric Use

Clinical studies of LEMTRADA did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

10 OVERDOSAGE

Two MS patients experienced serious reactions (headache, rash, and either hypotension or sinus tachycardia) after a single accidental infusion up to 60 mg of LEMTRADA. Doses of LEMTRADA greater than those recommended may increase the intensity and/or duration of infusion reactions or its immune effects. There is no known antidote for alemtuzumab overdosage.

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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11 DESCRIPTION

LEMTRADA (alemtuzumab) is a recombinant humanized IgG1 kappa monoclonal antibody directed against the cell surface glycoprotein, CD52. Alemtuzumab has an approximate molecular weight of 150kD. LEMTRADA is produced in mammalian cell (Chinese hamster ovary) suspension culture in a nutrient medium containing neomycin. Neomycin is not detectable in the final product. LEMTRADA is a sterile, clear and colorless to slightly yellow, solution (pH 7.2±0.2) for infusion.

Each 1 mL of solution contains alemtuzumab 10 mg, dibasic sodium phosphate (1.15 mg), disodium edetate dihydrate (0.0187 mg), polysorbate 80 (0.1 mg), potassium chloride (0.2 mg), potassium dihydrogen phosphate (0.2 mg), sodium chloride (8 mg), and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which alemtuzumab exerts its therapeutic effects in multiple sclerosis is unknown but is presumed to involve binding to CD52, a cell surface antigen present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

12.2 Pharmacodynamics

Effects of LEMTRADA on the Lymphocyte Population

LEMTRADA depletes circulating T and B lymphocytes after each treatment course. In clinical trials, the lowest cell counts occurred 1 month after a course of treatment at the time of the first post-treatment blood count. Lymphocyte counts then increased over time. B cell counts usually recovered within 6 months; T cell counts increased more slowly and usually remained below baseline 12 months after treatment. Approximately 60% of patients had total lymphocyte counts below the lower limit of normal 6 months after each treatment course and 20% had counts below the lower limit of normal after 12 months.

Reconstitution of the lymphocyte population varies for the different lymphocyte subtypes. At Month 1 in clinical trials, the mean CD4+ lymphocyte count was 40 cells per microliter, and, at Month 12, 270 cells per microliter. At 36 months, approximately half of patients had CD4+ lymphocyte counts that remained below the lower limit of normal.

Cardiac Electrophysiology

In a study of 53 MS patients, alemtuzumab 12 mg per day for 5 days caused no changes in the QTc interval greater than 20ms. An average 22 to 26 beats-per-minute increase in heart rate was observed for at least 2 hours after the first but not subsequent infusions.

12.3 Pharmacokinetics

The pharmacokinetics of LEMTRADA were evaluated in a total of 148 patients with relapsing forms of MS who received 12 mg/day on 5 consecutive days, followed by 12 mg/day on 3 consecutive days 12 months following the first treatment course.

Absorption

Serum concentrations increased with each consecutive dose within a treatment course, with the highest observed concentrations occurring following the last infusion of a treatment course. The mean maximum concentration was 3014 ng/mL on Day 5 of the first treatment course, and 2276 ng/mL on Day 3 of the second treatment course.

Distribution

LEMTRADA is largely confined to the blood and interstitial space with a central volume of distribution of 14.1 L.

Elimination

The elimination half-life was approximately 2 weeks and was comparable between courses. The serum concentrations were generally undetectable (< 60 ng/mL) within approximately 30 days following each treatment course.

Specific Populations

Age, race, or gender had no effect on the pharmacokinetics of LEMTRADA.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to assess the carcinogenic or genotoxic potential of LEMTRADA have not been conducted.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic male mice on 5 consecutive days prior to cohabitation with untreated wild-type females, no effect on fertility or reproductive performance was observed. However, adverse effects on sperm parameters (including abnormal morphology [detached rho head] and reduced total count and motility) were observed at both doses tested.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic female mice for 5 consecutive days prior to cohabitation with untreated wild-type males, there was a decrease in the average number of corpora lutea and implantation sites and an increase in post-implantation loss, resulting in fewer viable embryos at the higher dose tested.

14 CLINICAL STUDIES

The efficacy of LEMTRADA was demonstrated in two studies (Study 1 and 2) that evaluated LEMTRADA 12 mg in patients with relapsing-remitting multiple sclerosis (RRMS). LEMTRADA was administered by intravenous infusion once daily over a 5-day course, followed one year later by intravenous infusion once daily over a 3-day course. Both studies included patients who had experienced at least 2 relapses during the 2 years prior to trial entry and at least 1 relapse during the year prior to trial entry. Neurological examinations were performed every 12 weeks and at the time of suspected relapse. Magnetic resonance imaging (MRI) evaluations were performed annually.

Study 1

Study 1 was a 2 year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 1 had Expanded Disability Status Scale (EDSS) scores of 5 or less and had to have experienced at least one relapse while on interferon beta or glatiramer acetate therapy.

Patients were randomized to receive LEMTRADA (n=426) or interferon beta-1a (n=202). At baseline, the mean age was 36 years, the mean disease duration was 4.5 years, and the mean EDSS score was 2.7.

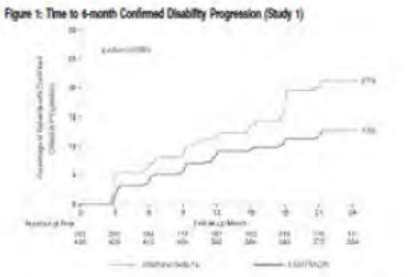
The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression. Confirmed disability progression was defined as at least a 1 point increase above baseline EDSS (1.5 point increase for patients with baseline EDSS of 0) sustained for 6 months. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. Time to onset of 6-month confirmed disability progression was significantly delayed with LEMTRADA treatment compared to interferon beta-1a. There was no significant difference between the treatment groups for the change in T2 lesion volume. The results of Study 1 are shown in Table 2 and Figure 1.

Table 2: Clinical and MRI Results of Study 1

	LEMTRADA (N=426)	Interferon beta-1a 44 mcg (N=202)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.26 49%	0.52	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	13% 42%	21%	0.0084
Percent of patients remaining relapse-free at Year 2	65%	47%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-1.3	-1.2	0.14

Figure 1: Time to 6-month Confirmed Disability Progression (Study 1)



Study 2

Study 2 was a 2-year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 2 had EDSS scores of 3 or less and no prior treatment for multiple sclerosis. Patients were randomized to receive LEMTRADA (n=376) or interferon beta-1a (n=187). At baseline, the mean age was 33 years, the mean disease duration was 2 years, and the mean EDSS score was 2.

The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression, as defined in Study 1. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. There was no significant difference between the treatment groups for the time to confirmed disability progression and for the primary MRI endpoint (change in T2 lesion volume). The results for Study 2 are shown in Table 3.

Table 3: Clinical and MRI Results of Study 2

	LEMTRADA (N=376)	Interferon beta-1a 44 mcg (N=187)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.18 55%	0.39	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	8% 30%	11%	0.22
Percent of patients remaining relapse-free at Year 2	78%	59%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-6.3	-6.5	0.31

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each LEMTRADA carton (NDC: 58468-0200-1) contains 1 single-use vial that delivers 12 mg/1.2 mL (10 mg/mL). The vial stopper is not made with natural rubber latex.

LEMTRADA is a sterile, clear and colorless to slightly yellow solution for infusion, containing no antimicrobial preservatives.

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16.2 Storage and Handling
Store LEMTRADA vials at 2°C to 8°C (36°F to 46°F). Do not freeze or shake. Store in original carton to protect from light.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Autoimmunity
- Advise patients to contact their healthcare provider promptly if they experience any symptoms of potential autoimmune disease. Give examples of important symptoms such as bleeding, easy bruising, petechiae, purpura, hematuria, edema, jaundice, or hemoptysis [see Warnings and Precautions (5.1)].
- Advise patients of the importance of monthly blood and urine tests for 48 months following the last course of LEMTRADA to monitor for signs of autoimmunity because early detection and prompt treatment can help prevent serious and potentially fatal outcomes associated with these events. Advise patients that monitoring may need to continue past 48 months if they have signs or symptoms of autoimmunity.
- Advise patients that LEMTRADA may cause hyperthyroid or hypothyroid disorders.
- Advise patients to contact their healthcare provider if they experience symptoms reflective of a potential thyroid disorder such as unexplained weight loss or gain, fast heartbeat or palpitations, eye swelling, constipation, or feeling cold.
- Advise women of childbearing potential of the risks of pregnancy with concomitant thyroid disease. Advise women of childbearing potential to discuss pregnancy planning with their doctor.

Infusion Reactions
- Advise patients that infusion reactions can occur after they leave the infusion center [see Warnings and Precautions (5.2)].
- Instruct the patient to remain at the infusion center for 2 hours after each LEMTRADA infusion, or longer at the discretion of the physician. Advise patients that symptoms of infusion reactions may occur after they leave the infusion center and to report these symptoms to their doctor.
- Advise patients to contact their healthcare provider promptly if they experience infusion reactions, which include swelling in the mouth or throat, difficulty breathing, weakness, abnormal heart rate (fast, slow, or irregular), chest pain, and rash.

Malignancies
- Advise patients that LEMTRADA may increase their risk of malignancies including thyroid cancer and melanoma [see Warnings and Precautions (5.3)].
- Advise patients to report symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, hoarseness or other voice changes that do not go away, trouble swallowing or breathing, or a constant cough not due to a cold.
- Advise patients that they should have baseline and yearly skin examinations.

LEMTRADA REMS Program
- LEMTRADA is available only through a restricted program called the LEMTRADA REMS Program [see Warnings and Precautions (5.4)]. Inform the patient of the following notable requirements:
  - Patients and providers must be enrolled in the program.
  - Patients must comply with the ongoing monitoring requirements.
  - Patients must report any side effects or symptoms to their doctor.
- LEMTRADA is available only at certified infusion centers participating in the program. Therefore, provide patients with information on the LEMTRADA REMS Program in order to locate an infusion center.
- Advise patients to read the LEMTRADA REMS material for patients, *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*.
- Instruct patients to carry the LEMTRADA REMS Patient Safety Information Card with them in case of an emergency.

Infections
- Advise patients to contact their healthcare provider if they develop symptoms of serious infection such as fever or swollen glands [see Warnings and Precautions (5.6)].
- Advise patients to complete any necessary immunizations at least 4 weeks prior to treatment with LEMTRADA [see Dosage and Administration (2.2)]. Advise patients that they should talk to their healthcare provider before taking any vaccine after recent treatment with LEMTRADA [see Warnings and Precautions (5.6)].
- Advise patients to take their prescribed medication for herpes prophylaxis as directed by their healthcare provider [see Warnings and Precautions (5.6)].
- Advise patients that yearly HPV screening is recommended [see Warnings and Precautions (5.9)].
- Advise patients to avoid or adequately heat foods that are potential sources of *Listeria monocytogenes* if they have had a recent course of LEMTRADA. The duration of increased risk for listeria infection after LEMTRADA administration is not known [see Warnings and Precautions (5.6)].

Pneumonitis
- Advise patients that pneumonitis has been reported in patients treated with LEMTRADA [see Warnings and Precautions (5.10)]. Advise patients to report symptoms of lung disease such as shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

Concomitant Use of Campath:
- Advise patients that alemtuzumab is the same drug as Campath for use in B-CLL. Patients should inform their healthcare provider if they have taken Campath [see Warnings and Precautions (5.11)].

Manufactured and distributed by:

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142

US License Number 1596

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MEDICATION GUIDE
LEMTRADA™ (lem-TRA-da)
(alemtuzumab)
injection for intravenous infusion

Read this Medication Guide before you start receiving LEMTRADA and before you begin each treatment course. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is the most important information I should know about LEMTRADA?
LEMTRADA can cause serious side effects, including:

1. **Serious autoimmune problems.** Some people receiving LEMTRADA develop a condition where the immune cells in your body attack other cells or organs in the body (autoimmunity) which can be serious and may cause death. Serious autoimmune problems may include:
   - **Immune thrombocytopenic purpura (ITP).** LEMTRADA may cause the number of platelets in your blood to be reduced (ITP). ITP can cause severe bleeding that, if not treated, may cause life-threatening problems. Call your healthcare provider right away if you have any of the following symptoms:
     - easy bruising
     - bleeding from a cut that is hard to stop
     - heavier menstrual periods than normal
     - bleeding from your gums or nose that is now or takes longer than usual to stop
     - small, scattered spots on your skin that are red, pink, or purple
   - **kidney problems.** LEMTRADA may cause a serious kidney problem, called anti-glomerular basement membrane disease. If this happens and you do not get treated, anti-glomerular basement membrane disease can lead to severe kidney damage, kidney failure that needs dialysis, a kidney transplant, or death. Call your healthcare provider right away if you have any of the following symptoms:
     - blood in the urine (red or tea-colored urine)
     - swelling in your legs or feet
     - coughing up blood

Side effects may happen while you receive LEMTRADA and for 4 years after you stop receiving LEMTRADA. Your healthcare provider will order blood and urine tests before you receive, while you are receiving, and every month for 4 years after you receive your last LEMTRADA infusion. You may need to continue these blood and urine tests after 4 years if you have any autoimmune signs or symptoms. The blood and urine tests will help your healthcare provider watch for signs and symptoms of serious autoimmune problems.

It is important to have your blood and urine tested, even if you are feeling well and do not have any symptoms from LEMTRADA and your multiple sclerosis. This may help your healthcare provider find any problems early and will increase your chances of getting better.

2. **Serious infusion reactions.** LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.

You will receive your infusion at a healthcare facility with equipment and staff trained to manage infusion reactions. You will be watched while you receive and for 2 hours after you receive LEMTRADA. **It is important** that you stay at the infusion center for 2 hours after your infusion is finished or longer if your healthcare provider decides you need to stay longer. If a serious infusion reaction happens while you are receiving LEMTRADA, your infusion may be stopped.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion, and after you have left the healthcare facility:
- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heart beat
- chest pain
- rash

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

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To lower your chances of getting a serious infusion reaction, your healthcare provider will give you a medicine called corticosteroids before your first 3 infusions of a treatment course. You may also be given other medicines before or after the infusion to try reduce your chances of those reactions or to treat them after they happen.

3. **Certain cancers.** Receiving LEMTRADA may increase your chance of getting some kinds of cancers, including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:

- new lump
- swelling in your neck
- pain in the front of your neck
- hoarseness or other voice changes that do not go away
- trouble swallowing or breathing
- cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA and each year while you are receiving treatment to monitor symptoms of skin cancer.

Because of your risk of autoimmunity, infusion reactions and the risk of some kinds of cancers, LEMTRADA is only available through a restricted program called the LEMTRADA Risk Evaluation and Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS Program.

- You and your healthcare provider must be enrolled in the LEMTRADA REMS Program.
- LEMTRADA can only be given at a certified healthcare facility that participates in the LEMTRADA REMS Program. Your healthcare provider can give you information on how to find a certified healthcare facility.
- Read the LEMTRADA REMS "What You Need to Know About LEMTRADA Treatment: A Patient Guide" and "What you Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide" after you are enrolled in the program.
- Carry your LEMTRADA REMS Patient Safety Information Card with you in case of an emergency.

What is LEMTRADA?

LEMTRADA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). Because of its risks, LEMTRADA is generally used in people who have tried 2 or more MS medicines that have not worked well enough. It is not known if LEMTRADA is safe and effective for use in children under 17 years of age.

Who should not receive LEMTRADA?

Do not receive LEMTRADA if you are infected with human immunodeficiency virus (HIV).

What should I tell my healthcare provider before receiving LEMTRADA?

Before receiving LEMTRADA, tell your healthcare provider if you:

- are taking a medicine called Campath®. Alemtuzumab the active ingredient in LEMTRADA is the same drug as Campath.
- have bleeding problems
- have thyroid problems
- have kidney problems
- have a recent history of infection
- have HIV
- have received a live vaccine in the past 6 weeks before receiving LEMTRADA or plan to receive any live vaccines. Ask your healthcare provider if you are not sure if your vaccine is a live vaccine.
- are pregnant or plan to become pregnant. LEMTRADA may harm your unborn baby. You should use birth control while receiving LEMTRADA and for 4 months after your course of treatment.
- are breastfeeding or plan to breastfeed. It is not known if LEMTRADA passes into your breast milk. You and your healthcare provider should decide if you should receive LEMTRADA or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

LEMTRADA and other medicines may affect each other causing side effects. Especially tell your healthcare provider if you take medicines that increase your chance of getting infections, including medicines used to treat cancer or to control your immune system.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How will I receive LEMTRADA?

- LEMTRADA is given through a needle placed in your vein (IV infusion).
- It takes about 4 hours to receive a full dose of LEMTRADA each day.
- You will receive LEMTRADA over 2 treatment courses.
- You will receive LEMTRADA for 5 days in a row (consecutive) for the first treatment course and then for 3 days in a row (consecutive) about 1 year later for your second treatment course.

What are the possible side effects of LEMTRADA?

LEMTRADA may cause serious side effects including:

- See **"What is the most important information I should know about LEMTRADA?"**
- **thyroid problems.** Some people who receive LEMTRADA may get thyroid problems including an overactive thyroid (hyperthyroidism) or an underactive thyroid (hypothyroidism). Your healthcare provider will do blood tests to check how your thyroid is working. Call your healthcare provider if you have any of the symptoms of thyroid problems.

Symptoms of **hyperthyroidism** may include:

- excessive sweating
- unexplained weight loss
- eye swelling
- nervousness
- fast heartbeat

Symptoms of **hypothyroidism** may include:

- unexplained weight gain
- feeling cold
- worsening tiredness
- constipation

- **low blood counts (cytopenias).** LEMTRADA may cause a decrease in some types of blood cells. Some people with these low blood counts have increased infections. Symptoms of cytopenias may include:

- weakness
- chest pain
- yellowing of the skin or whites of eyes (jaundice)
- dark urine
- fast heartbeat

Your healthcare provider will do blood tests to check for cytopenias. Call your healthcare provider right away if you have symptoms listed above.

- **serious infections.** LEMTRADA may cause you to have serious infections while you receive and after receiving a treatment course. Serious infections may include:
  - **herpes viral infections.** Some people taking LEMTRADA have an increased chance of getting herpes viral infections. Your healthcare provider will prescribe medicines to reduce your chances of getting these infections. Take these medicines exactly as your healthcare provider tells you to.
  - **human papilloma virus (HPV).** Females have an increased chance of getting a cervical HPV infection. If you are a female, you should have an HPV screening each year.
  - **tuberculosis.** Your healthcare provider should check you for tuberculosis before you receive LEMTRADA.
  - **fungal infections.**
  - **listeria.** People who receive LEMTRADA have an increased chance of getting an infection caused by the bacteria, listeria. Avoid foods that may be a source for listeria (for example, deli meat, unpasteurized milk and cheese products, or undercooked meat, seafood or poultry) or make sure that the food you eat which may contain listeria is heated well if you receive treatment with LEMTRADA.

Call your healthcare provider right away if you have symptoms of a serious infection, such as fever or swollen glands. You may need to go to the hospital for treatment if you got a serious infection. It is

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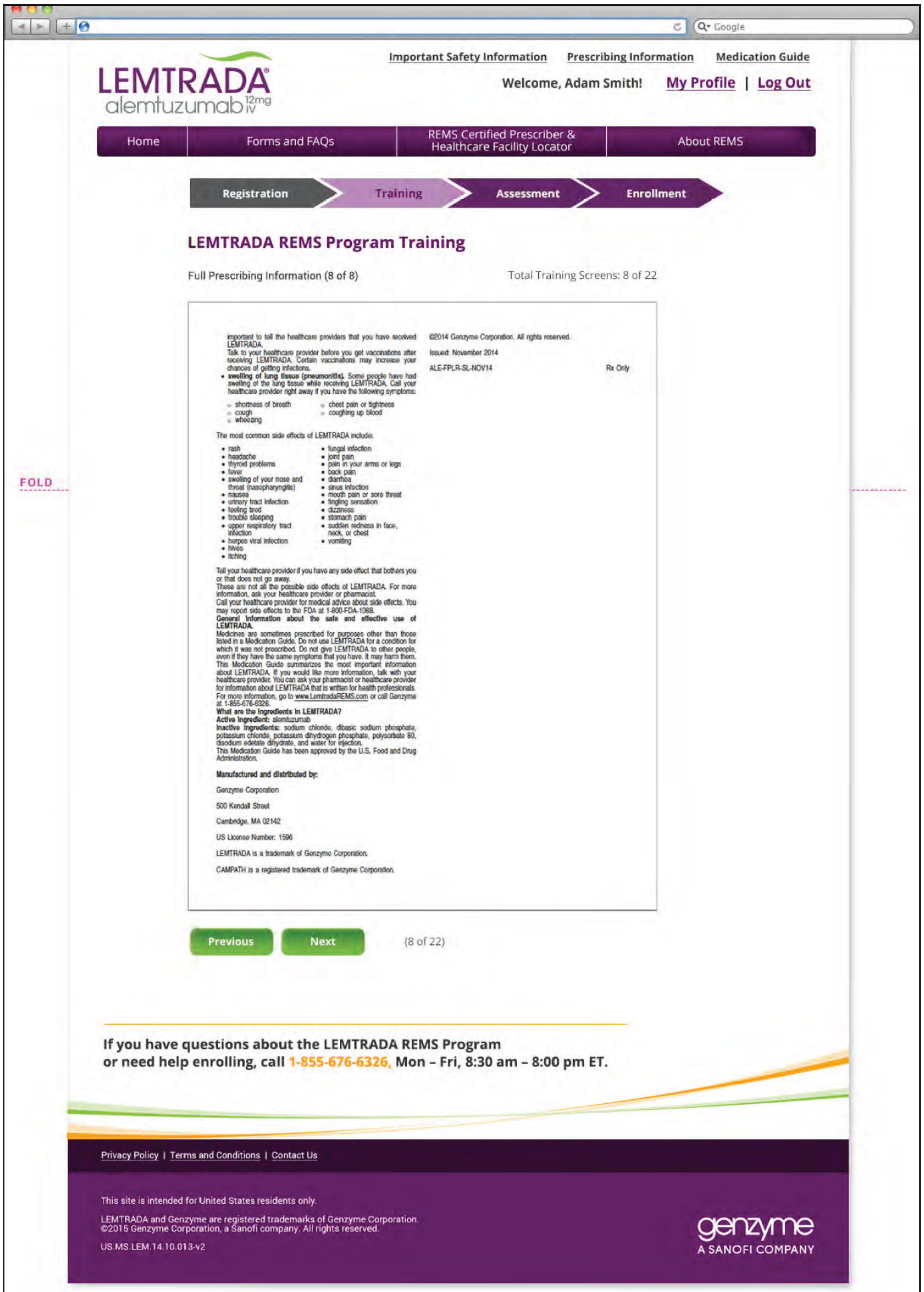
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important to tell the healthcare providers that you have received LEMTRADA.
Talk to your healthcare provider before you get vaccinations after receiving LEMTRADA. Certain vaccinations may increase your chances of getting infections.
• swelling of lung tissue (pneumonitis). Some people have had swelling of the lung tissue while receiving LEMTRADA. Call your healthcare provider right away if you have the following symptoms:
○ shortness of breath
○ cough
○ wheezing
○ chest pain or tightness
○ coughing up blood
The most common side effects of LEMTRADA include:
• rash
• headache
• thyroid problems
• fever
• swelling of your nose and throat (nasopharyngitis)
• nausea
• urinary tract infection
• feeling tired
• trouble sleeping
• upper respiratory tract infection
• herpes viral infection
• hives
• itching
• fungal infection
• joint pain
• pain in your arms or legs
• back pain
• diarrhea
• sinus infection
• mouth pain or sore throat
• tingling sensation
• dizziness
• stomach pain
• sudden redness in face, neck, or chest
• vomiting
Tell your healthcare provider if you have any side effect that bothers you or that does not go away.
These are not all the possible side effects of LEMTRADA. For more information, ask your healthcare provider or pharmacist.
Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.
General information about the safe and effective use of LEMTRADA.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use LEMTRADA for a condition for which it was not prescribed. Do not give LEMTRADA to other people, even if they have the same symptoms that you have. It may harm them. This Medication Guide summarizes the most important information about LEMTRADA. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about LEMTRADA that is written for health professionals. For more information, go to www.LemtradaREMS.com or call Genzyme at 1-855-676-6326.
What are the ingredients in LEMTRADA?
Active ingredient: alemtuzumab
Inactive ingredients: sodium chloride, dibasic sodium phosphate, potassium chloride, potassium dihydrogen phosphate, polysorbate 80, disodium edetate dihydrate, and water for injection.
This Medication Guide has been approved by the U.S. Food and Drug Administration.
Manufactured and distributed by:
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Cambridge, MA 02142
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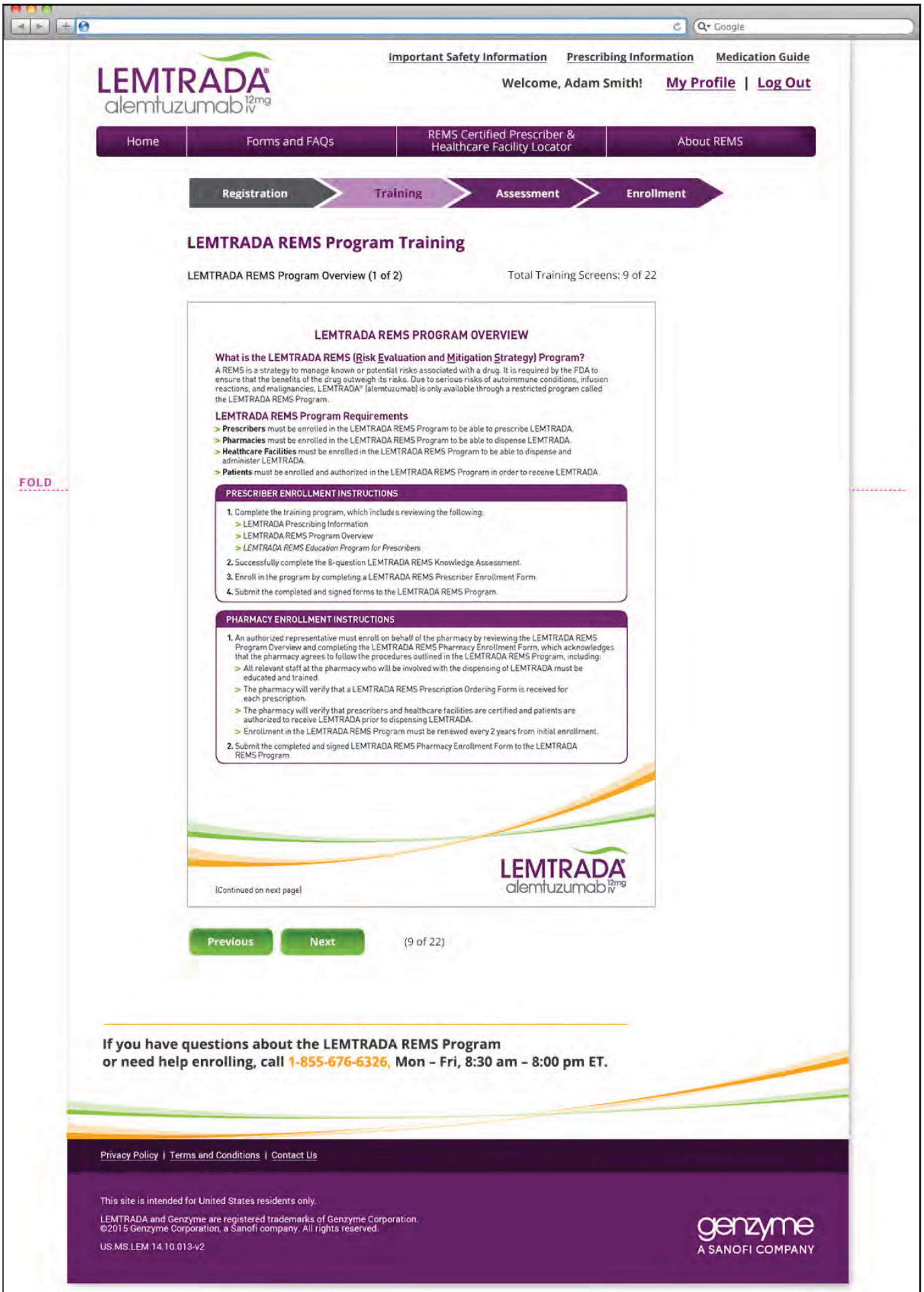

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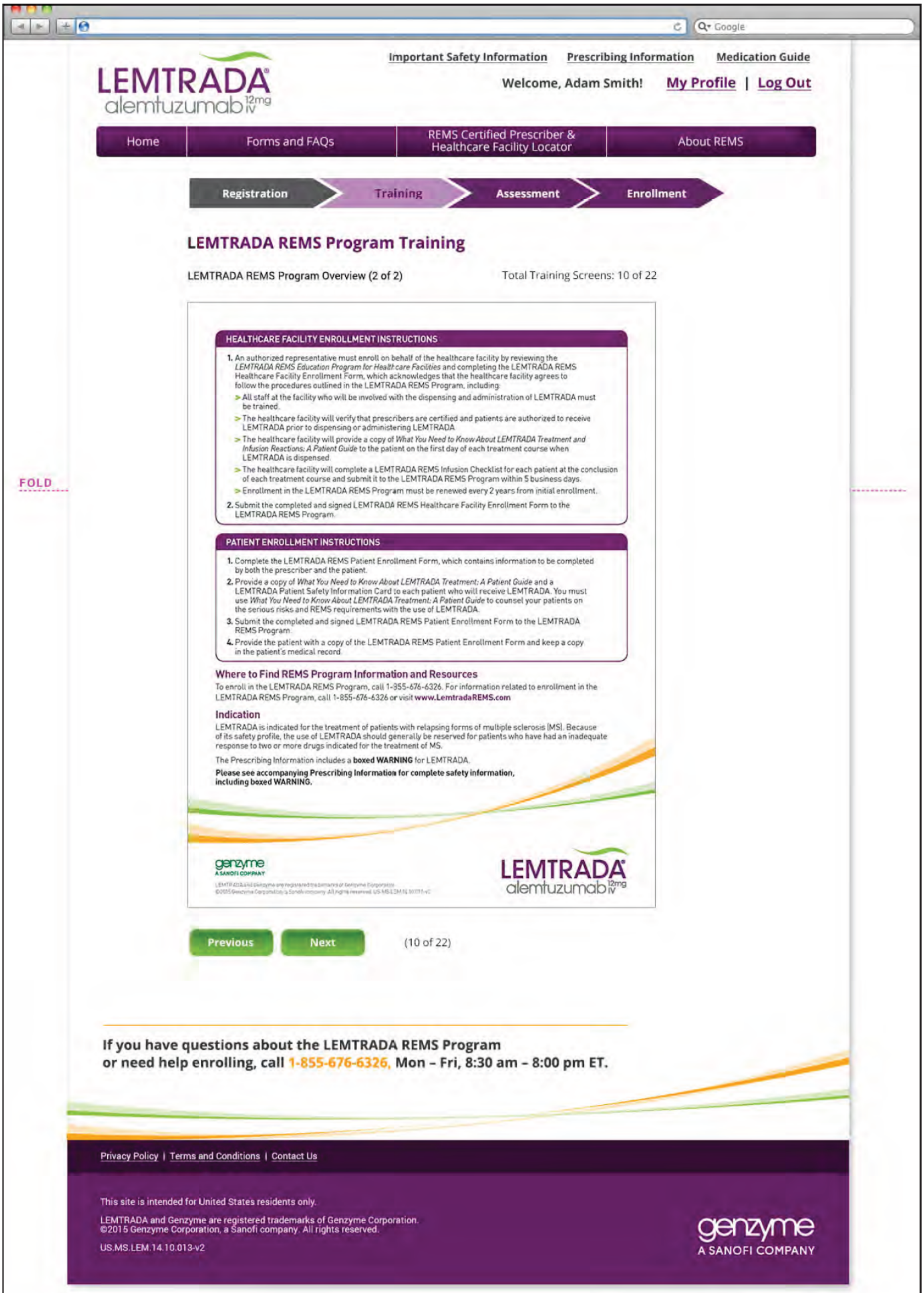

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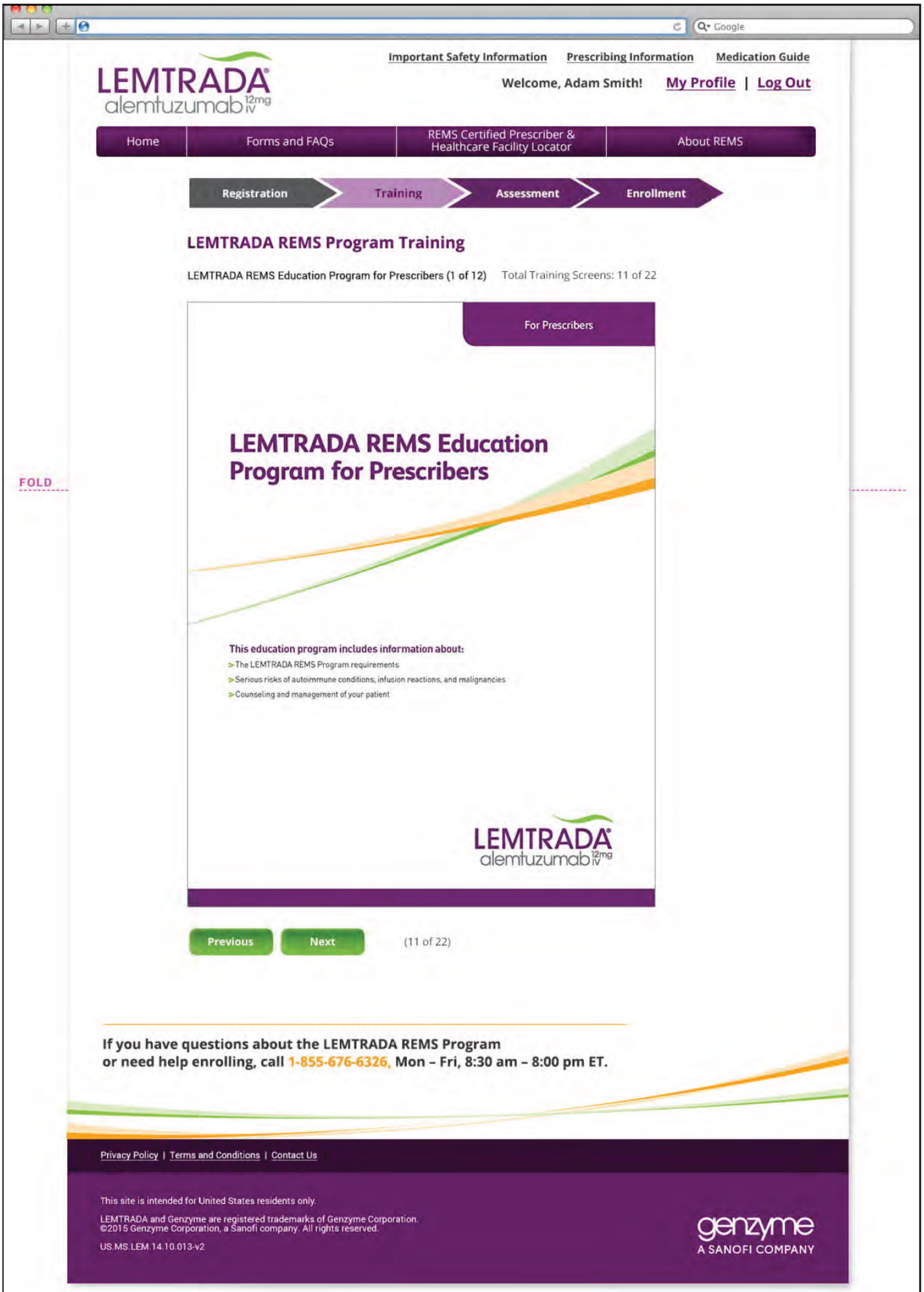

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What Is the LEMTRADA REMS Program?

A REMS (Risk Evaluation and Mitigation Strategy) is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions and malignancy, LEMTRADA is only available through a restricted program called the LEMTRADA REMS Program.

This brochure has been developed as part of the LEMTRADA REMS Program to help educate prescribers about the risks associated with LEMTRADA and how to help mitigate these risks through periodic monitoring for, and prompt identification of, signs and symptoms of these events.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

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Steps for Prescriber Certification and Enrollment in the LEMTRADA REMS Program

1. Complete the training program, which includes reviewing the following materials:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - LEMTRADA REMS Education Program for Prescribers
2. Successfully complete the 8-question Knowledge Assessment
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form
4. Submit the completed and signed forms to the LEMTRADA REMS Program

The LEMTRADA REMS Program Overview, Knowledge Assessment, LEMTRADA Prescribing Information, and other REMS materials are available online at **www.LemtradaREMS.com** or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program, call 1-855-676-6326 or go to **www.LemtradaREMS.com**

Genzyme will send confirmation of a prescriber's enrollment in the LEMTRADA REMS Program, including the prescriber's assigned LEMTRADA REMS Program identification number.

You will not be able to prescribe LEMTRADA without completing your certification in the LEMTRADA REMS Program.

You should understand that if you fail to comply with the Program requirements, you may no longer be able to participate in the Program.

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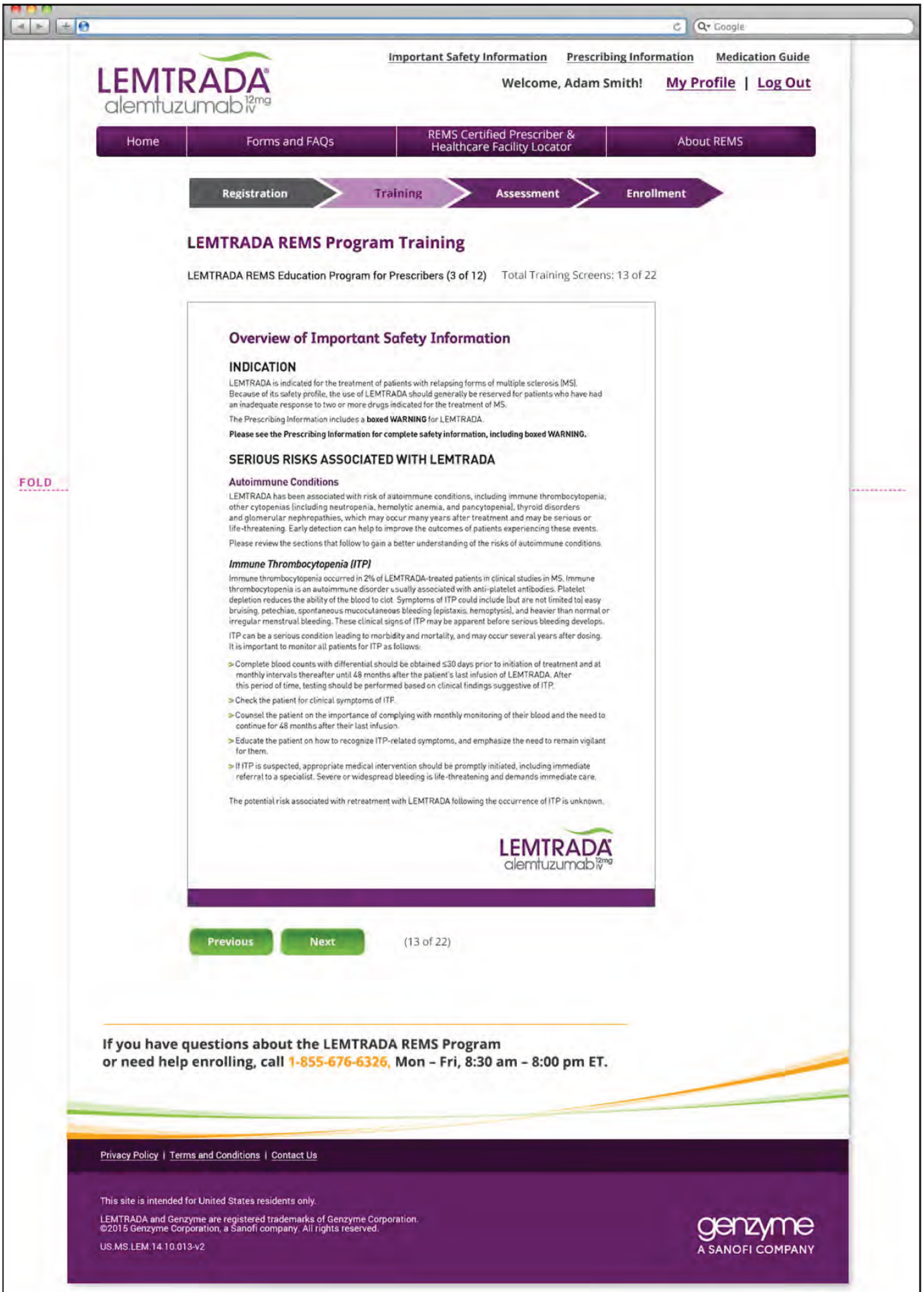

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Potential Clinical Presentations of ITP

Note: These pictures are only a guide in order to show examples of bruises or petechiae. The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

Petechiae are small, scattered, "pinprick" spots under the skin that are red, pink or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

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Other Autoimmune Cytopenias

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Use the monthly CBC results to monitor for cytopenias. If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

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Glomerular Nephropathies

Glomerular nephropathies, including anti-glomerular basement membrane (anti-GBM) disease, have been reported after treatment with LEMTRADA in multiple sclerosis patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation, and this may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria.

While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, it is important that the monthly tests are conducted.

- Serum creatinine levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.
- Urinalysis with urine cell counts should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies. In menstruating females, consider the timing of urinalysis to avoid false positives. The observation of clinically significant changes from baseline in serum creatinine, unexplained hematuria, and/or proteinuria should prompt further evaluation for nephropathies, including referral to a specialist.
- Early detection and treatment of nephropathies may decrease the risk of poor outcomes.
- Immediate referral to a specialist for further assessment for patients with suspected nephropathy is strongly recommended.

Thyroid Disorders

During clinical trials, autoimmune thyroid disorders including Graves' disease, hyperthyroidism, and hypothyroidism were reported. Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies.

Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention.

It is important to monitor all patients for thyroid disorders as follows:

- Thyroid function tests such as thyroid-stimulating hormone (TSH) levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.
- Additionally, watch out for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness, and newly occurring constipation (hypothyroidism).

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- Thyroid disease poses special risks in women who become pregnant. Untreated thyroid disease can cause harm to the unborn and newborn baby. Special caution should be taken for pregnant women with Graves' disease, as maternal thyroid-stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause transient neonatal Graves' disease. The HCP responsible for managing the patient's pregnancy must be made aware of the increased risk of thyroid disorders due to the patient's LEMTRADA treatment, and the need for these to be appropriately treated.

Strategies to Mitigate the Risk of Autoimmune Conditions

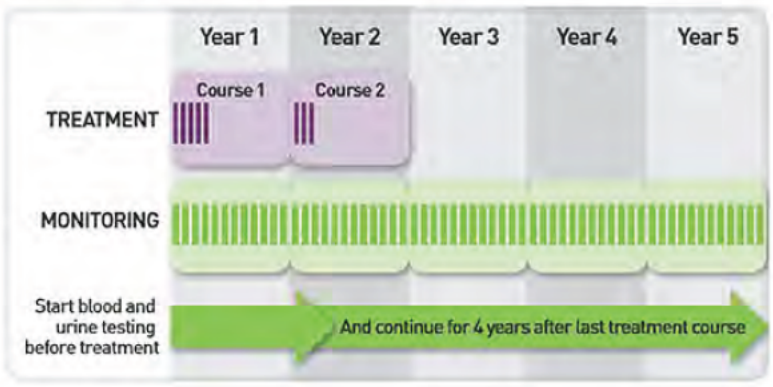
In order to minimize possible risks and side effects of LEMTRADA, prescribers and patients must commit to 48 months of follow-up after the last infusion of LEMTRADA. It is important that patients understand that they should continue with the monitoring, even if they are feeling well.

Creating a partnership between you and your patient, along with careful review of the patient education tool (*What You Need to Know About LEMTRADA Treatment: A Patient Guide*) with your patient, will help patients to:

- Comply with periodic tests
- Identify and report symptoms early
- Receive prompt and appropriate treatment if needed

To enhance your understanding of the duration of the effects of treatment and the length of required follow-up, please refer to the diagrams below titled ***Overview of LEMTRADA Treatment*** and ***Overview of LEMTRADA Monitoring.***

Overview of LEMTRADA Treatment



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Overview of LEMTRADA Monitoring

Condition	Activity	Timing	
Immune Thrombocytopenia (ITP)	Complete blood count with differential	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Serum creatinine	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Urinalysis with microscopy	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Thyroid Disorders	Thyroid function tests (such as TSH)	Prior to initiating LEMTRADA treatment	Every 3 months until 48 months after last infusion

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Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients, including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before the infusion and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. The duration of the infusion may be extended if clinically indicated. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

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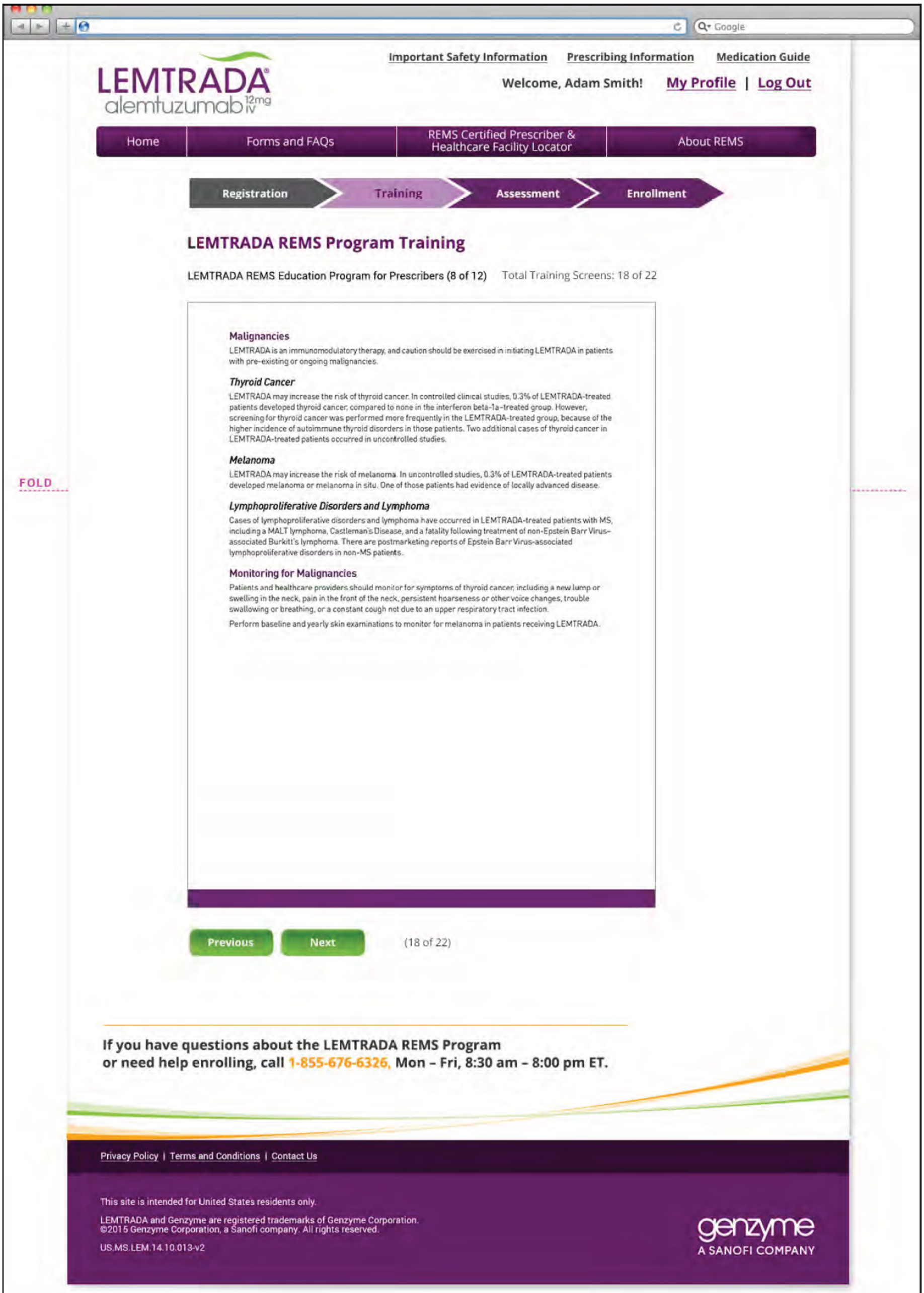

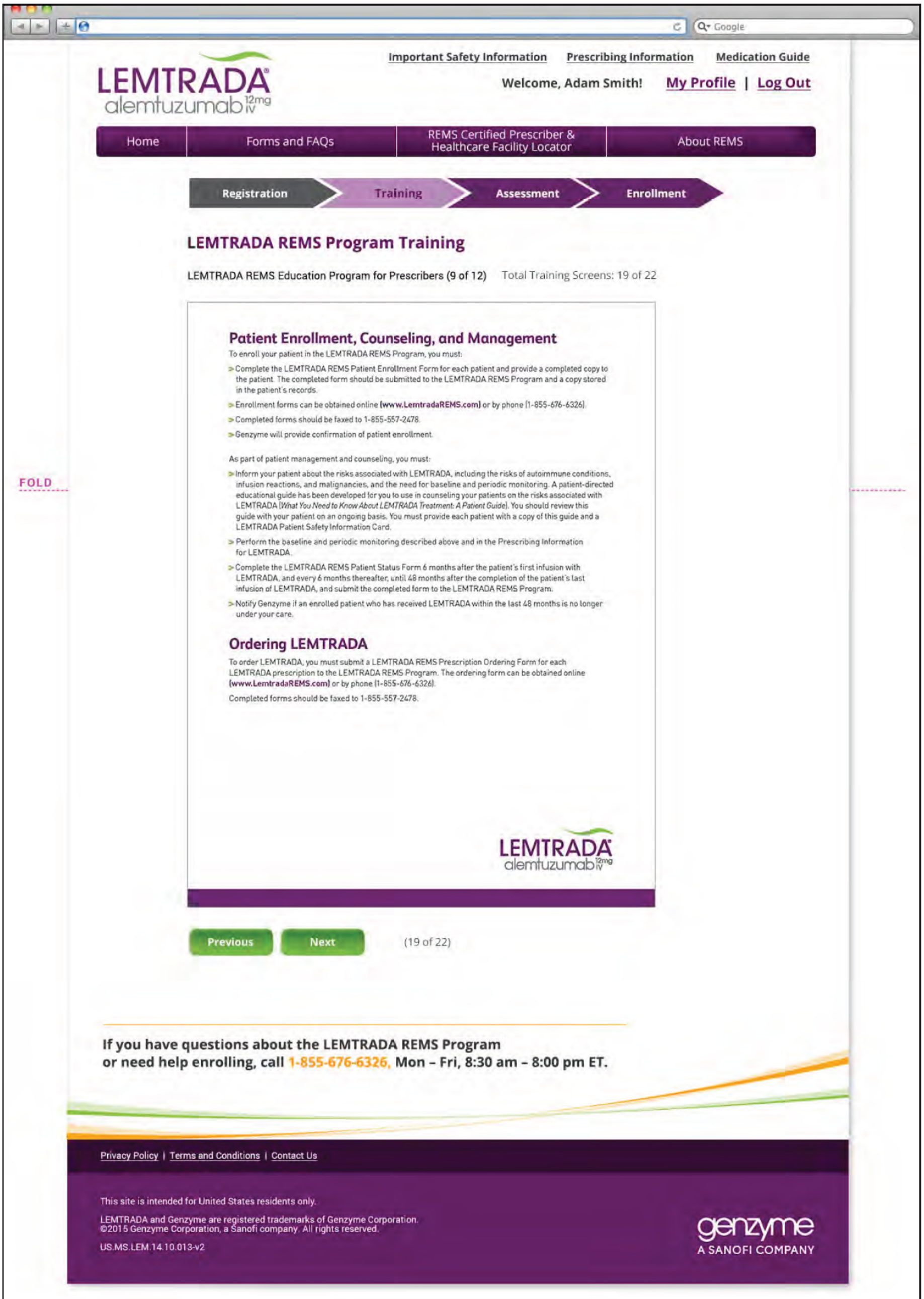
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Patient Enrollment, Counseling, and Management
To enroll your patient in the LEMTRADA REMS Program, you must:
> Complete the LEMTRADA REMS Patient Enrollment Form for each patient and provide a completed copy to the patient. The completed form should be submitted to the LEMTRADA REMS Program and a copy stored in the patient's records.
> Enrollment forms can be obtained online (www.LemtradaREMS.com) or by phone (1-855-676-6326).
> Completed forms should be faxed to 1-855-557-2478.
> Genzyme will provide confirmation of patient enrollment.
As part of patient management and counseling, you must:
> Inform your patient about the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies, and the need for baseline and periodic monitoring. A patient-directed educational guide has been developed for you to use in counseling your patients on the risks associated with LEMTRADA (What You Need to Know About LEMTRADA Treatment: A Patient Guide). You should review this guide with your patient on an ongoing basis. You must provide each patient with a copy of this guide and a LEMTRADA Patient Safety Information Card.
> Perform the baseline and periodic monitoring described above and in the Prescribing Information for LEMTRADA.
> Complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the completion of the patient's last infusion of LEMTRADA, and submit the completed form to the LEMTRADA REMS Program.
> Notify Genzyme if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care.
Ordering LEMTRADA
To order LEMTRADA, you must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription to the LEMTRADA REMS Program. The ordering form can be obtained online (www.LemtradaREMS.com) or by phone (1-855-676-6326).
Completed forms should be faxed to 1-855-557-2478.
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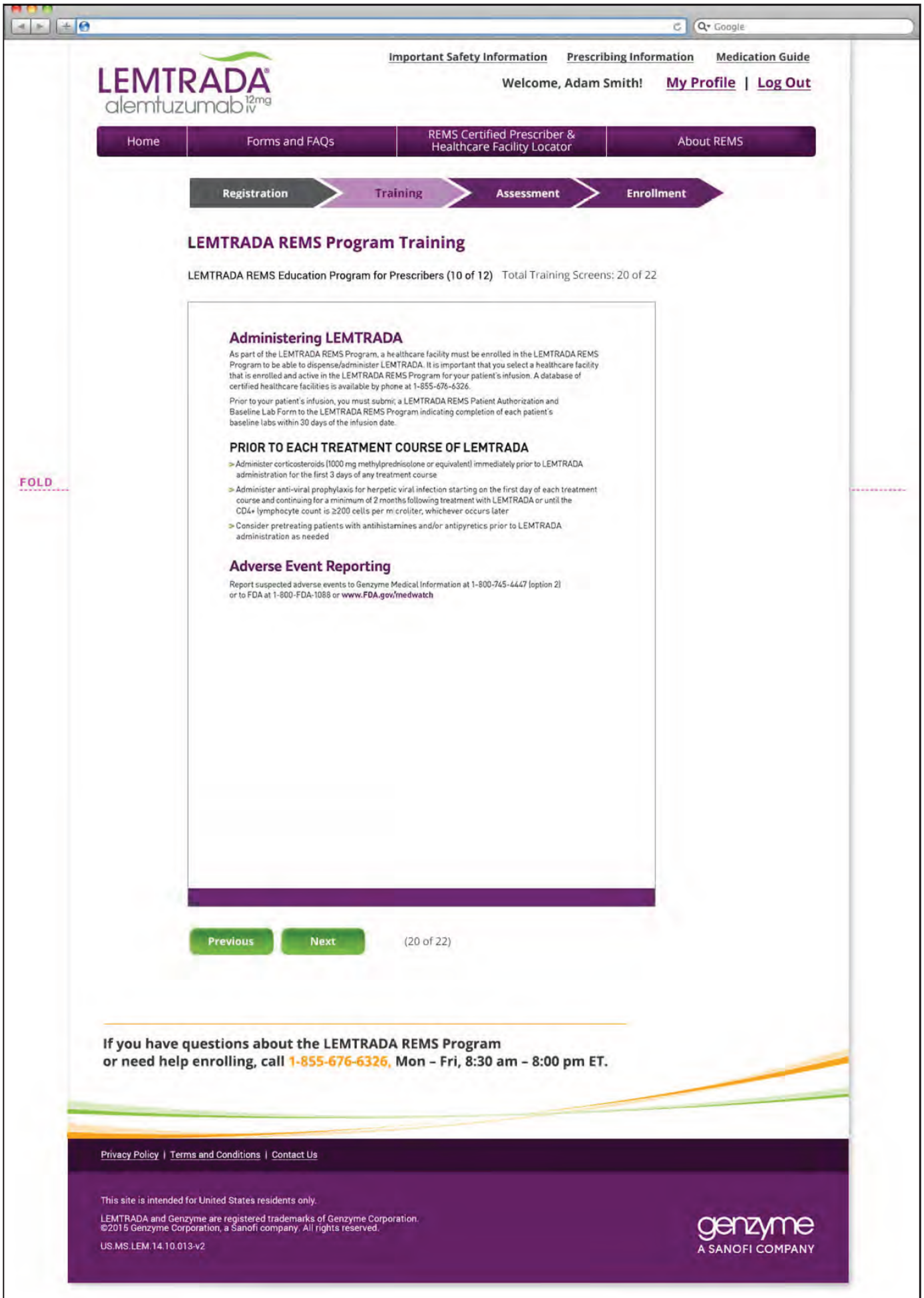
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Administering LEMTRADA
As part of the LEMTRADA REMS Program, a healthcare facility must be enrolled in the LEMTRADA REMS Program to be able to dispense/administer LEMTRADA. It is important that you select a healthcare facility that is enrolled and active in the LEMTRADA REMS Program for your patient's infusion. A database of certified healthcare facilities is available by phone at 1-855-676-6326.
Prior to your patient's infusion, you must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form to the LEMTRADA REMS Program indicating completion of each patient's baseline labs within 30 days of the infusion date.
PRIOR TO EACH TREATMENT COURSE OF LEMTRADA
Administer corticosteroids (1000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA administration for the first 3 days of any treatment course
Administer anti-viral prophylaxis for herpetic viral infection starting on the first day of each treatment course and continuing for a minimum of 2 months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥200 cells per microliter, whichever occurs later
Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed
Adverse Event Reporting
Report suspected adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or to FDA at 1-800-FDA-1088 or www.FDA.gov/medwatch
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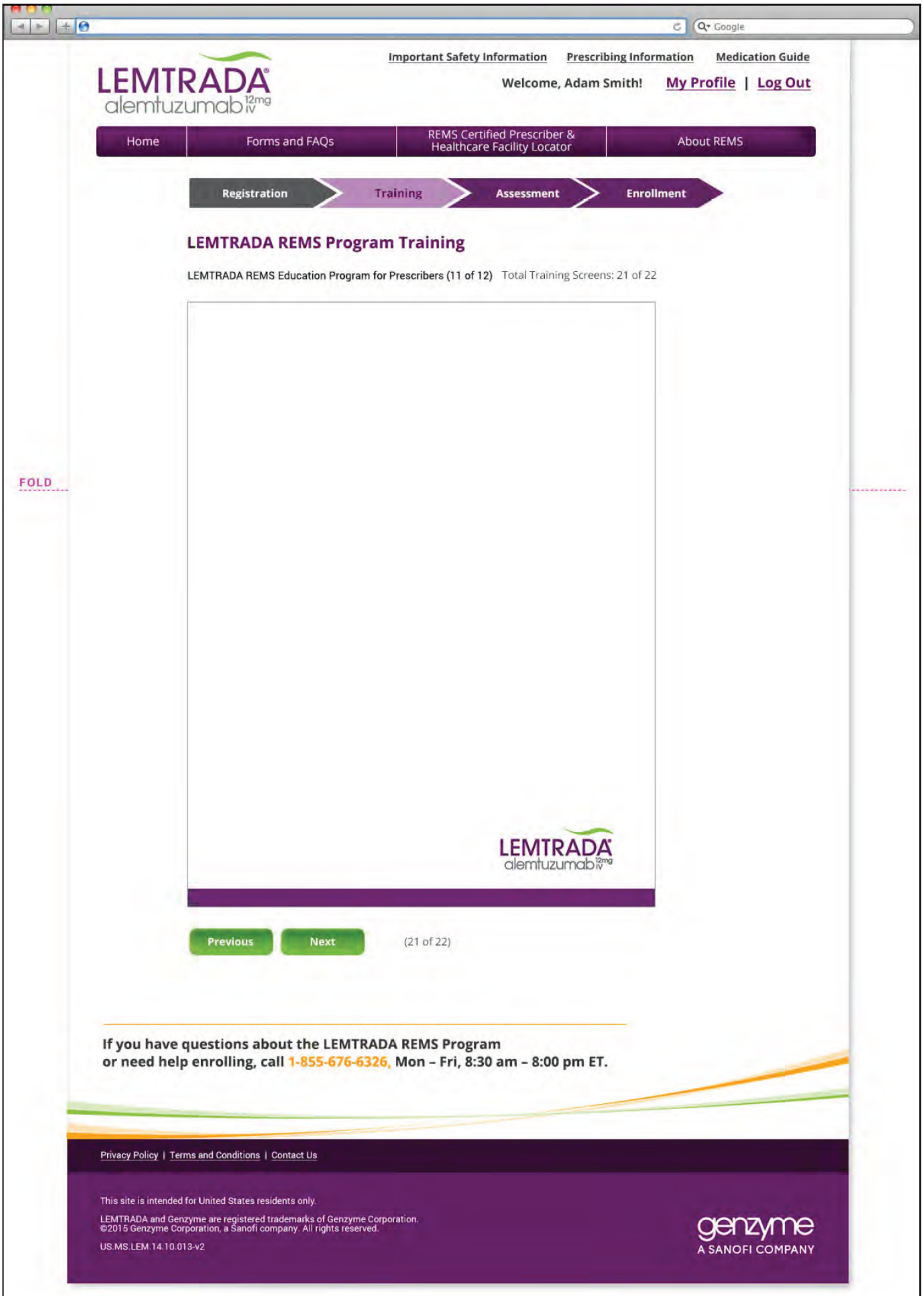

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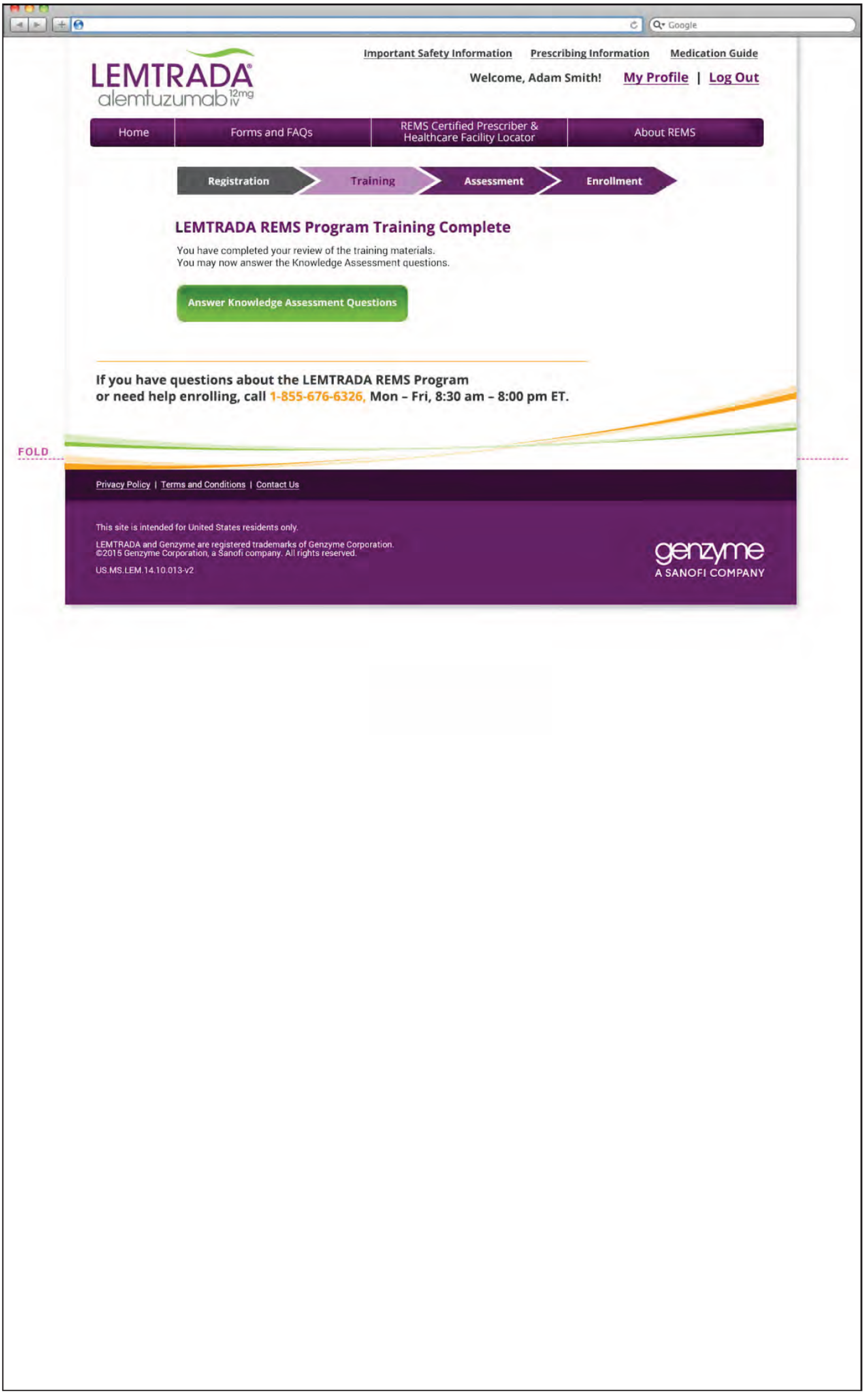

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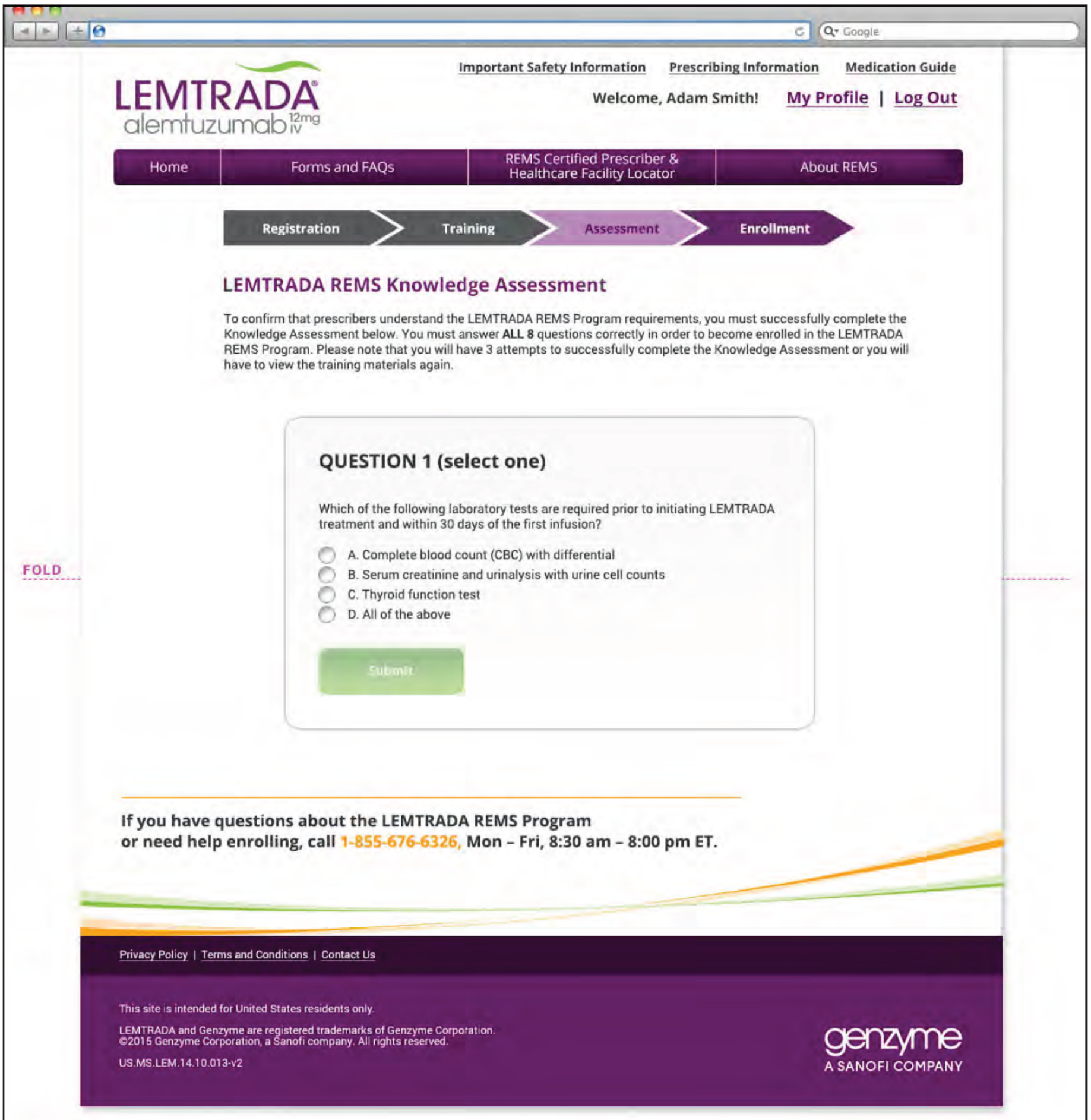

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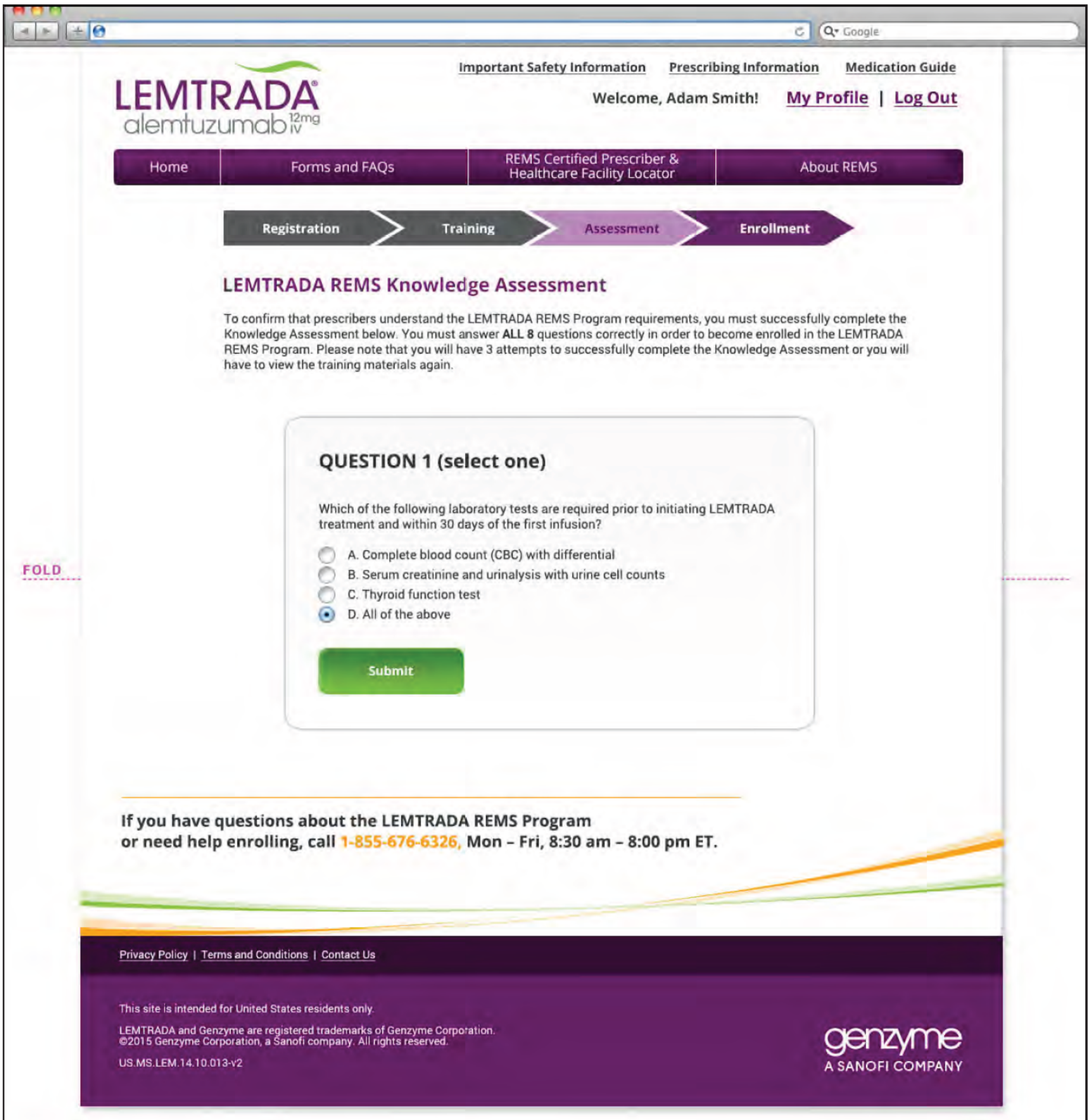

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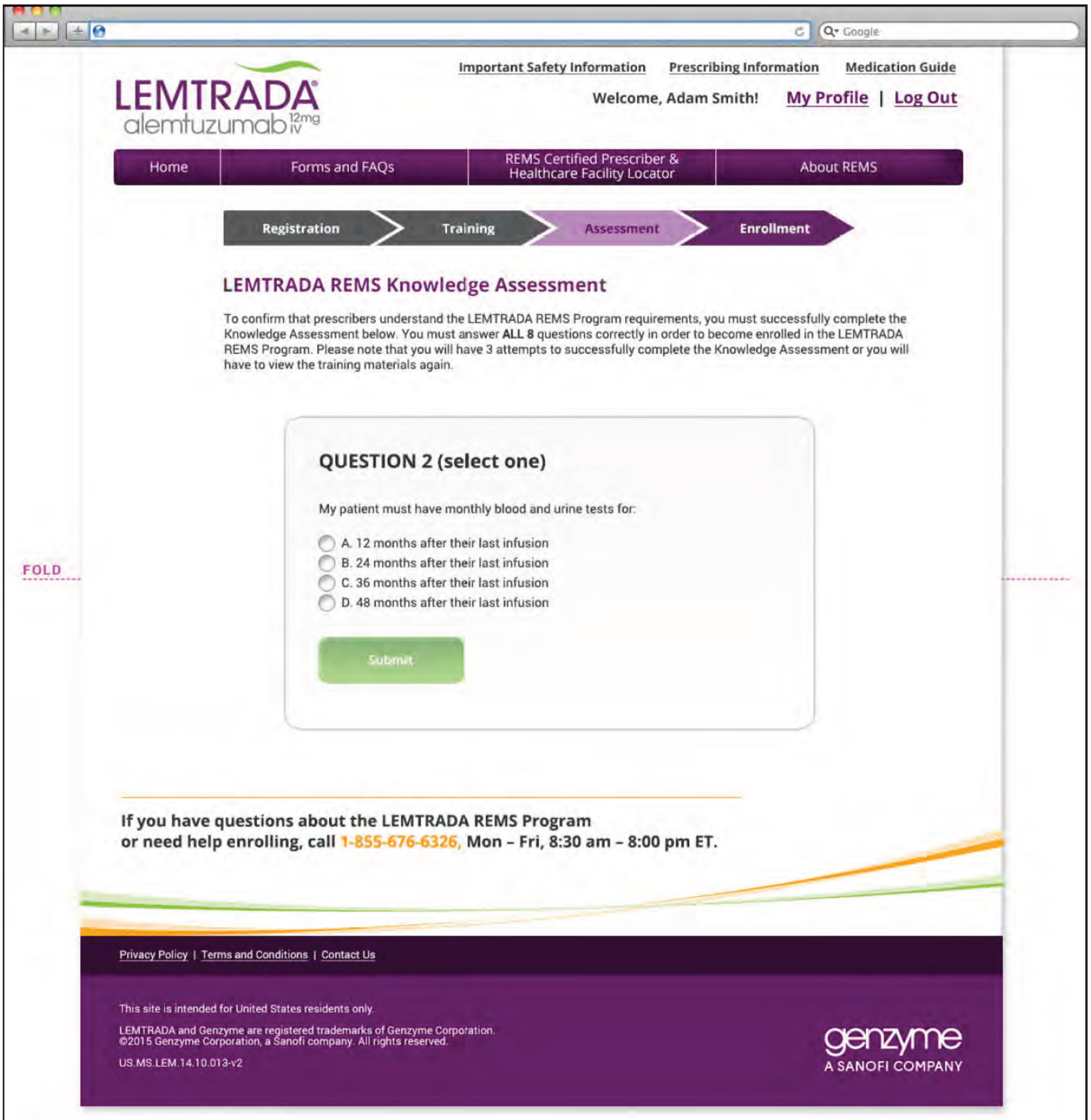

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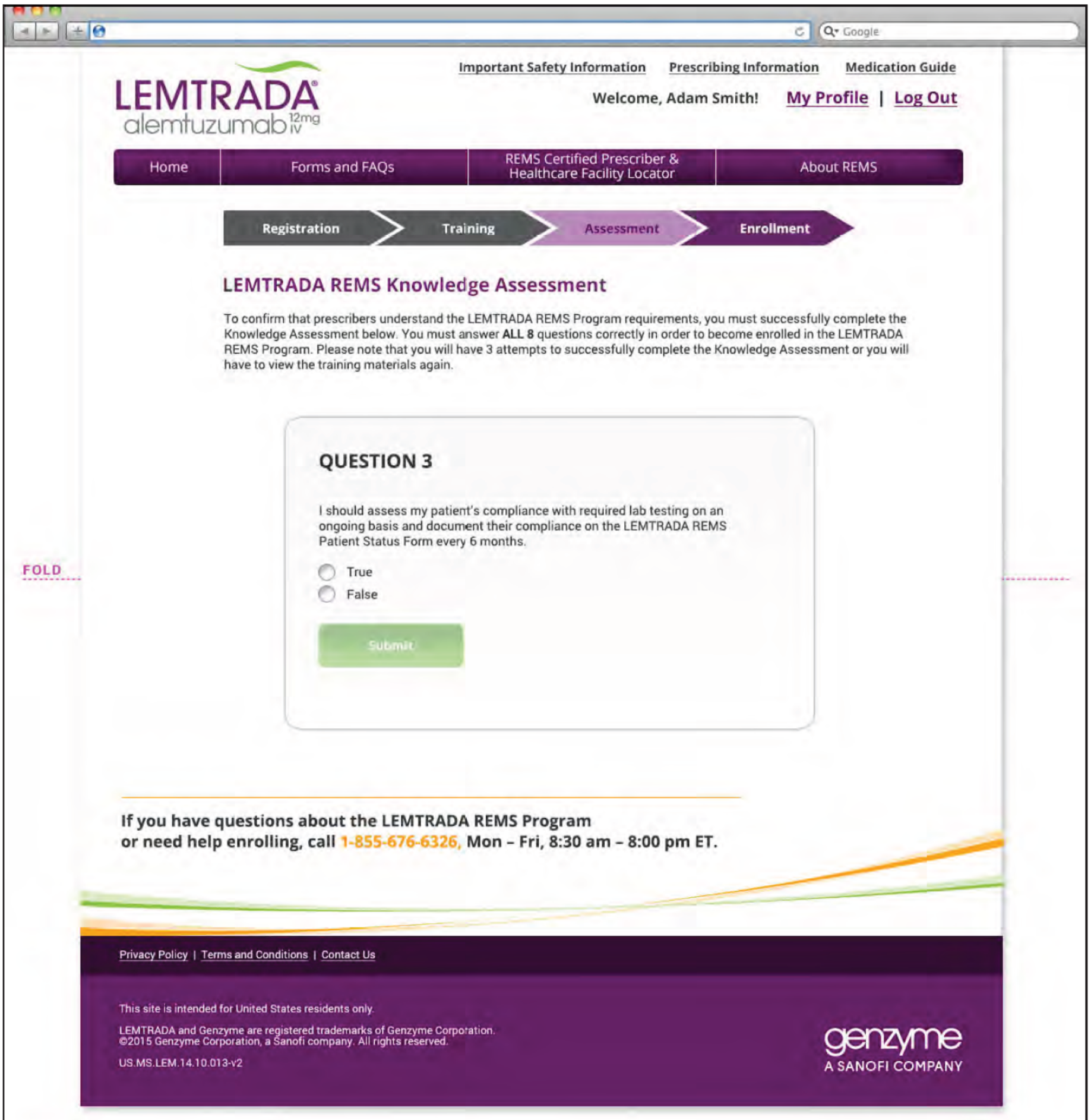

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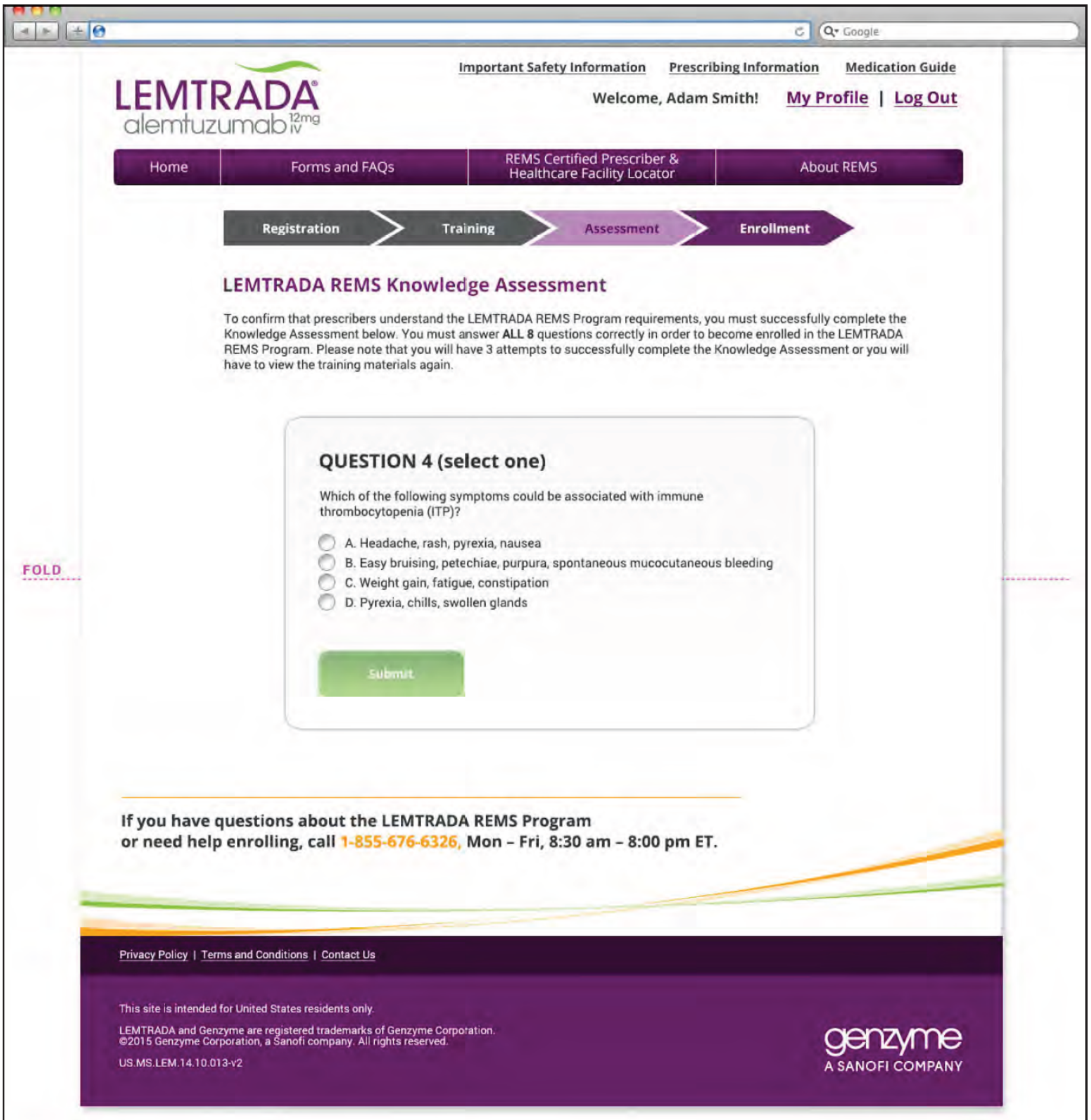

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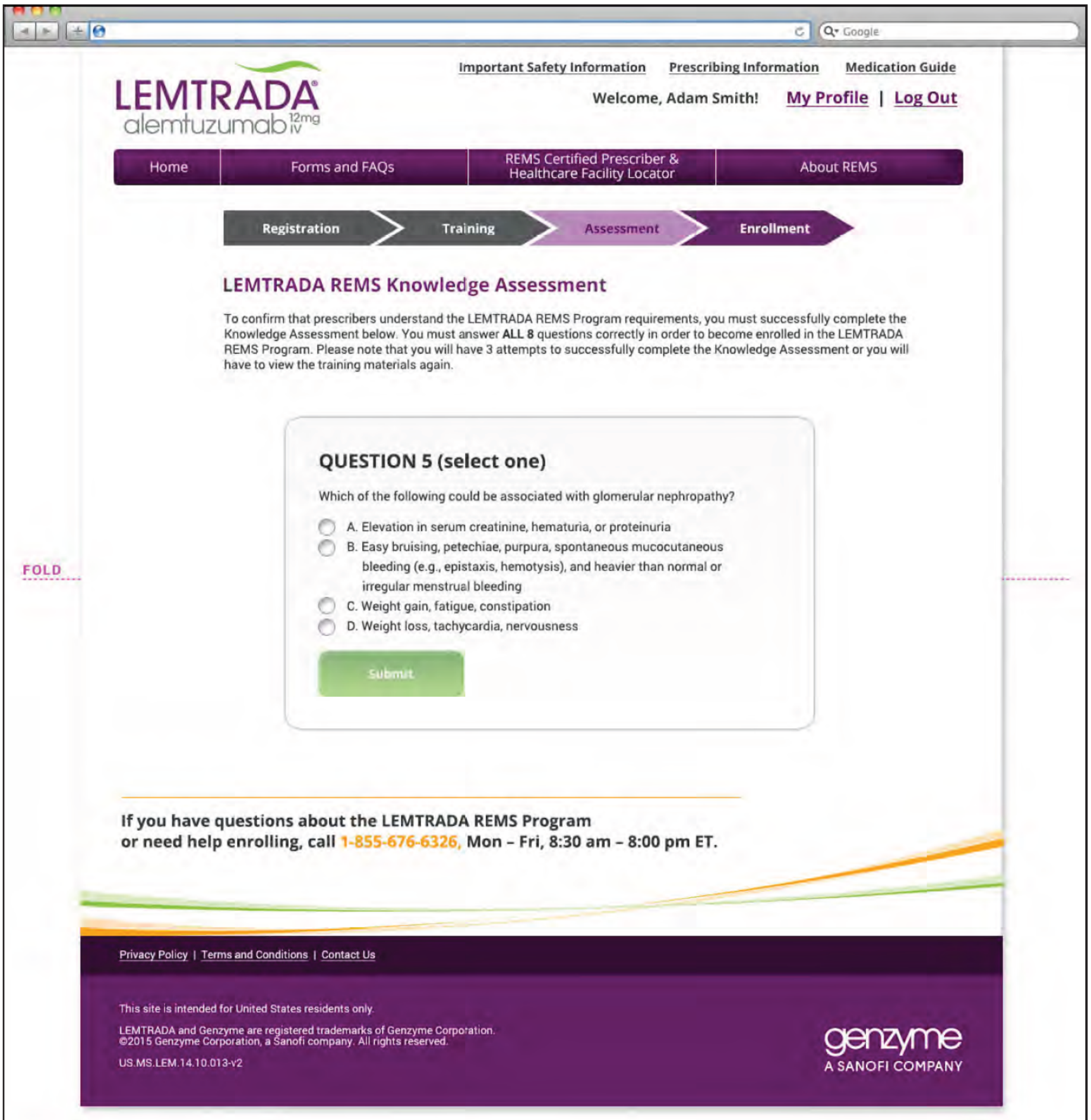

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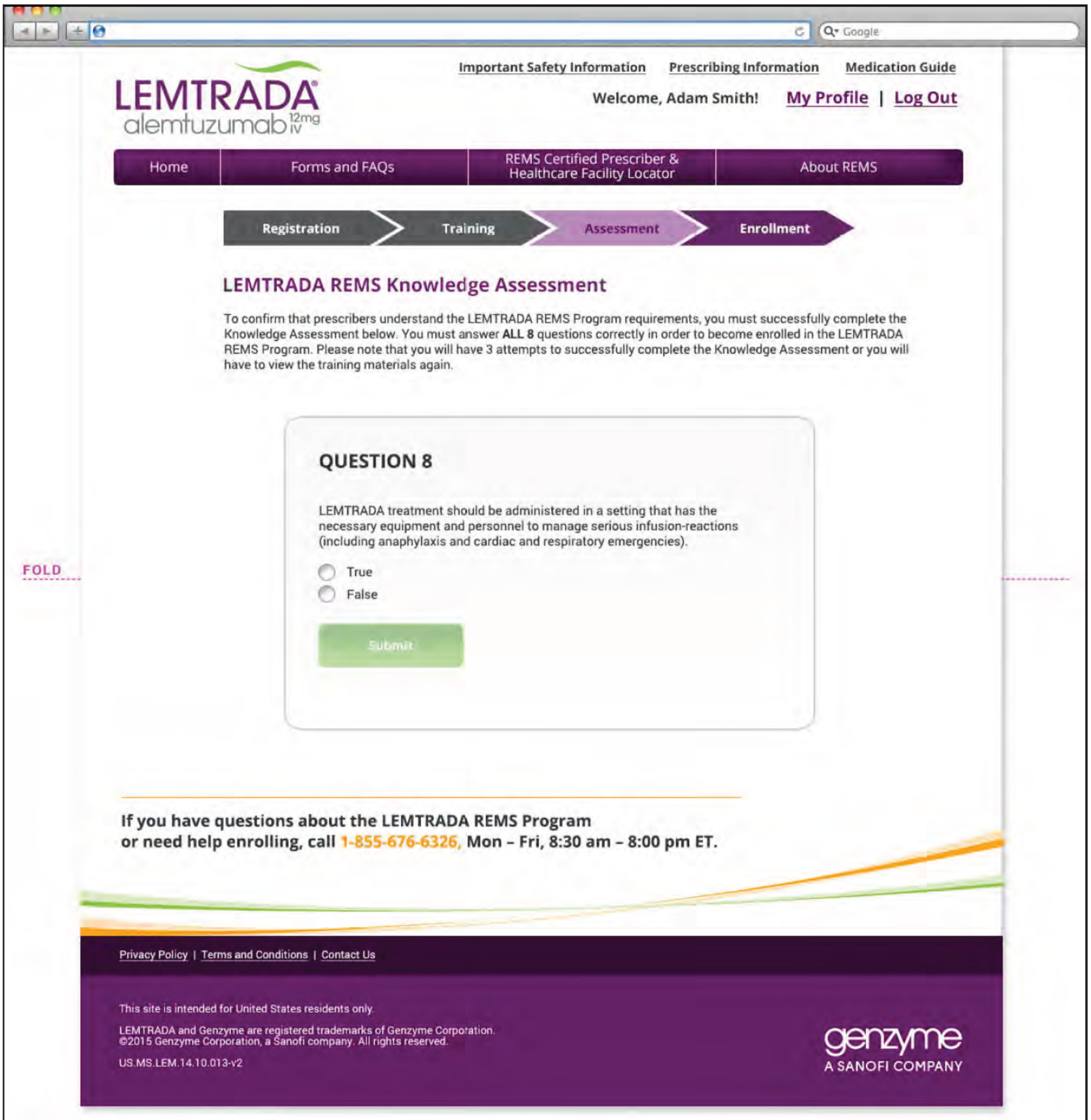
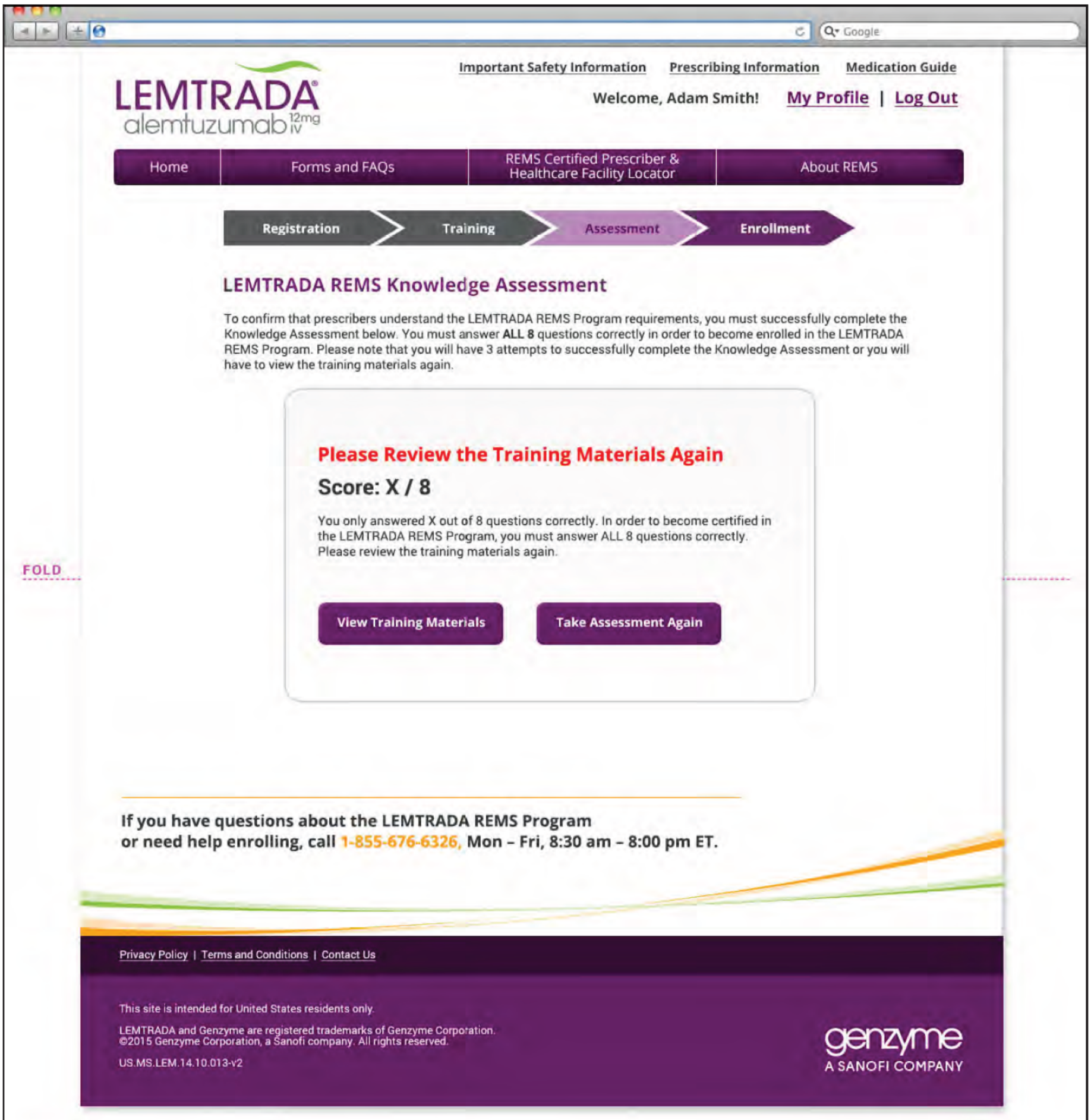
LEMTRADA REMS Desktop - Prescriber Training, Assessment Question 8



LEMTRADA REMS Desktop - Prescriber Training, Failed Assessment



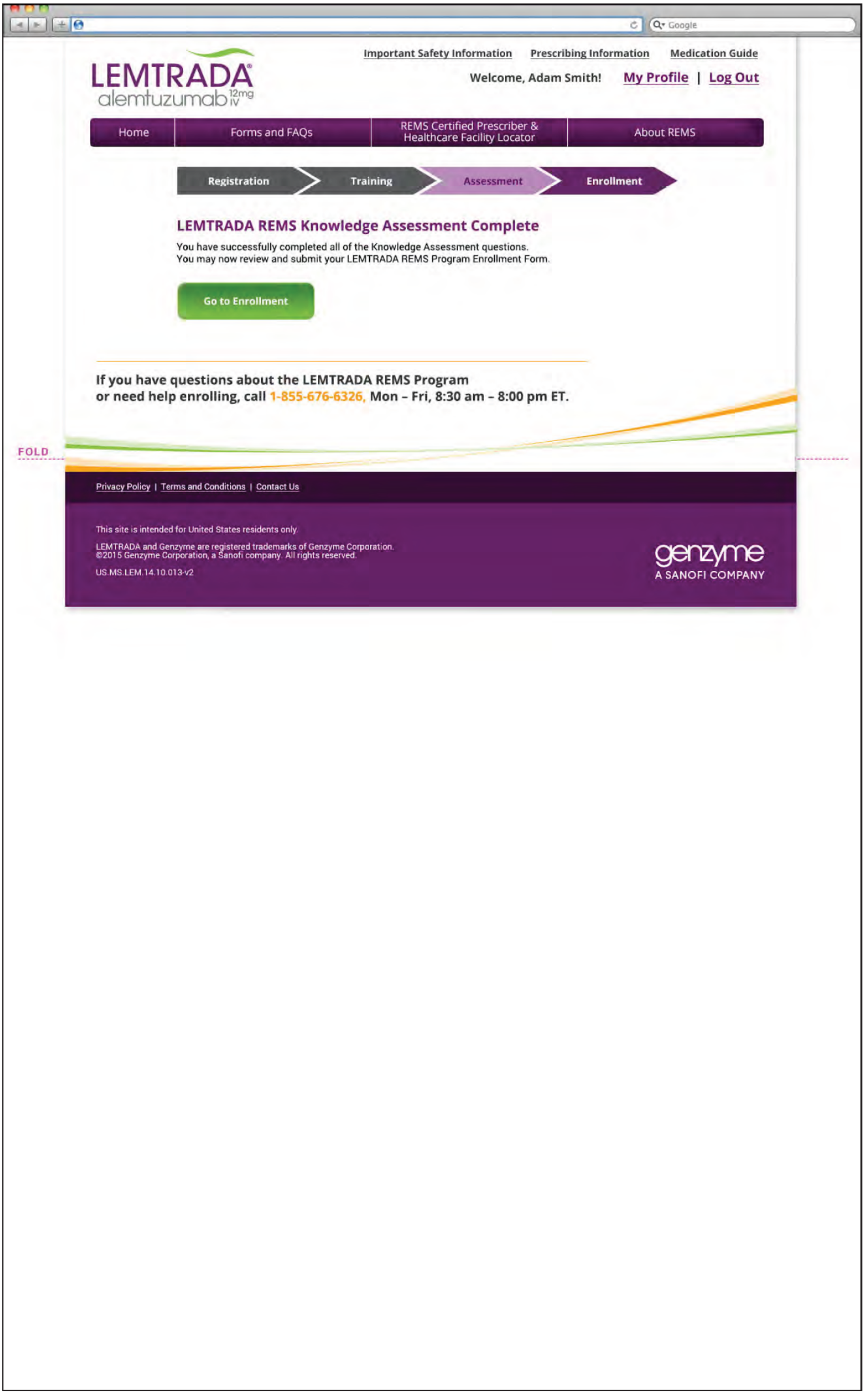
LEMTRADA REMS Desktop - Prescriber Training, Failed the Assessment 3 Times



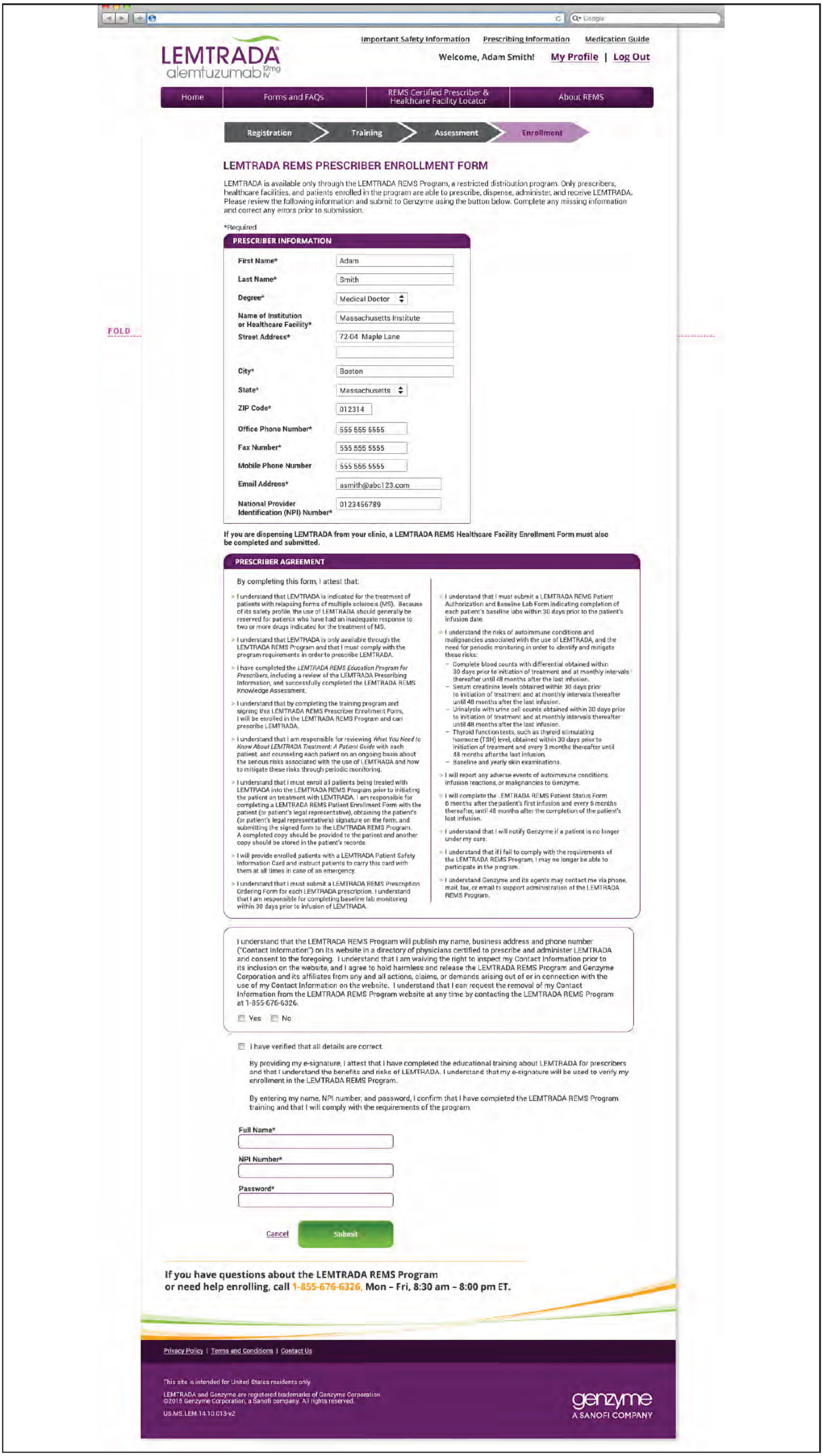
LEMTRADA REMS Desktop - Prescriber Training, Failed the Assessment 6 Times



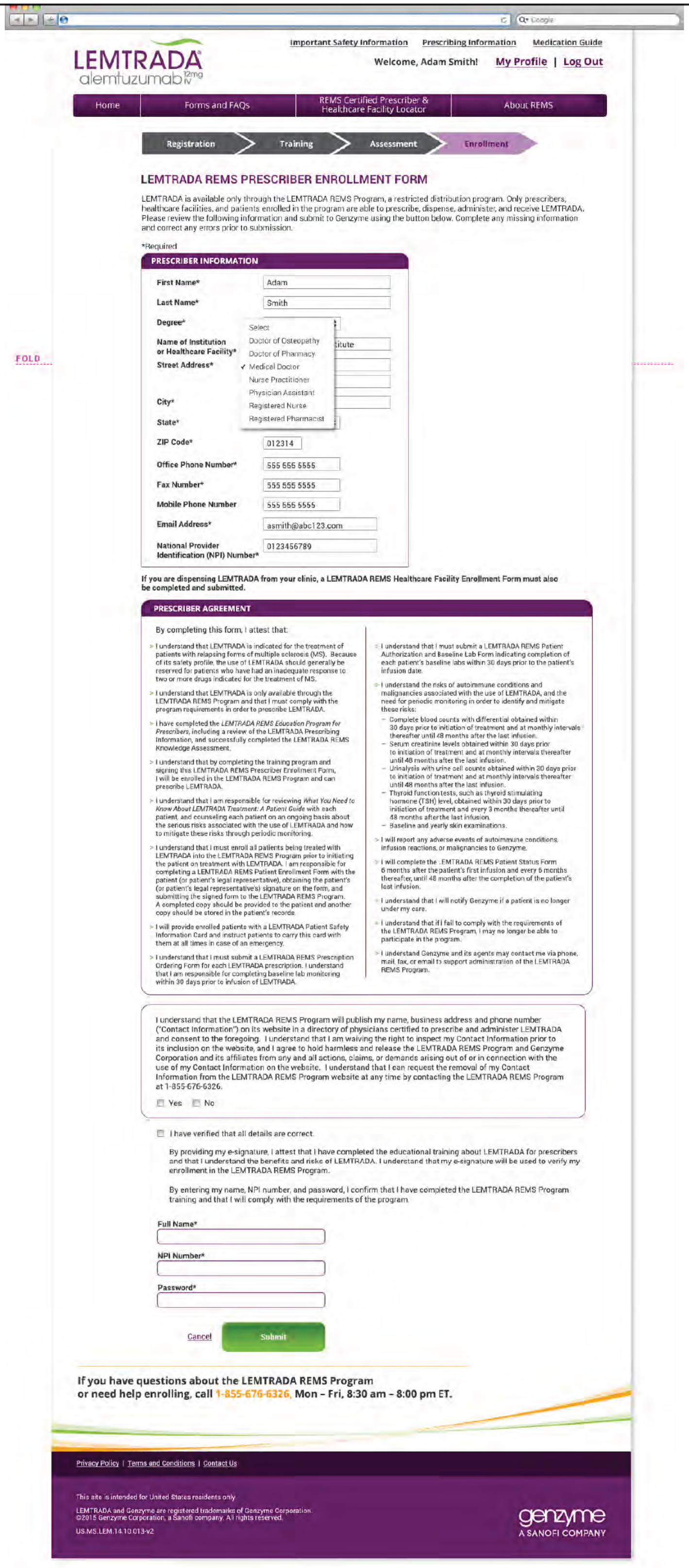
LEMTRADA REMS Desktop - Prescriber Training, Assessment Complete



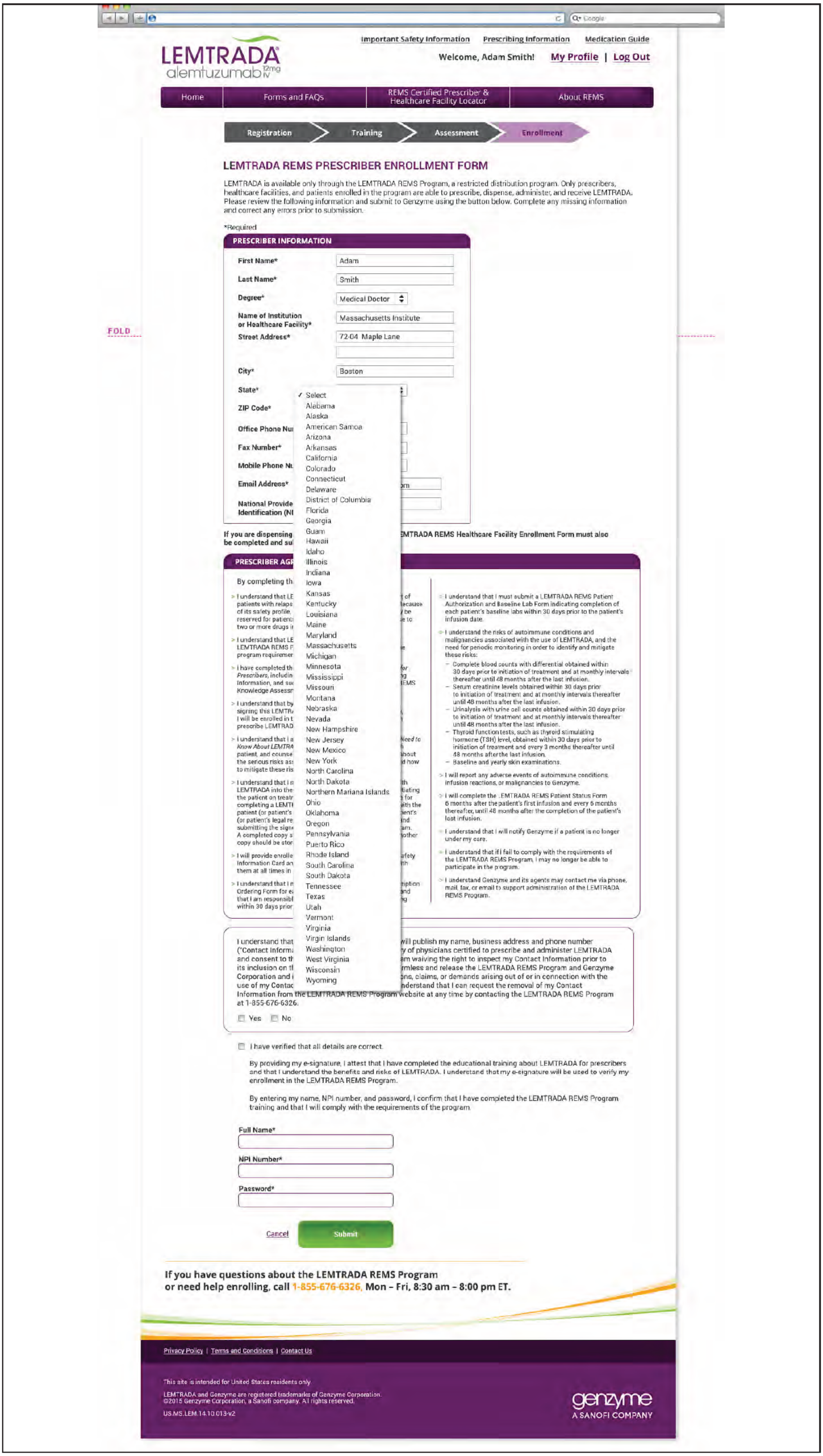
LEMTRADA REMS Desktop - Prescriber Training, Enrollment



LEMTRADA REMS Desktop - Prescriber Training, Enrollment, Degree Dropdown

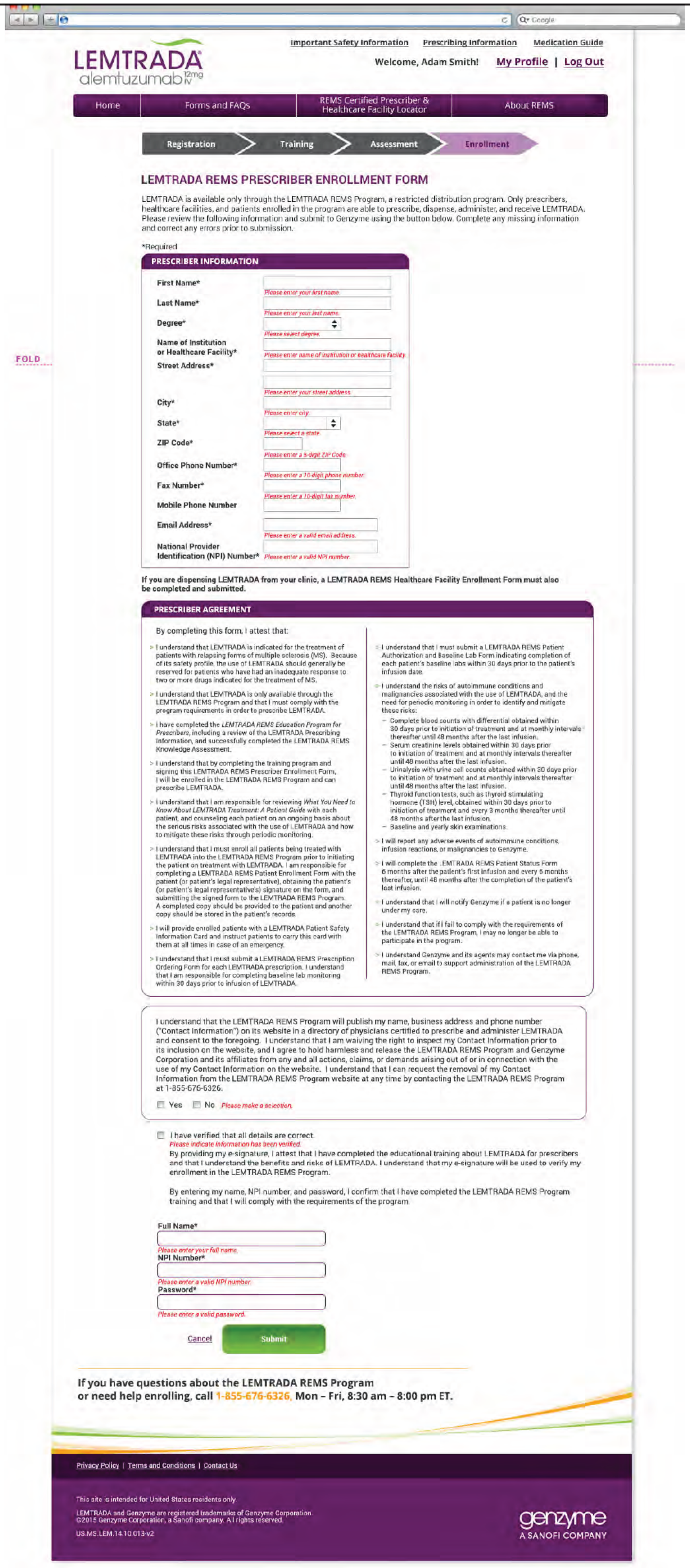


LEMTRADA REMS Desktop - Prescriber Training, Enrollment, State Dropdown

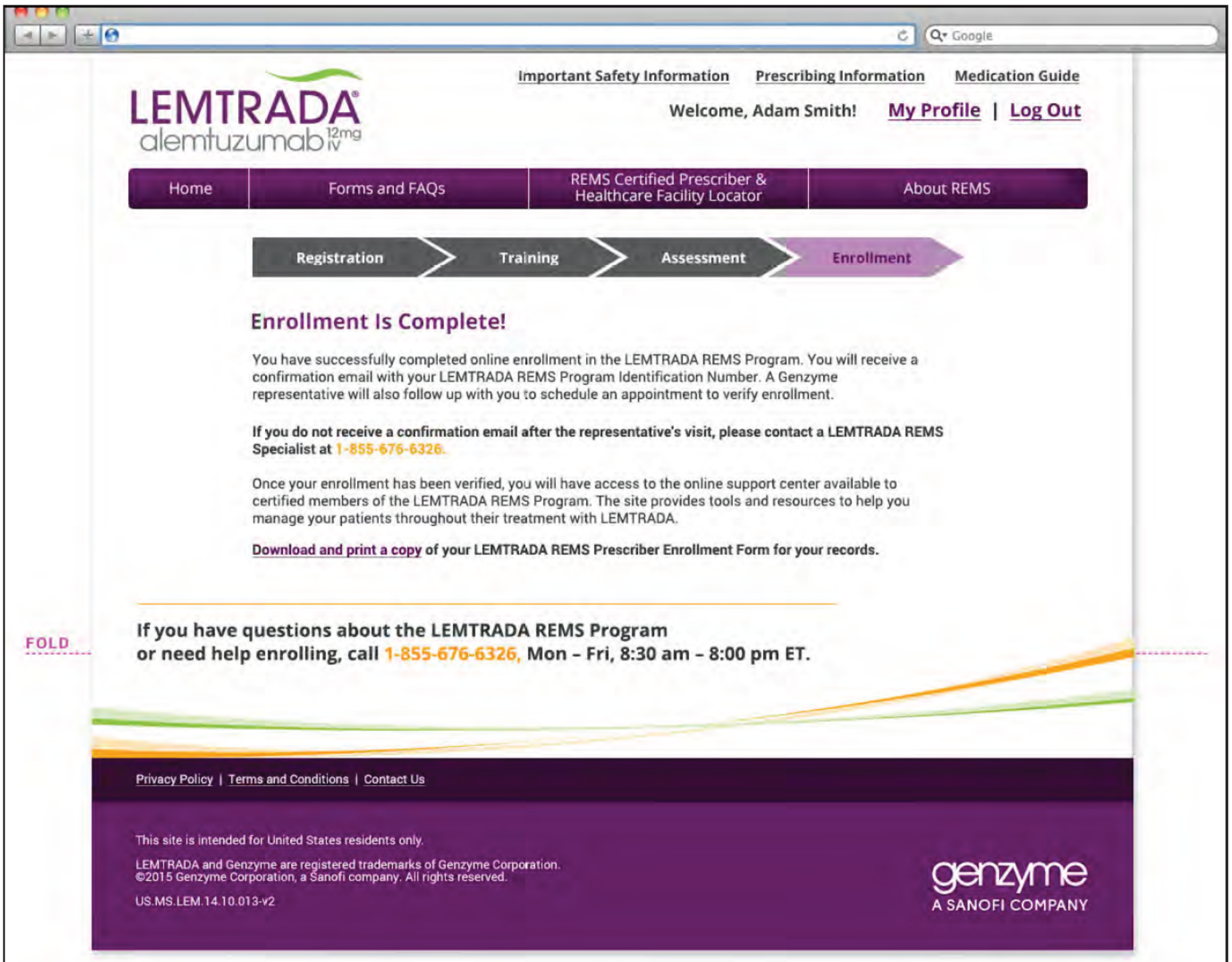


Reference ID: 3821900

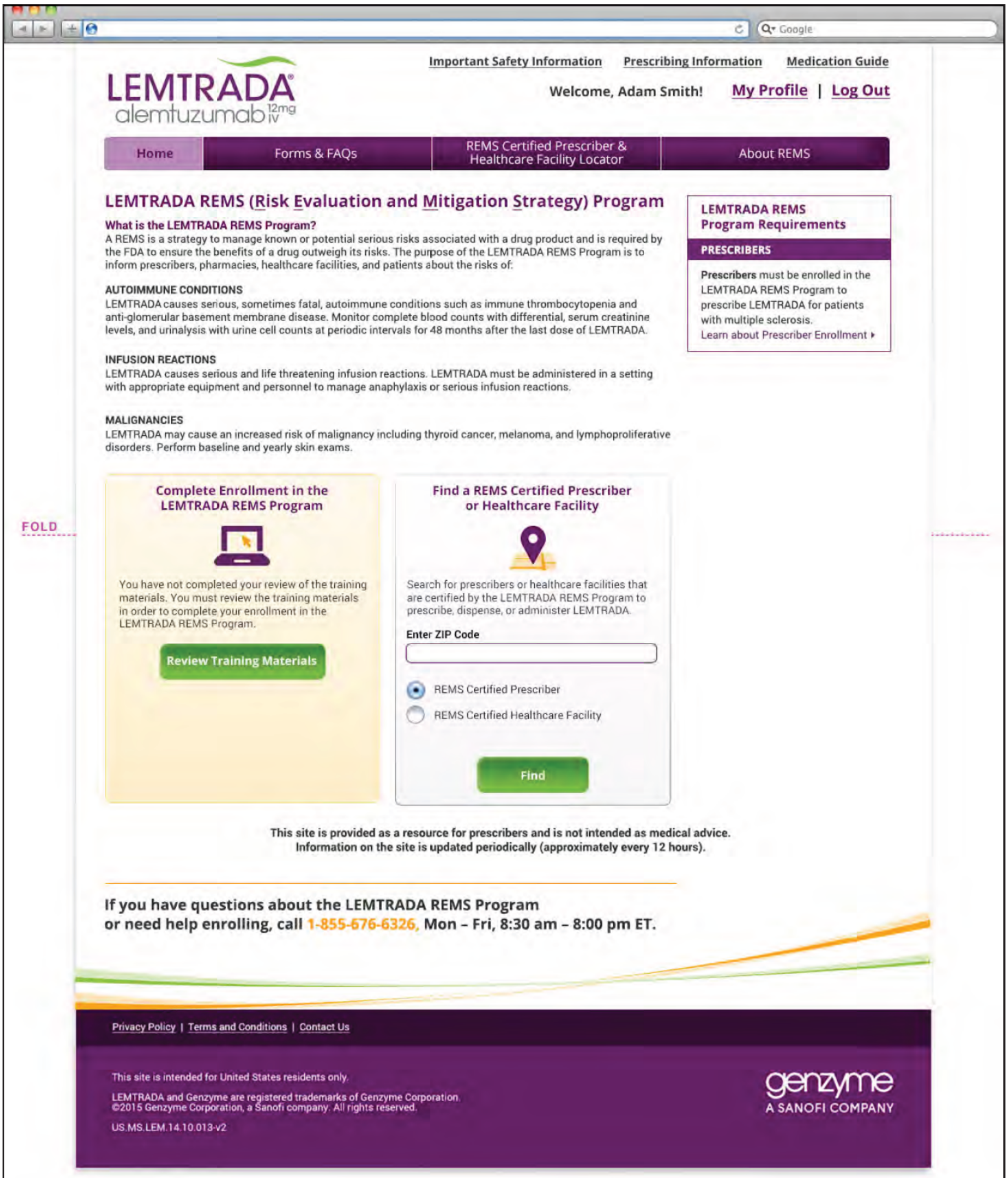
LEMTRADA REMS Desktop - Prescriber Training, Enrollment Error



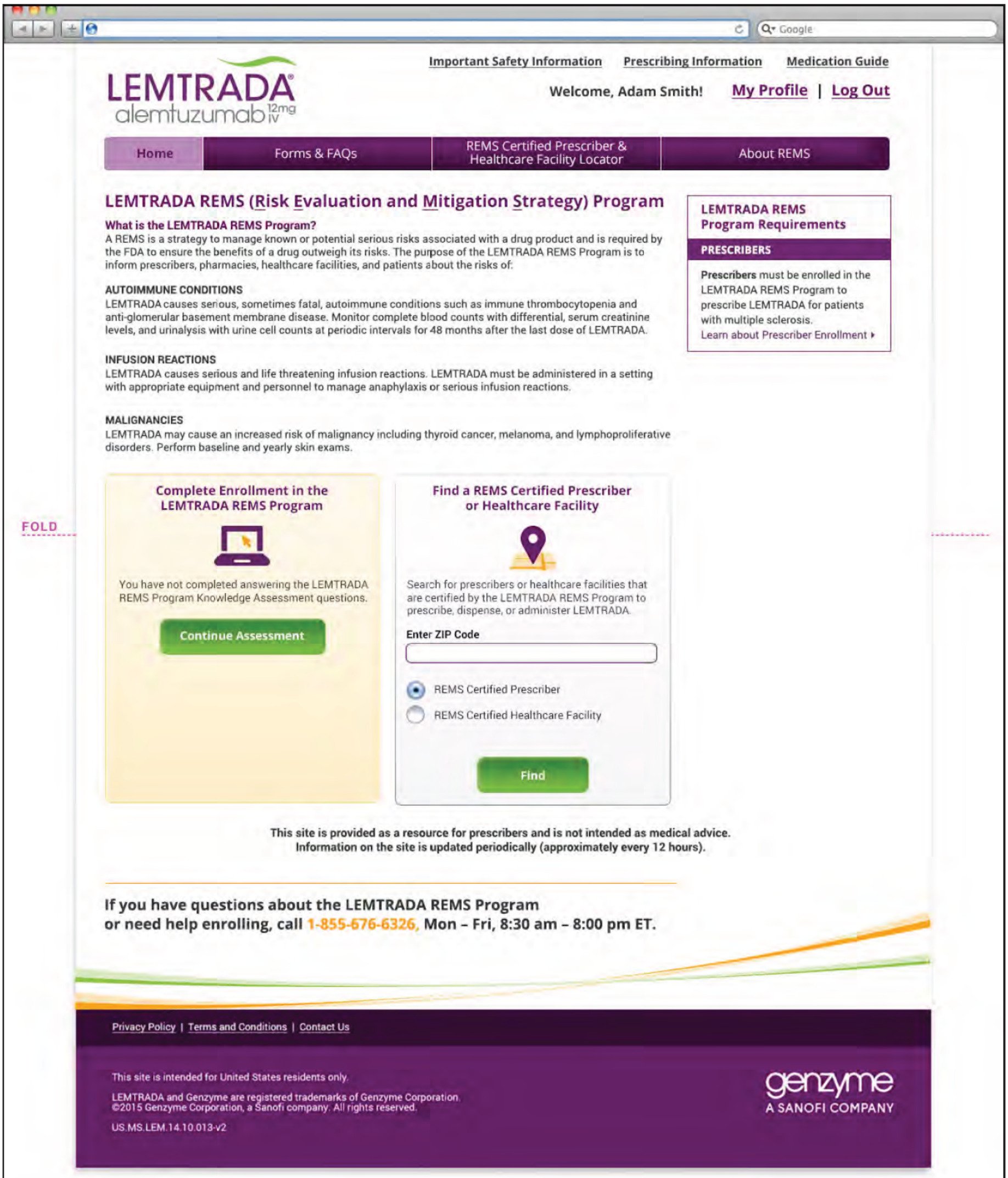
LEMTRADA REMS Desktop - Prescriber Training, Enrollment Complete



LEMTRADA REMS Desktop - Enrolled, Pre-REMS Cert, Training Incomplete



LEMTRADA REMS Desktop - Enrolled, Pre-REMS Cert, Assessment Incomplete



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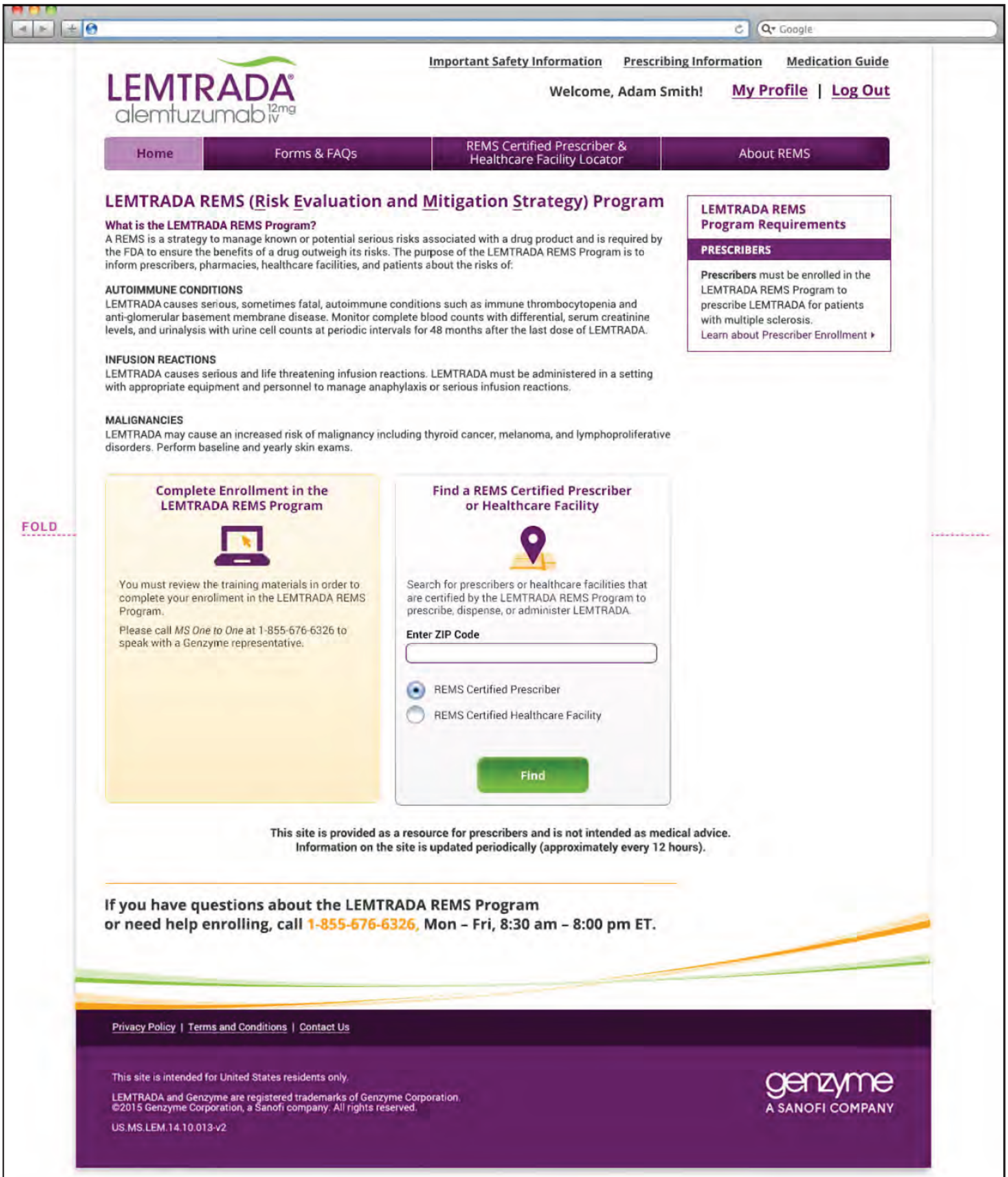

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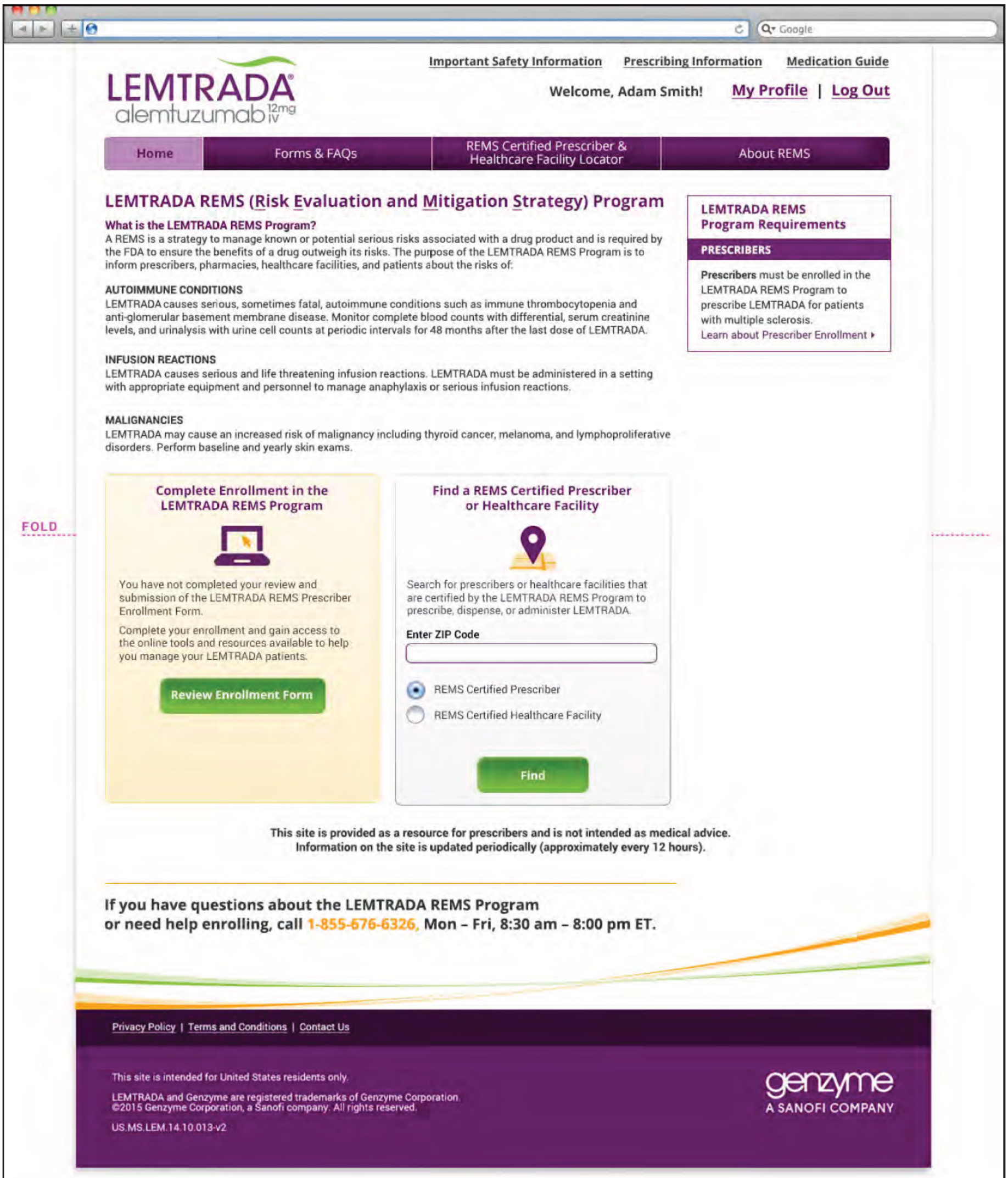
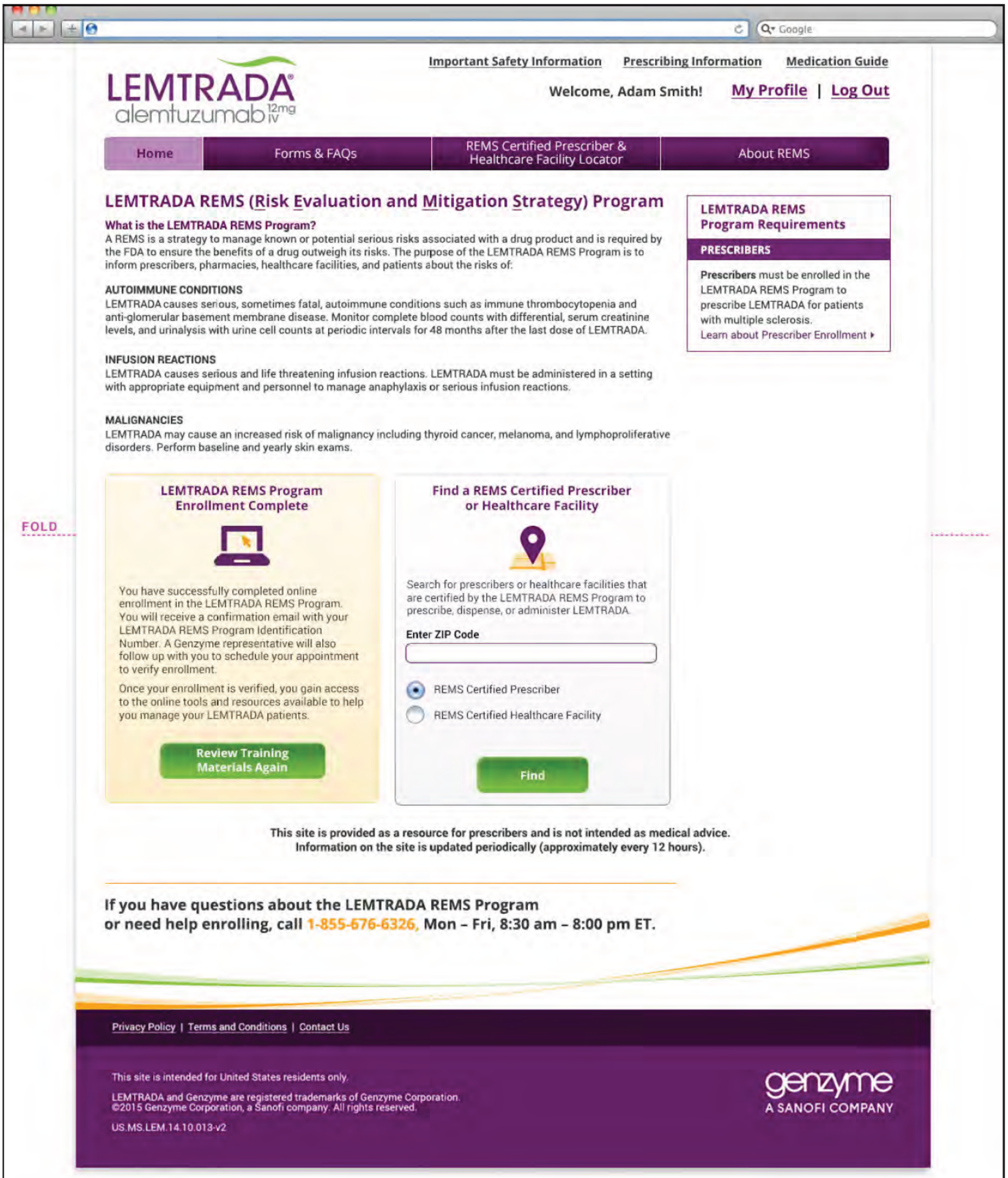


LEMTRADA REMS Desktop - Enrolled, Pre-REMS Cert, Enrollment Complete



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LEMTRADA REMS Program Training

Full Prescribing Information (1 of 8)

Total Training Screens: 1 of 22

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- LEMTRADA is available only through a restricted distribution program. (5.4)

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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*Sections or subsections omitted from the full prescribing information are not listed.

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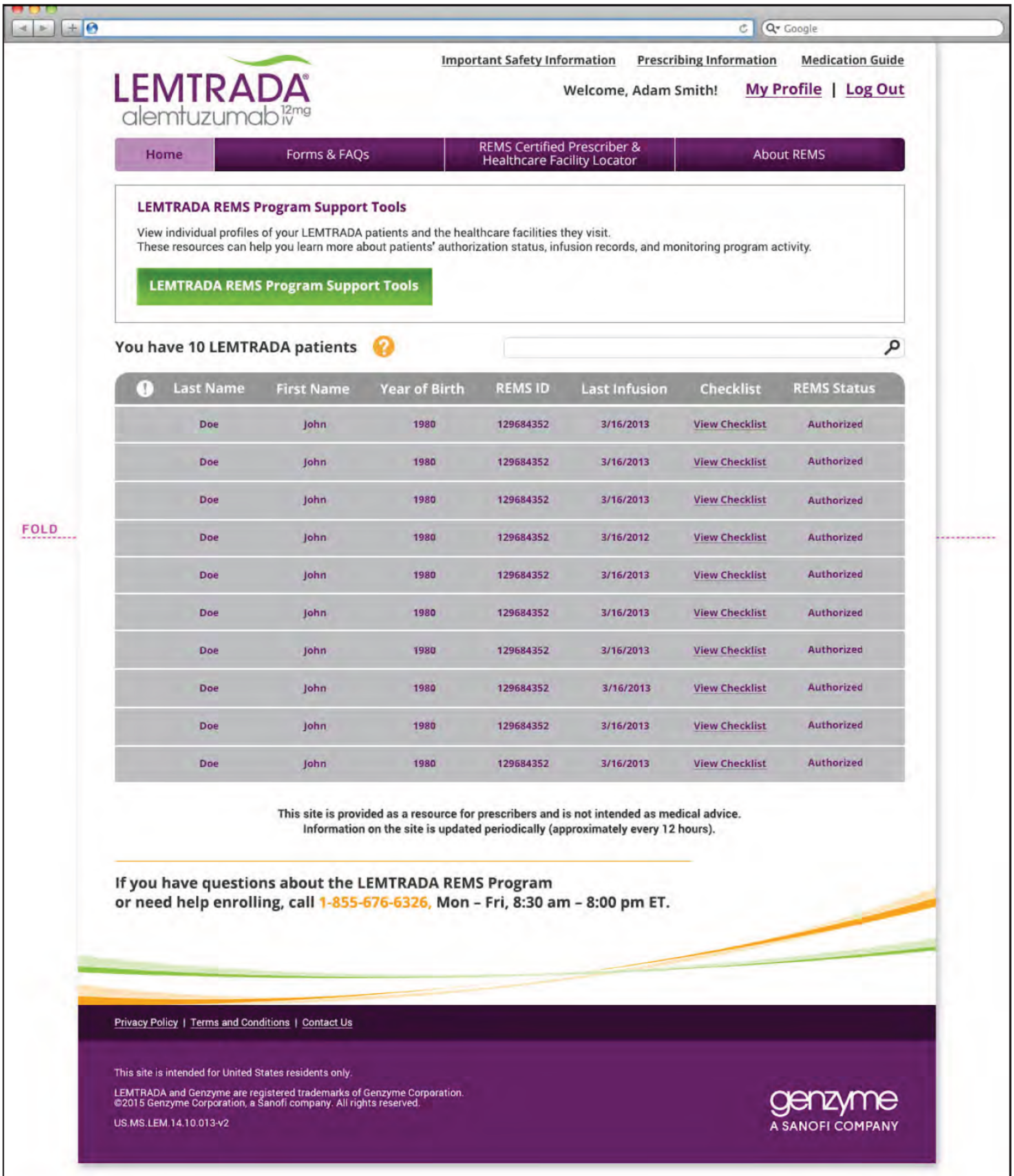
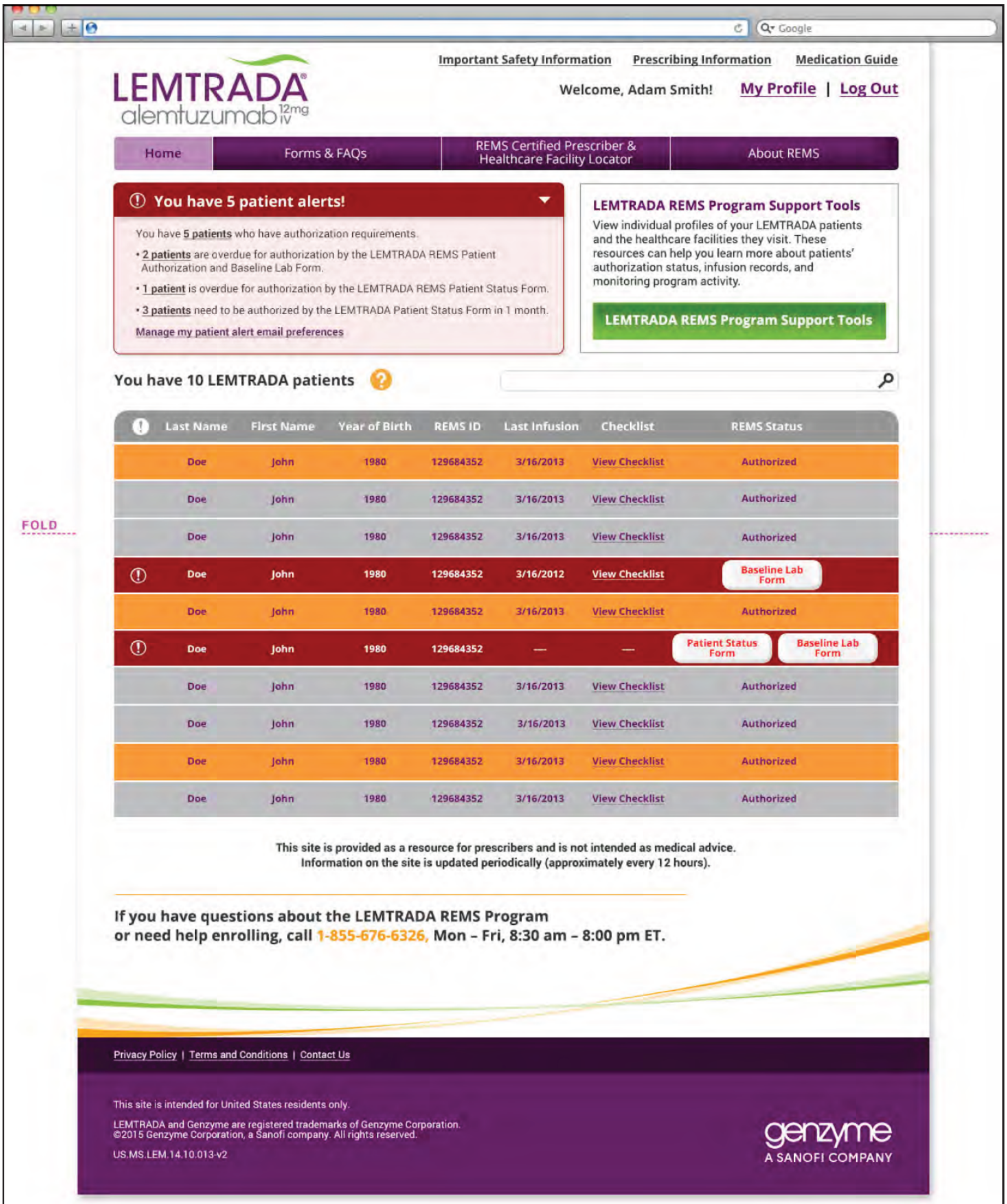
PRESCRIBER DASHBOARD PAGES

LEMTRADA REMS Desktop - Prescriber Dashboard, My Patients - No Patient Alerts



LEMTRADA REMS Desktop - Prescriber Dashboard, My Patients, Alert Expanded



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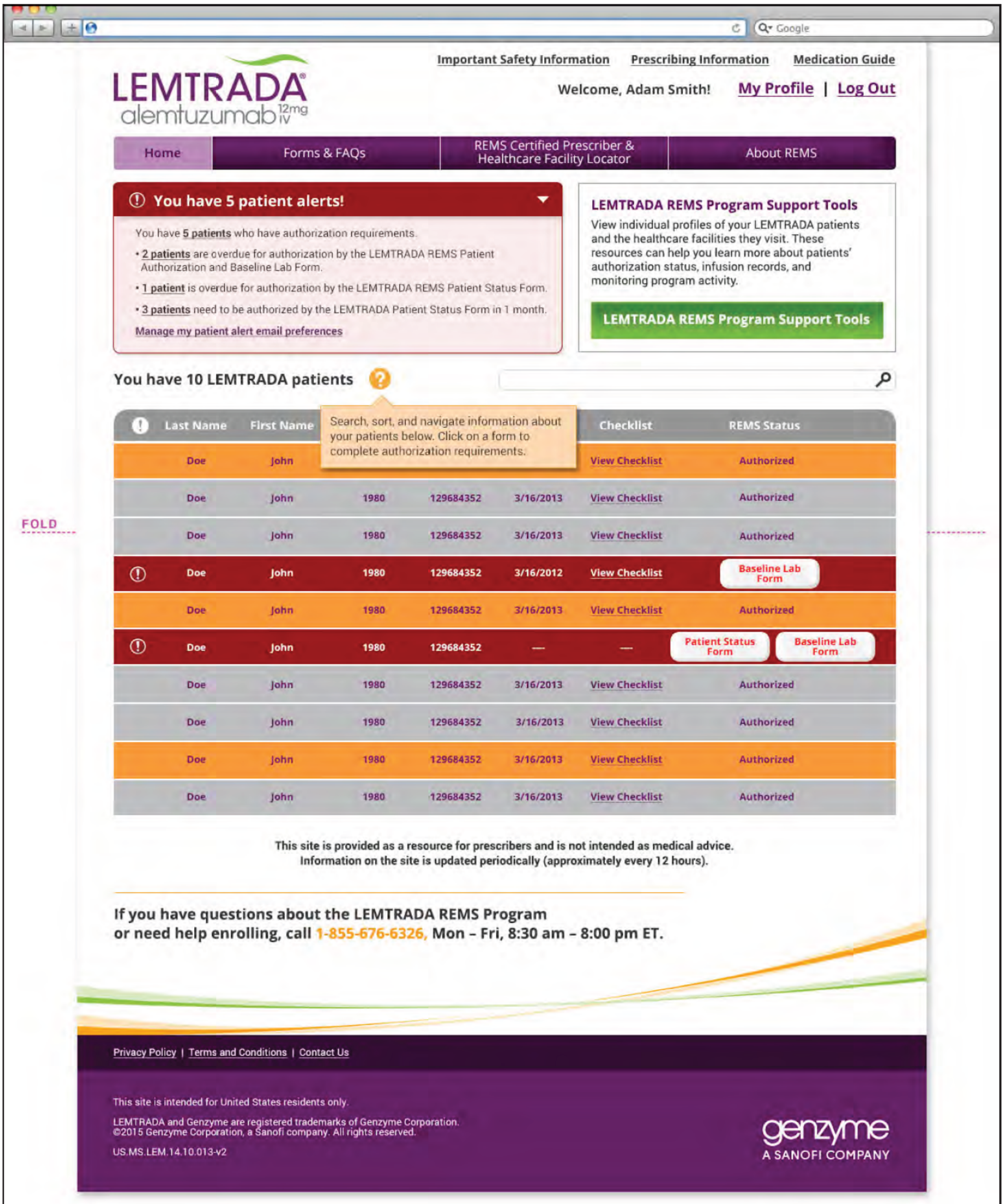

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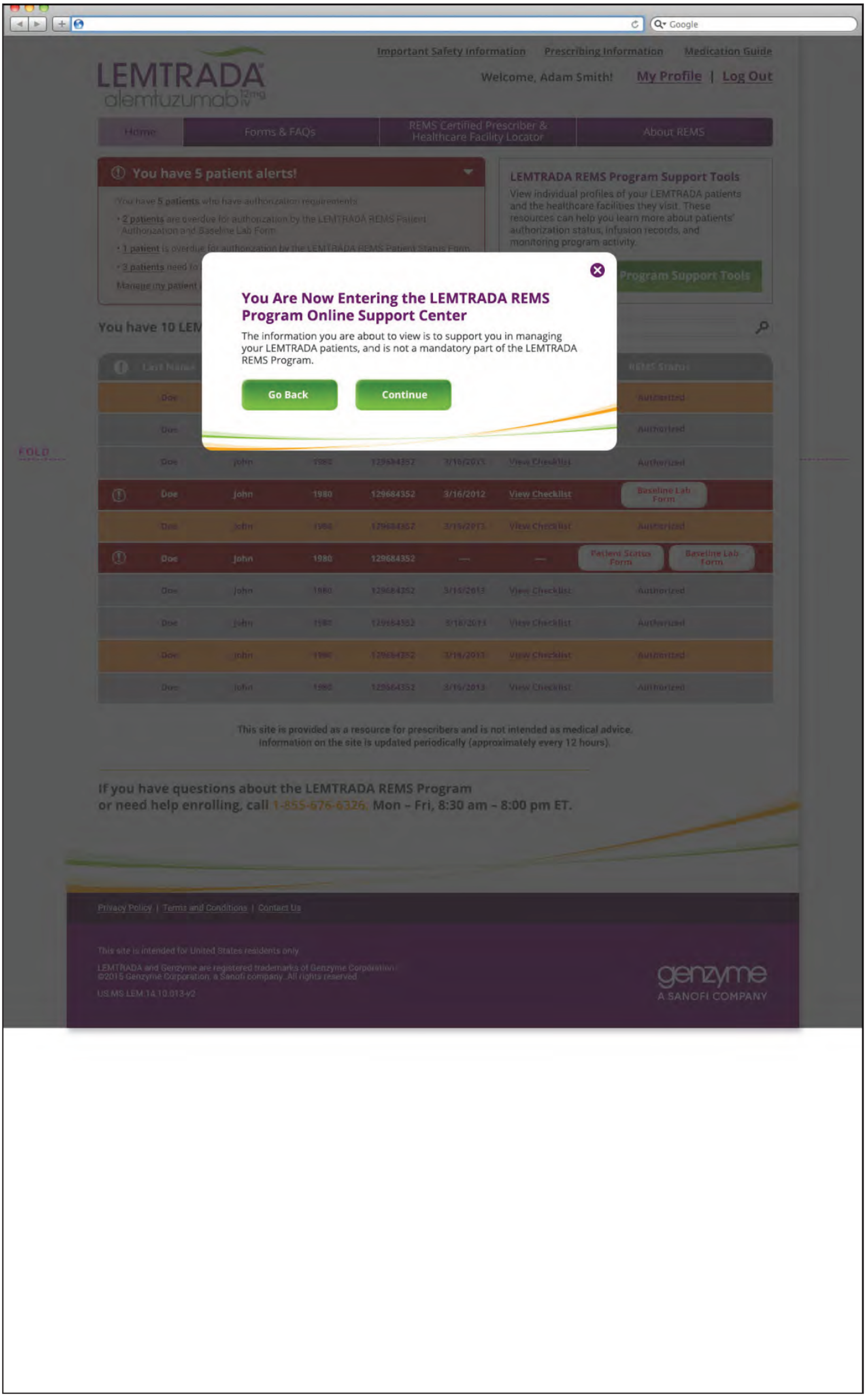
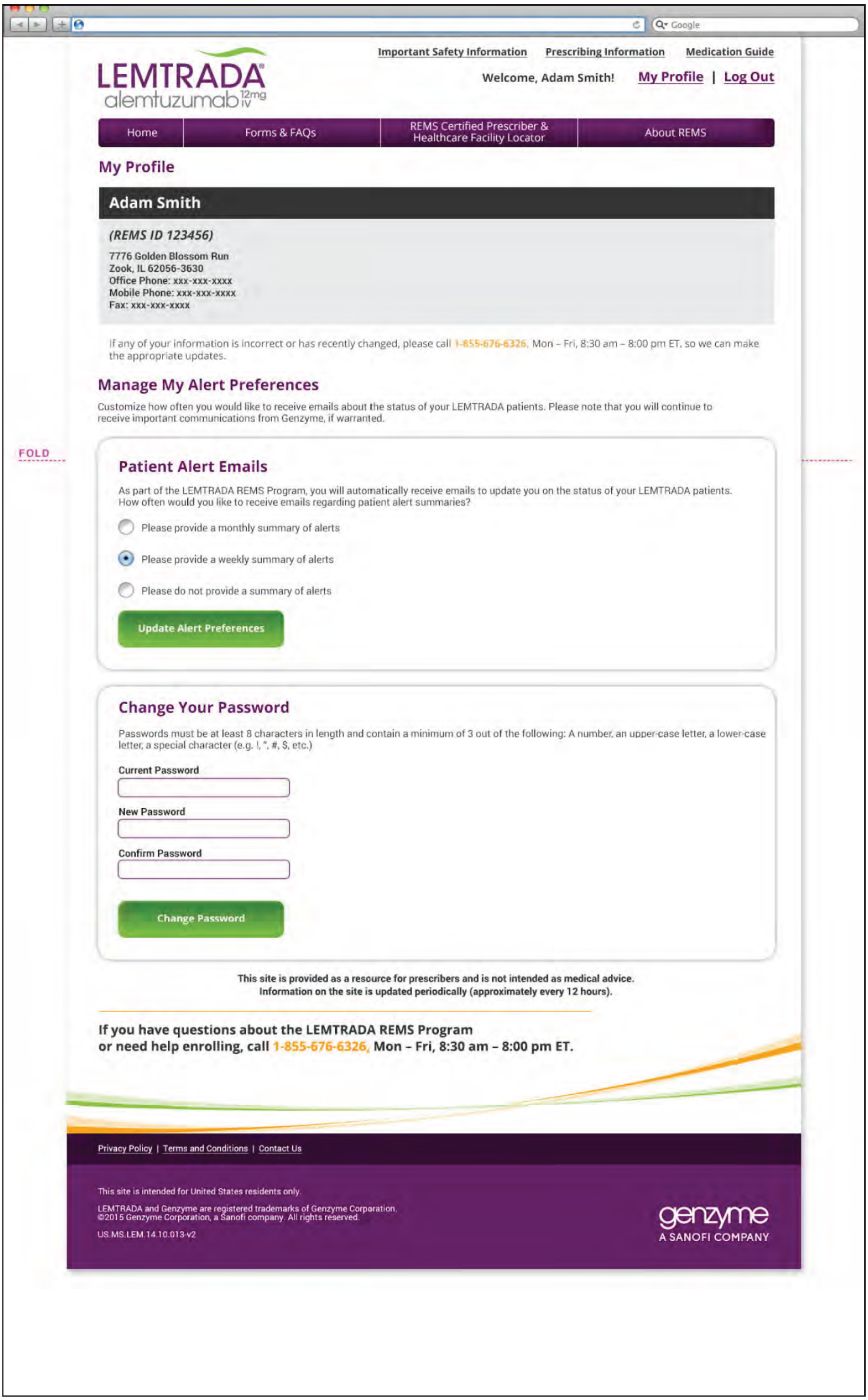
LEMTRADA REMS Desktop - Prescriber Dashboard, View Patient List - External Monitoring Interstitial Page



LEMTRADA REMS Desktop - Prescriber Dashboard, My Profile



LEMTRADA REMS Desktop - Prescriber Dashboard, My Profile, Error

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My Profile

Adam Smith

(REMS ID 123456)

7776 Golden Blossom Run
Zook, IL 62056-3630
Office Phone: xxx-xxx-xxxx
Mobile Phone: xxx-xxx-xxxx
Fax: xxx-xxx-xxxx

If any of your information is incorrect or has recently changed, please call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET, so we can make the appropriate updates.

Manage My Alert Preferences

Customize how often you would like to receive emails about the status of your LEMTRADA patients. Please note that you will continue to receive important communications from Genzyme, if warranted.

FOLD

Patient Alert Emails

As part of the LEMTRADA REMS Program, you will automatically receive emails to update you on the status of your LEMTRADA patients. How often would you like to receive emails regarding patient alert summaries?

- ○ Please provide a monthly summary of alerts
- ◉ Please provide a weekly summary of alerts
- ○ Please do not provide a summary of alerts

Update Alert Preferences

Change Your Password

Passwords must be at least 8 characters in length and contain a minimum of 3 out of the following: A number, an upper-case letter, a lower-case letter, a special character (e.g. !, ", #, $, etc.)

Current Password

Please enter password.

New Password

Please enter a valid password.

Confirm Password

Please confirm new password.

Change Password

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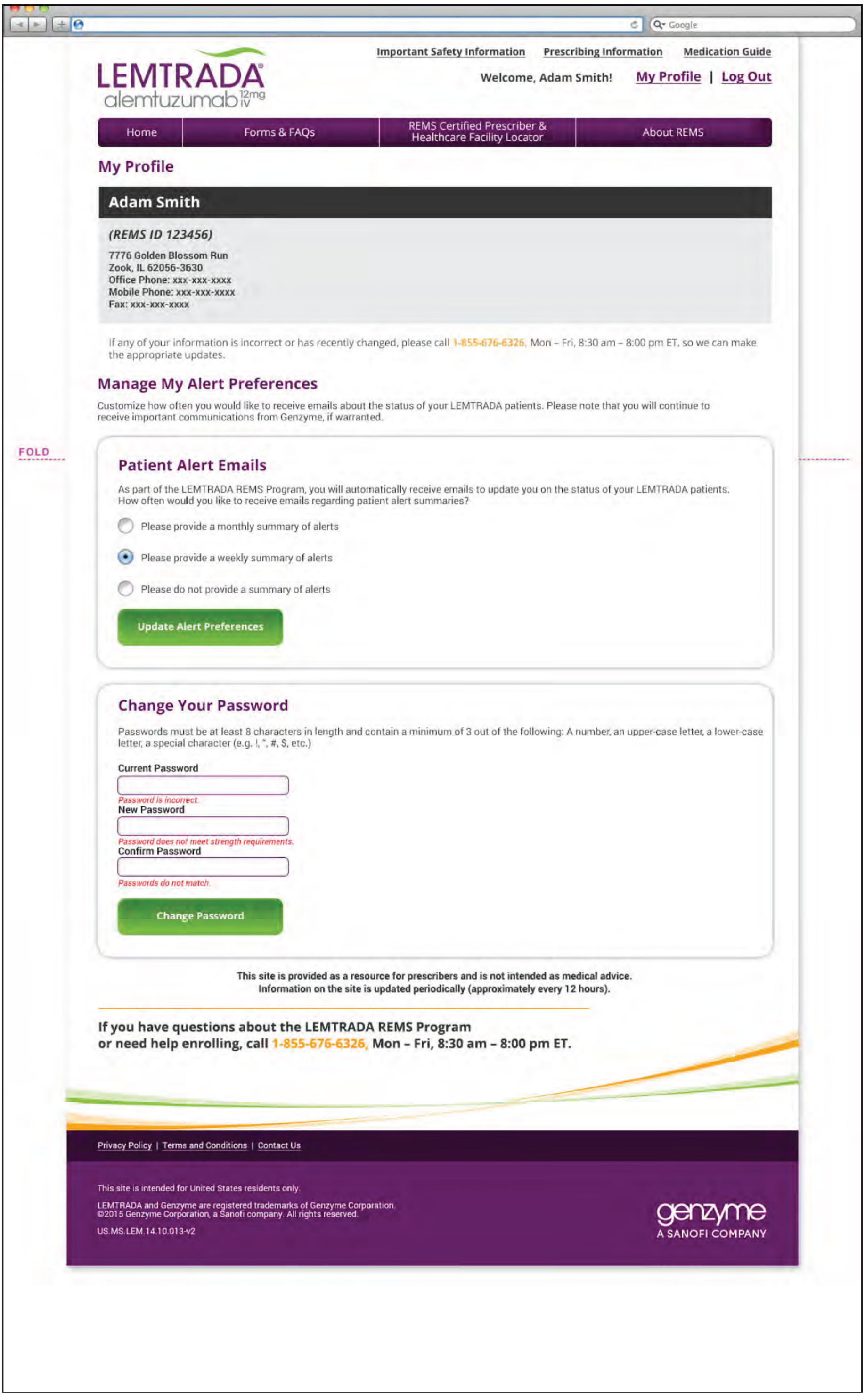
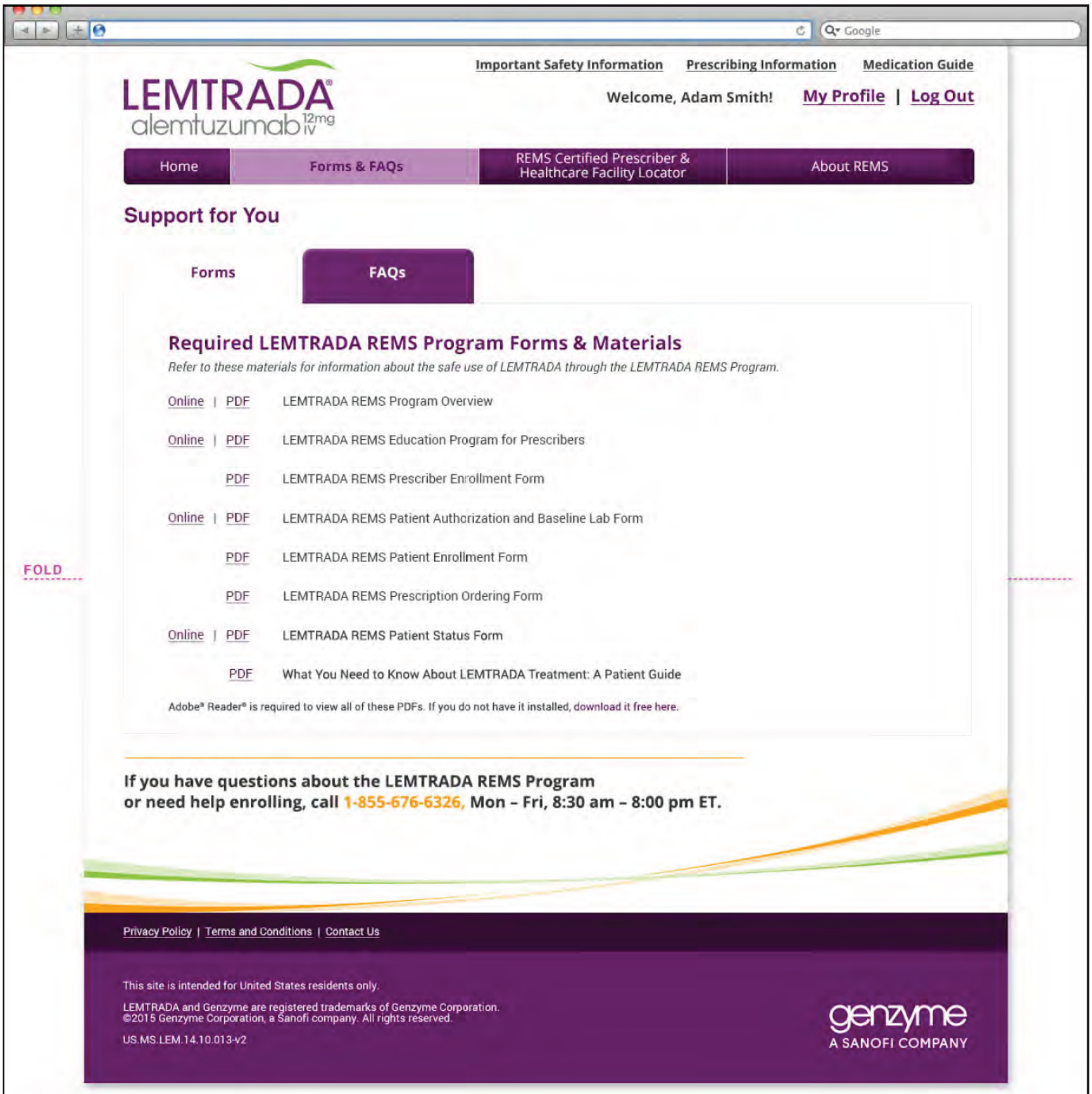


LEMTRADA REMS Desktop - Prescriber Dashboard, Support - Forms



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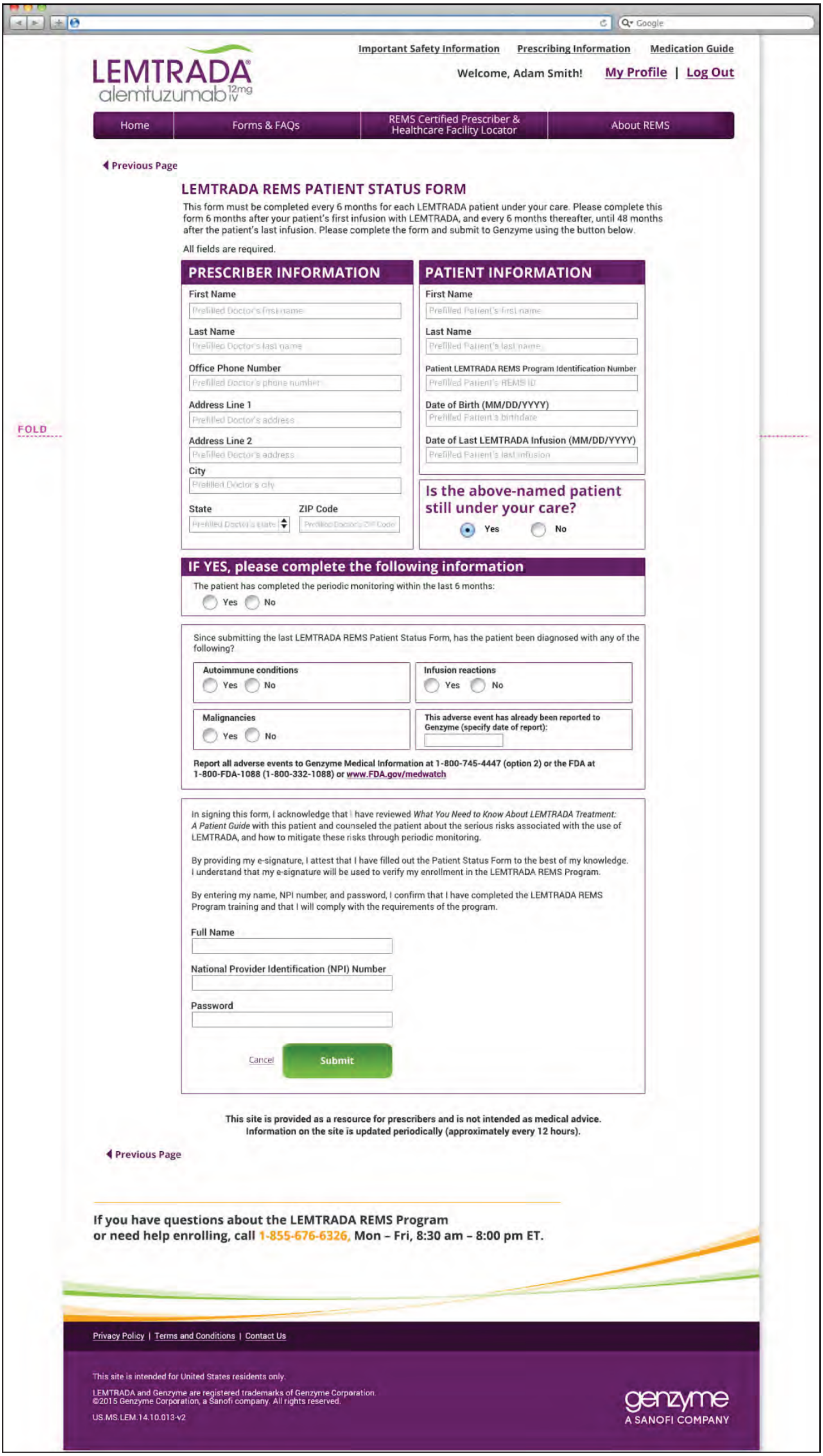
LEMTRADA REMS Desktop - Prescriber Dashboard, Patient Status Form, Yes Selected



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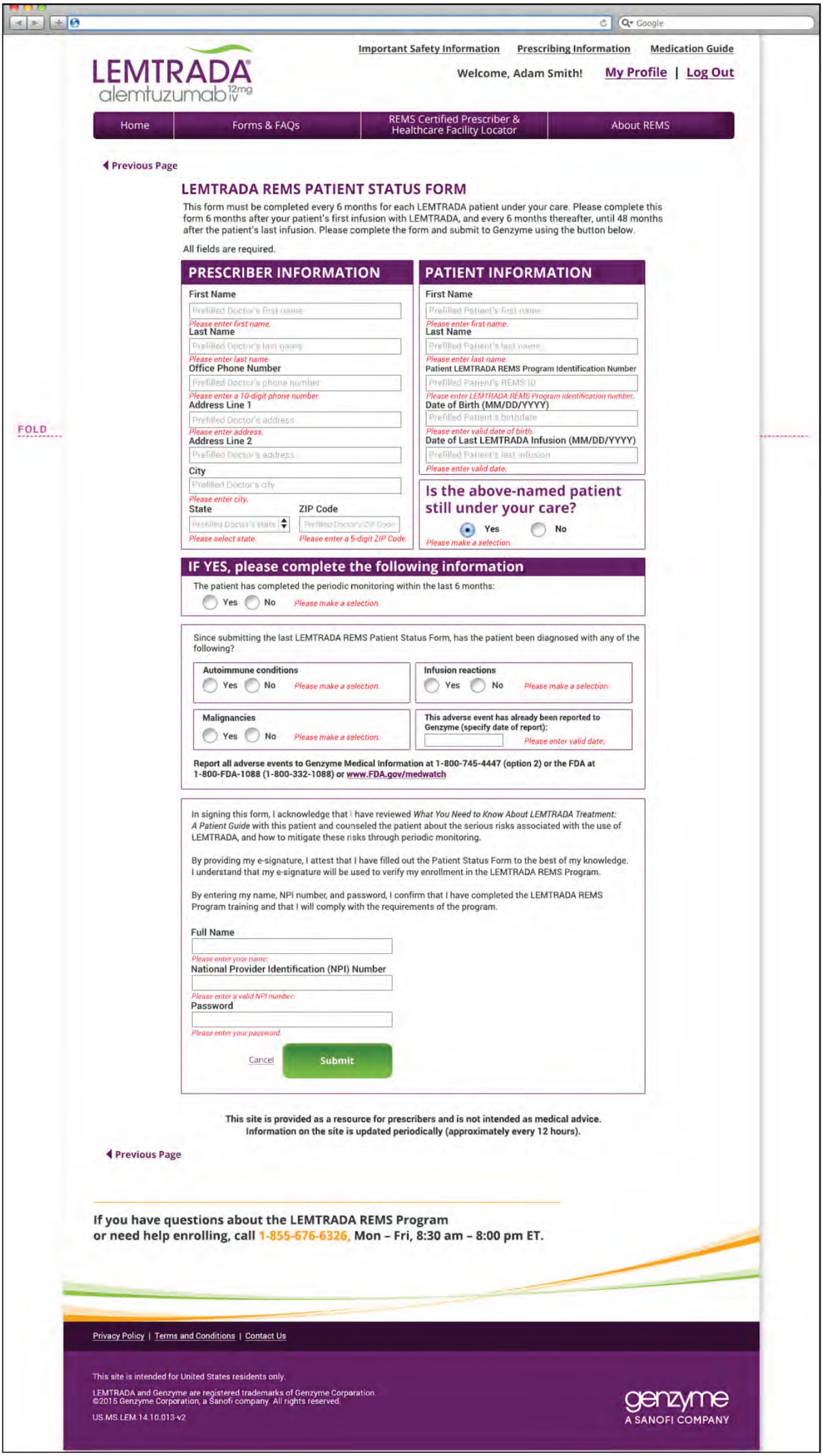
LEMTRADA REMS Desktop - Prescriber Dashboard, Patient Status Form, Yes Selected - Error



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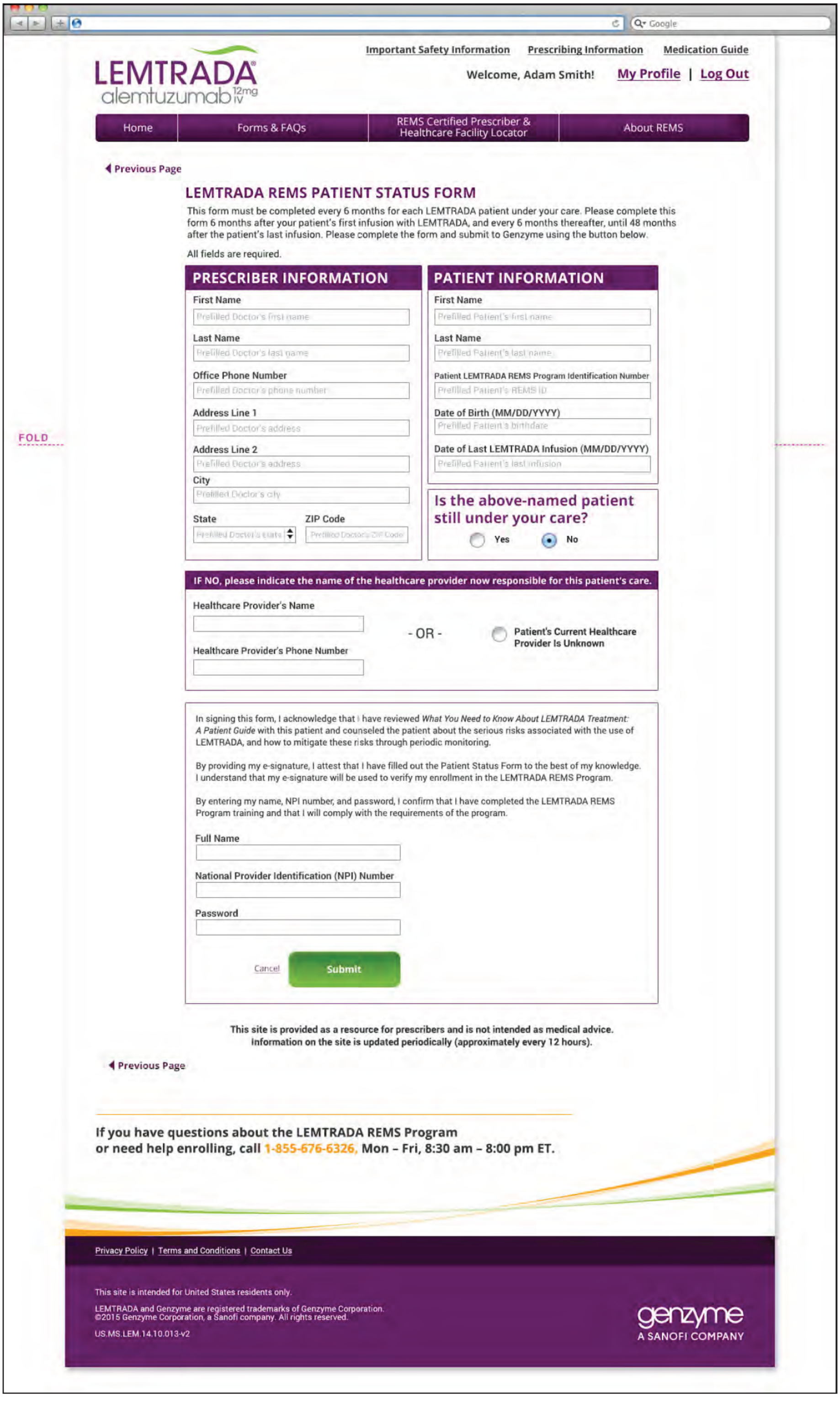

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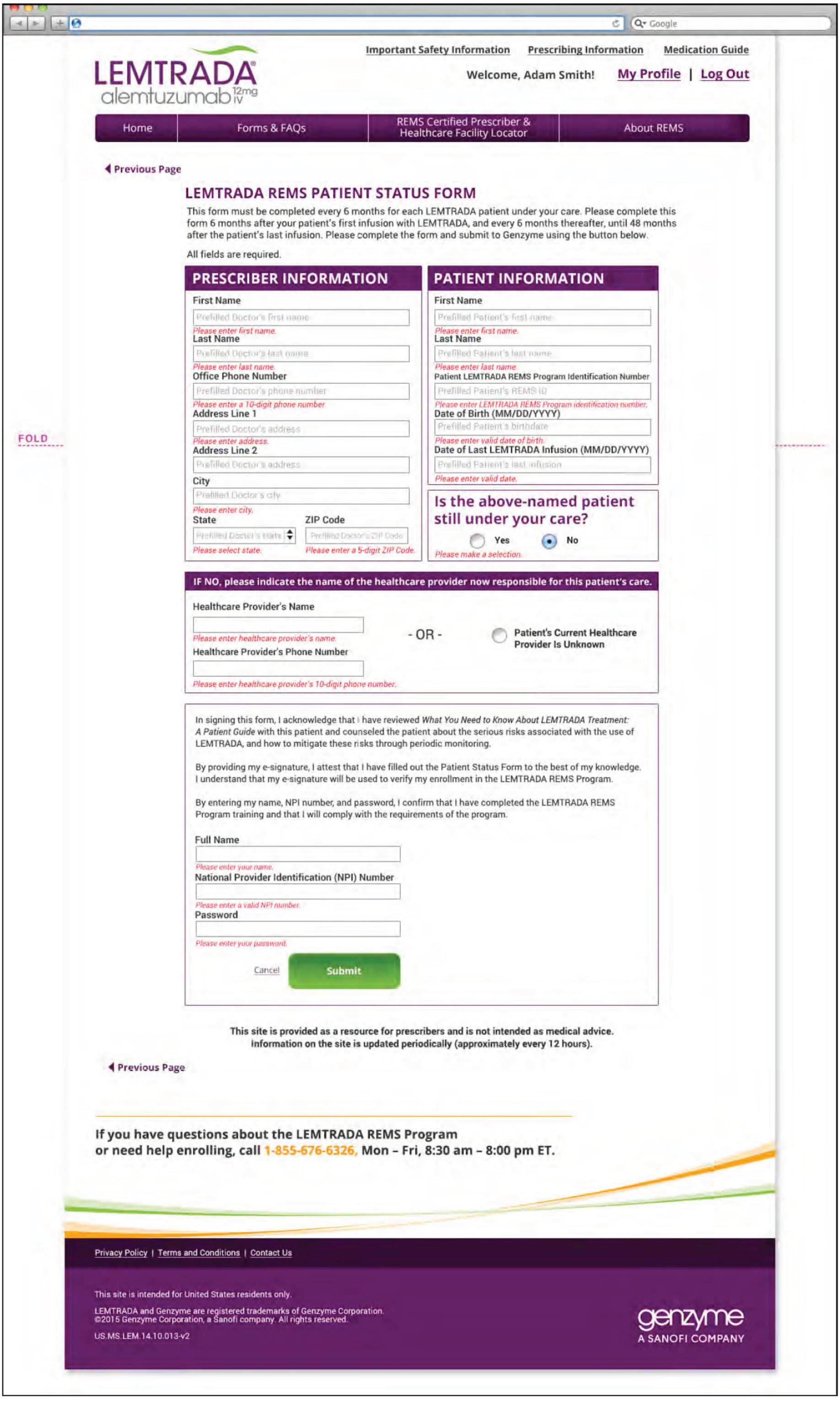

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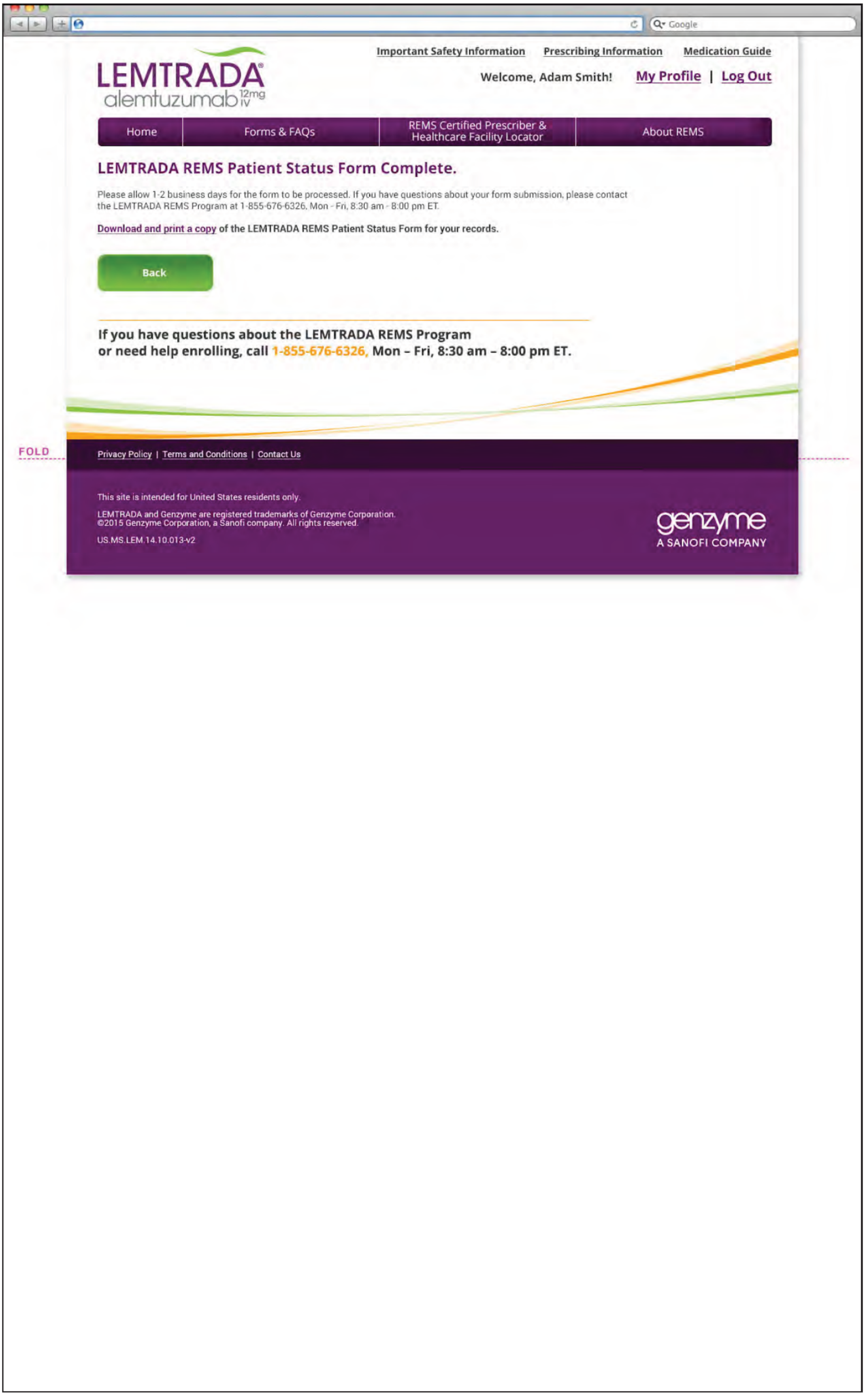
LEMTRADA REMS Desktop - Prescriber Dashboard, Patient Status Form Confirmation



LEMTRADA REMS Desktop - Prescriber Dashboard, Patient Authorization and Baseline Lab Form

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LEMTRADA REMS PATIENT AUTHORIZATION AND BASELINE LAB FORM

This form must be completed within 30 days prior to the first infusion date of each LEMTRADA patient's treatment course. Please complete the form and submit to Genzyme using the button below.

All fields are required.

PRESCRIBER INFORMATION

First Name
Prefilled Doctor's first name

Last Name
Prefilled Doctor's last name

Office Phone Number
Prefilled Doctor's phone number

Address Line 1
Prefilled Doctor's address

Address Line 2
Prefilled Doctor's address

City
Prefilled Doctor's city

State
Prefilled Doctor's state

ZIP Code
Prefilled Doctor's ZIP Code

Prescriber LEMTRADA REMS Identification Number
Prefilled Doctor's REMS ID

PATIENT INFORMATION

First Name

Last Name

Patient LEMTRADA REMS Program Identification Number

Date of Birth (MM/DD/YYYY)

FOLD

PRESCRIPTION INFORMATION

Select one

- Initial course (1 vial [12 mg/day]) X 5 consecutive days
  Total number of vials ordered
- Subsequent course (1 vial [12 mg/day]) X 3 consecutive days
  Total number of vials ordered

AUTHORIZATION AND BASELINE LABS

Do you authorize LEMTRADA treatment for the above-referenced patient?

Yes No

Do you attest that required baseline laboratory testing has been completed prior to LEMTRADA treatment and within 30 days of the patient's first infusion?

Yes No

By providing my e-signature, I attest that I have filled out the Patient Authorization and Baseline Lab Form to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name

National Provider Identification (NPI) Number

Password

Cancel Submit

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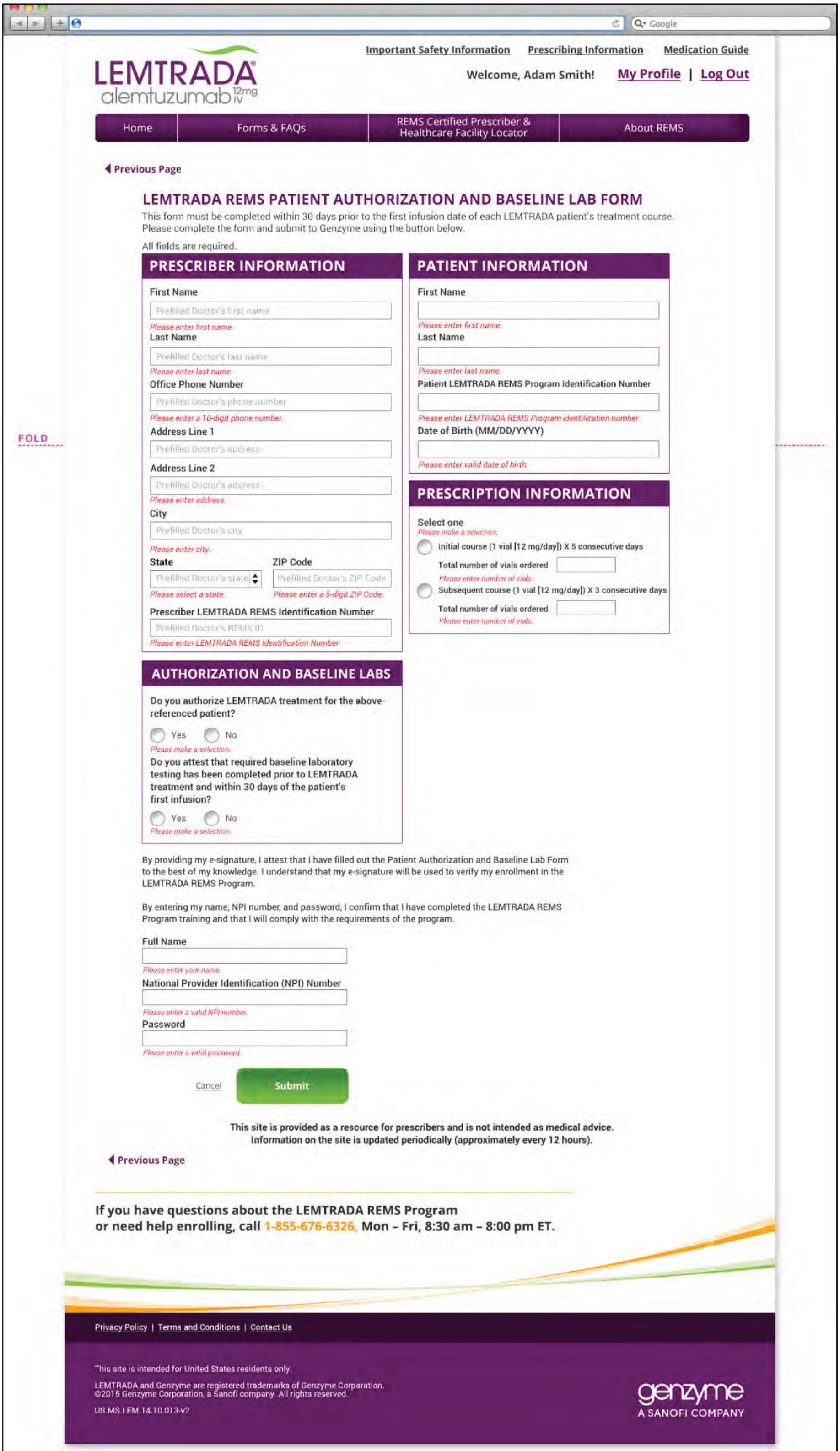

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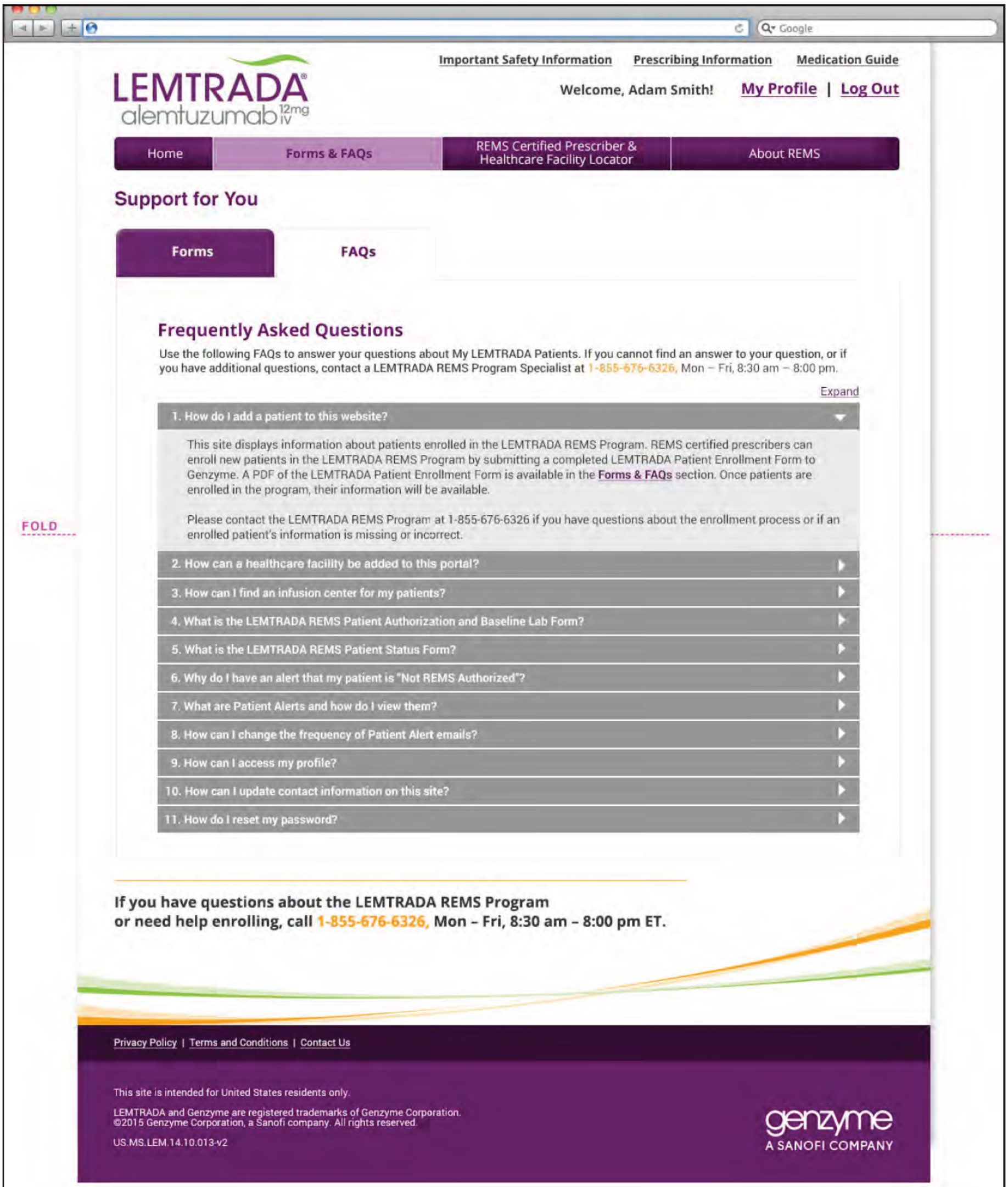
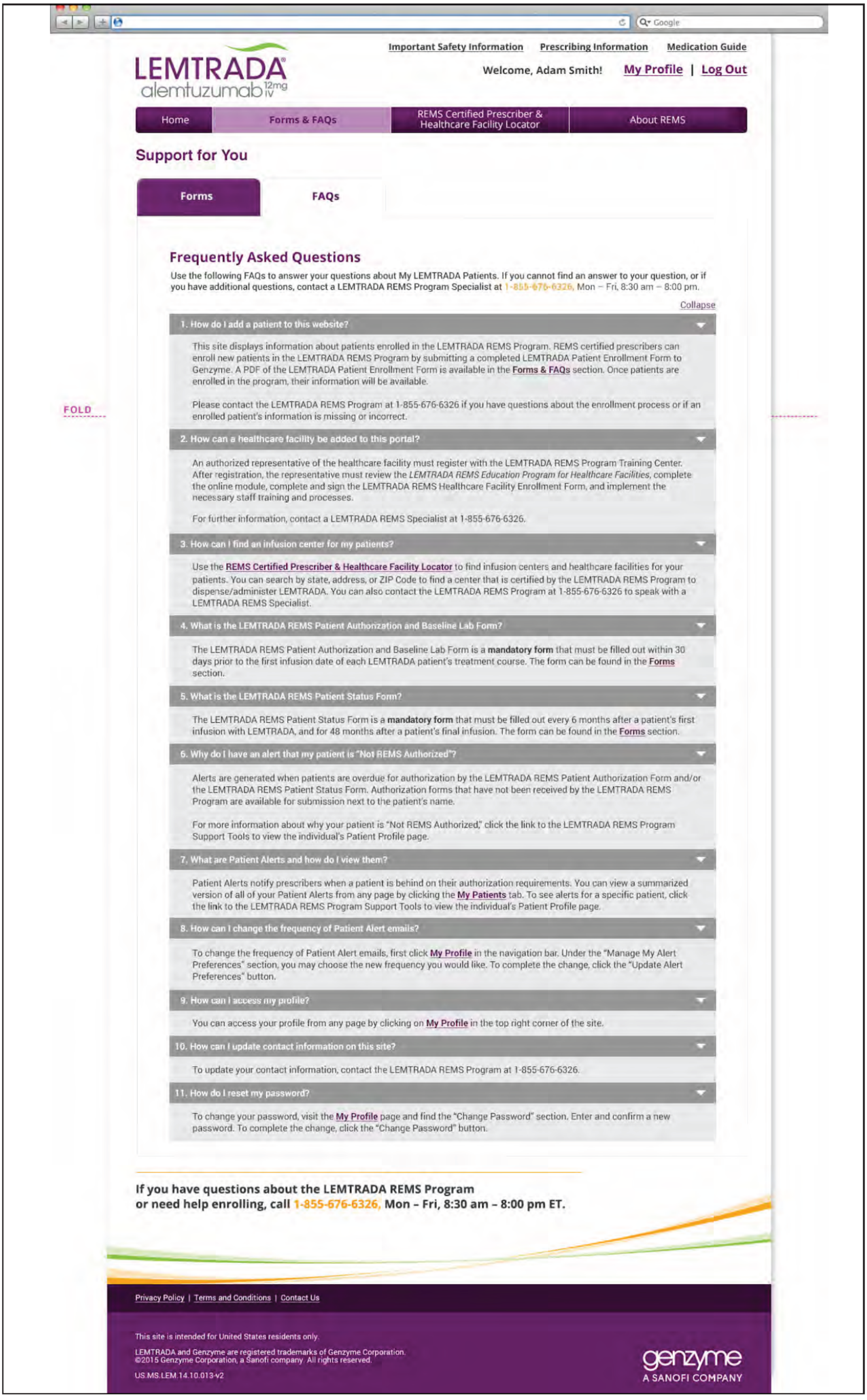
LEMTRADA REMS Desktop - Prescriber Dashboard, Patient Authorization and Baseline Lab Form Conf.



LEMTRADA REMS Desktop - Prescriber Dashboard, Support - FAQs



LEMTRADA REMS Desktop - Prescriber Dashboard, Support - FAQs Expanded



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REMS Certified Prescriber & Healthcare Facility Locator

Search for prescribers or healthcare facilities that are enrolled and certified in the LEMTRADA REMS Program and able to prescribe or dispense/administer LEMTRADA.

Please enter street address, city, state, or ZIP Code you would like to search for.

New Search: Street address, city, state, or ZIP Code

REMS Certified Prescribers | REMS Certified Healthcare Facilities

Certified Prescriber Name
Address
Address
P. (888) - 888 - 8888

Certified Prescriber Name
Address
Address
P. (888) - 888 - 8888

Certified Prescriber Name
Address
Address
P. (888) - 888 - 8888

Certified Prescriber Name
Address
Address
P. (888) - 888 - 8888

Certified Prescriber Name
Address
Address
P. (888) - 888 - 8888



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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Desktop - Prescriber Dashboard, REMS Certified Prescriber and Healthcare Facility Locator

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LEMTRADA® alemtuzumab 12mg IV

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REMS Certified Prescriber & Healthcare Facility Locator

Search for prescribers or healthcare facilities that are enrolled and certified in the LEMTRADA REMS Program and able to prescribe or dispense/administer LEMTRADA.

Please enter street address, city, state, or ZIP Code you would like to search for.

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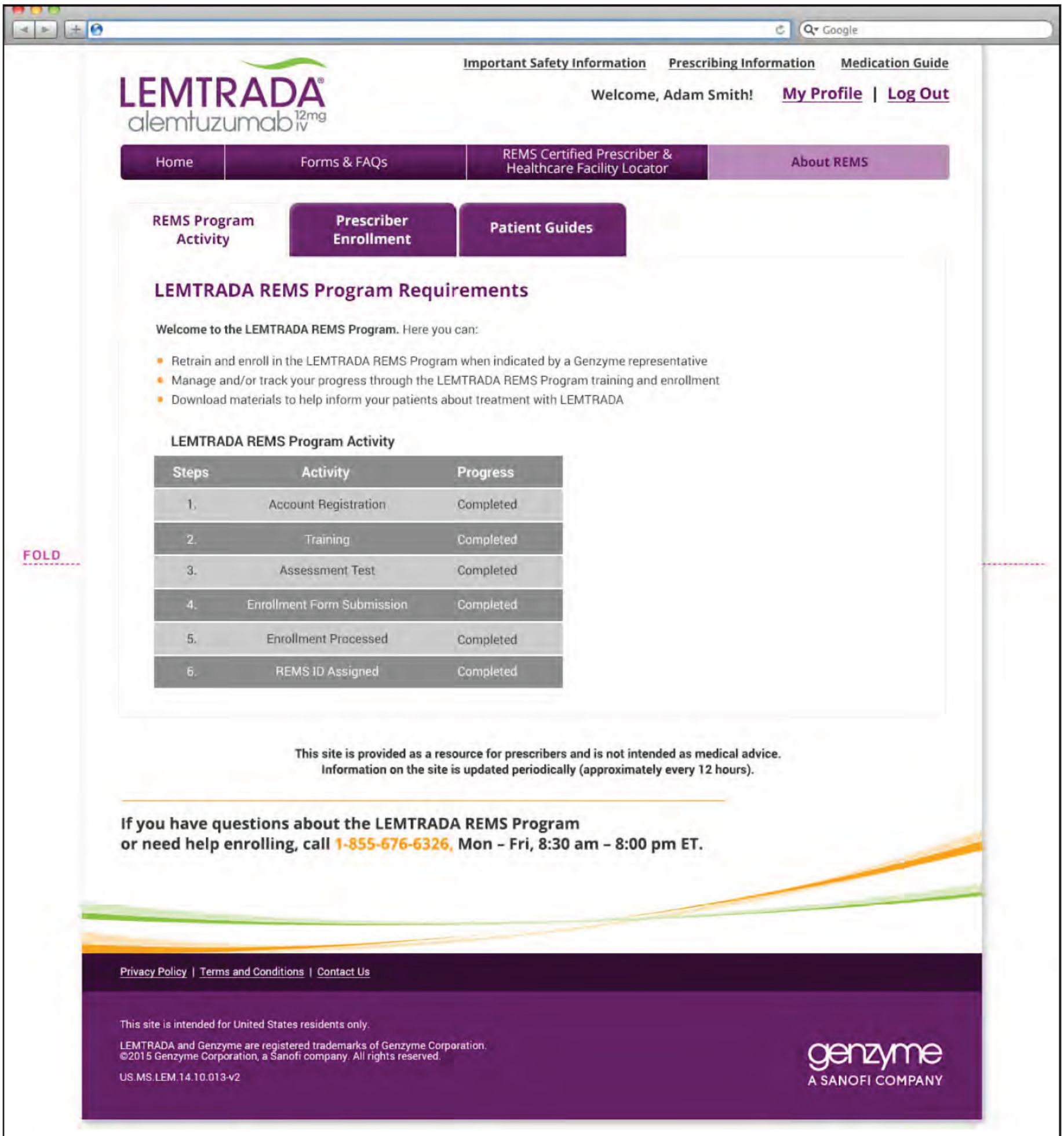
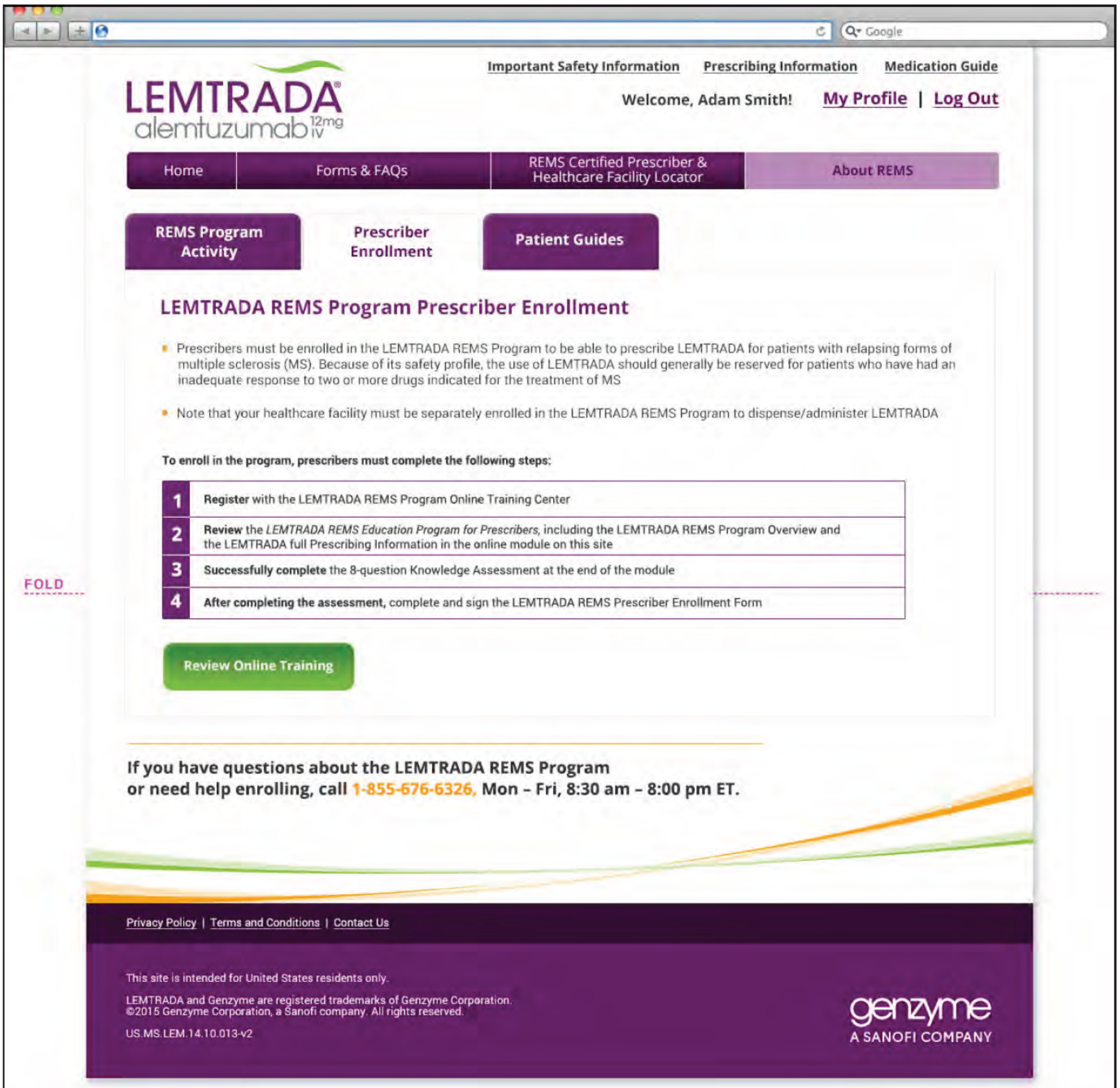
LEMTRADA REMS Desktop - Prescriber Dashboard, REMS Program Activity



LEMTRADA REMS Desktop - Prescriber Dashboard, About REMS - Prescriber Enrollment



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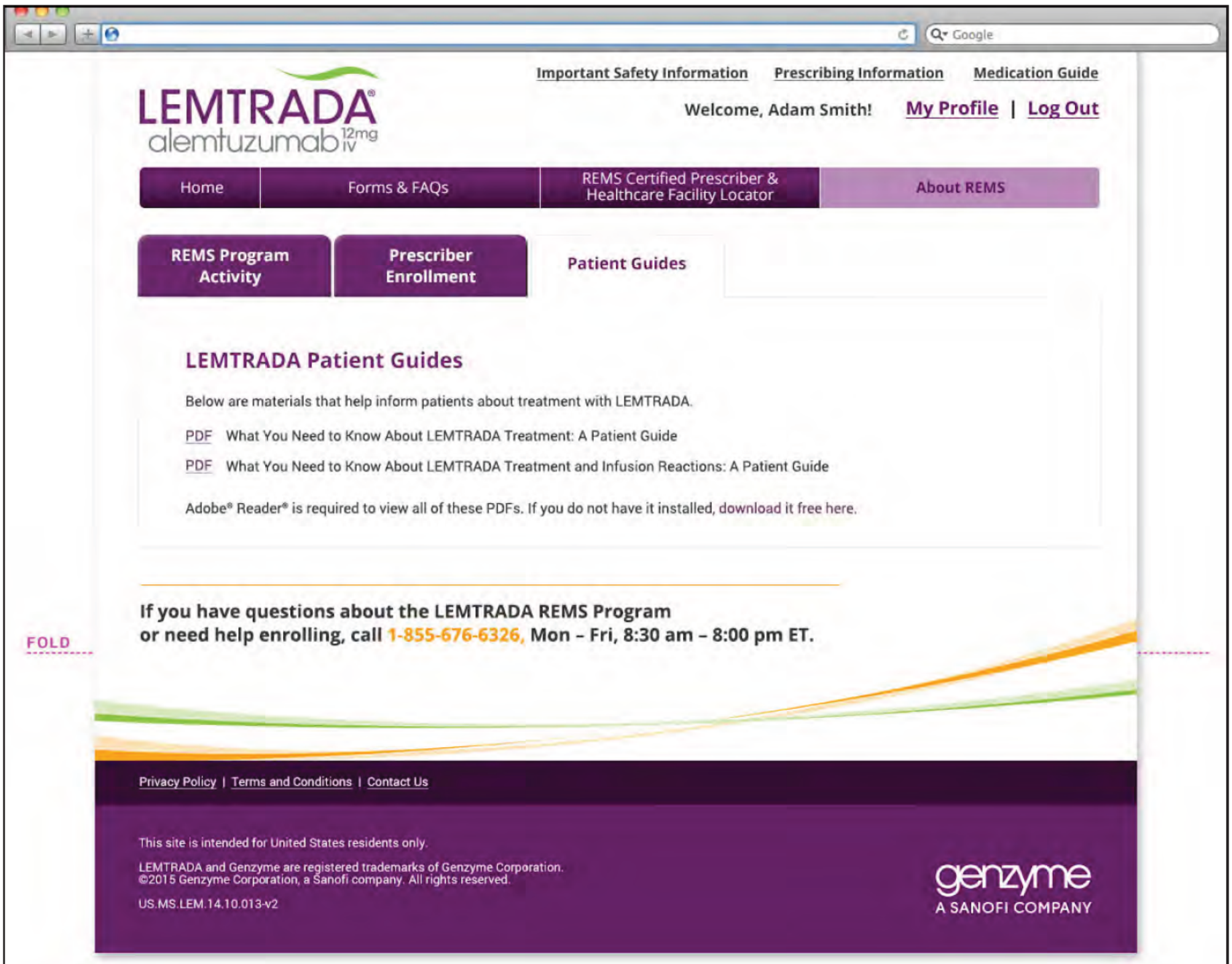
LEMTRADA REMS Desktop - Prescriber Dashboard, About REMS - Patient Guides

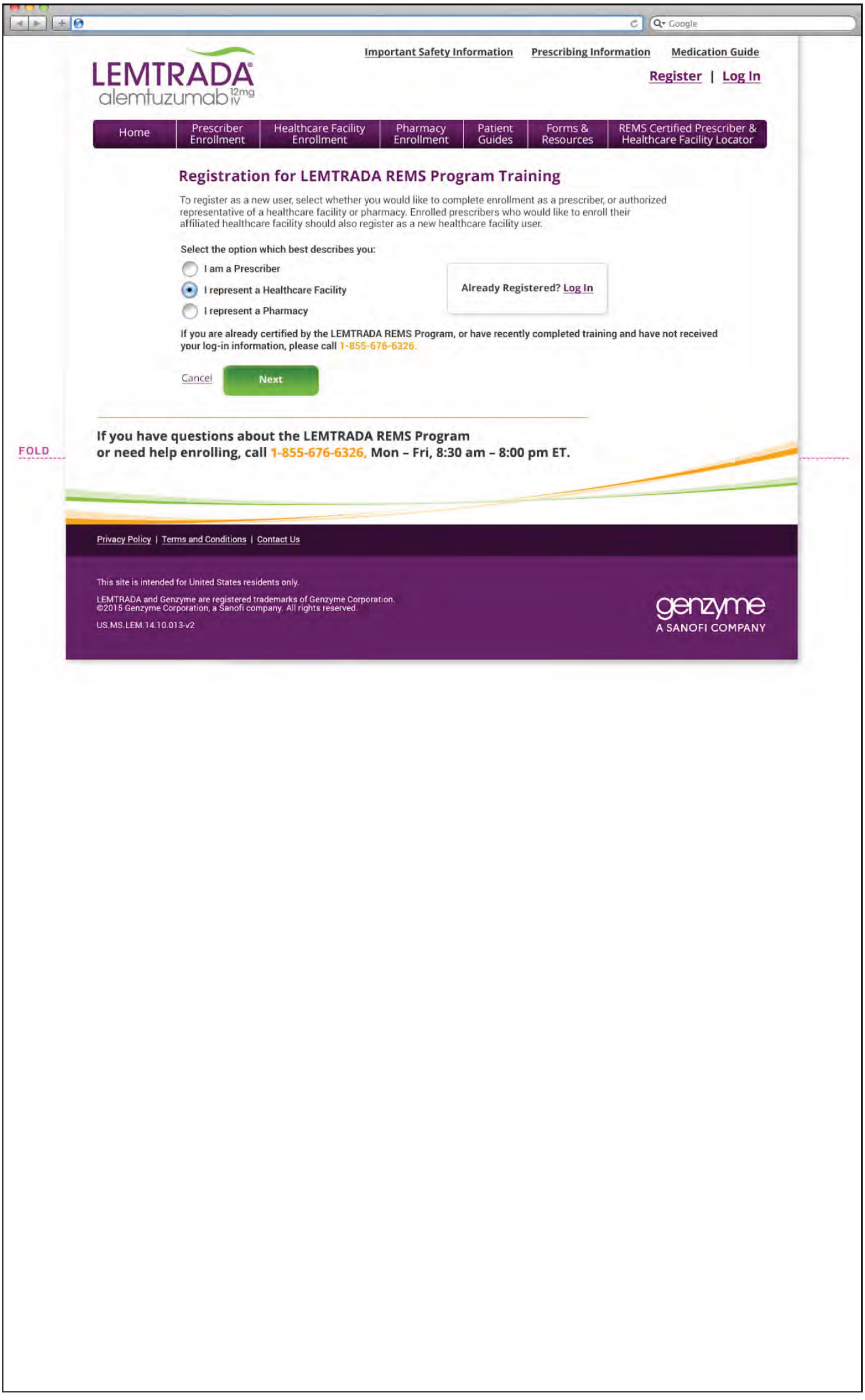


LEMTRADA REMS DESKTOP

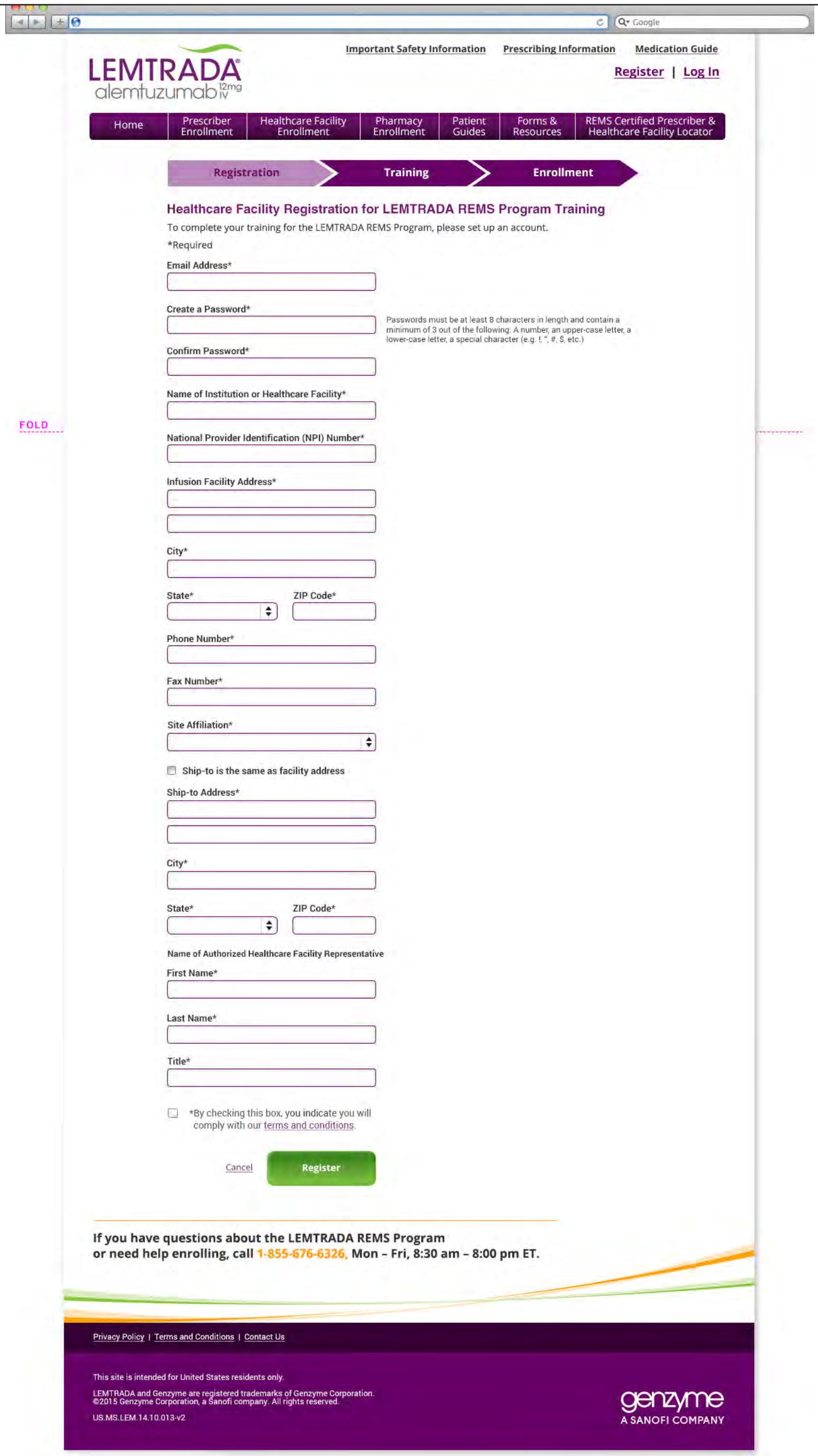
REMS Certified Healthcare Facility Pages Only

HEALTHCARE FACILITY TRAINING PAGES

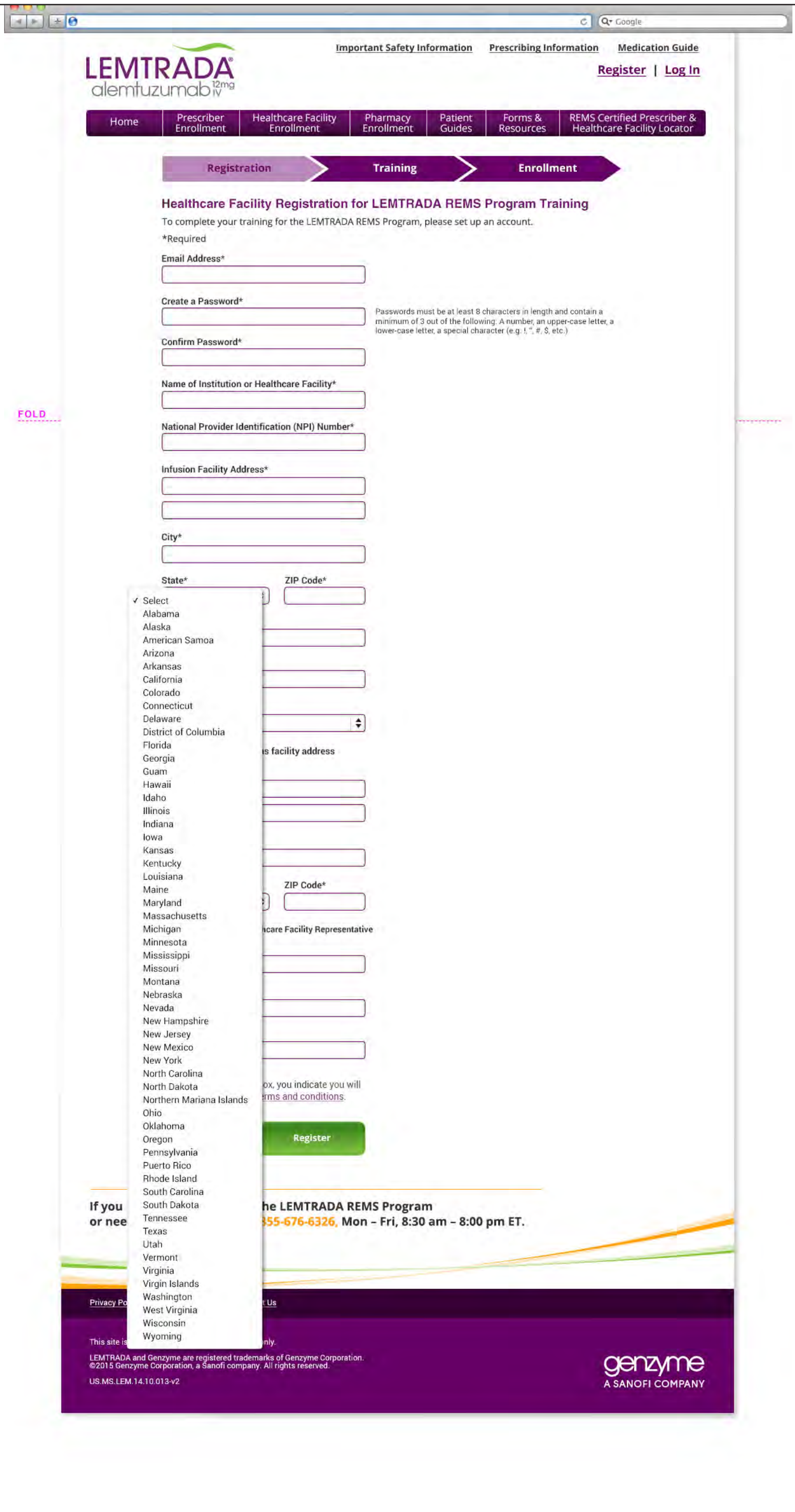
LEMTRADA REMS Desktop - HCF Training - Registration Home Selection



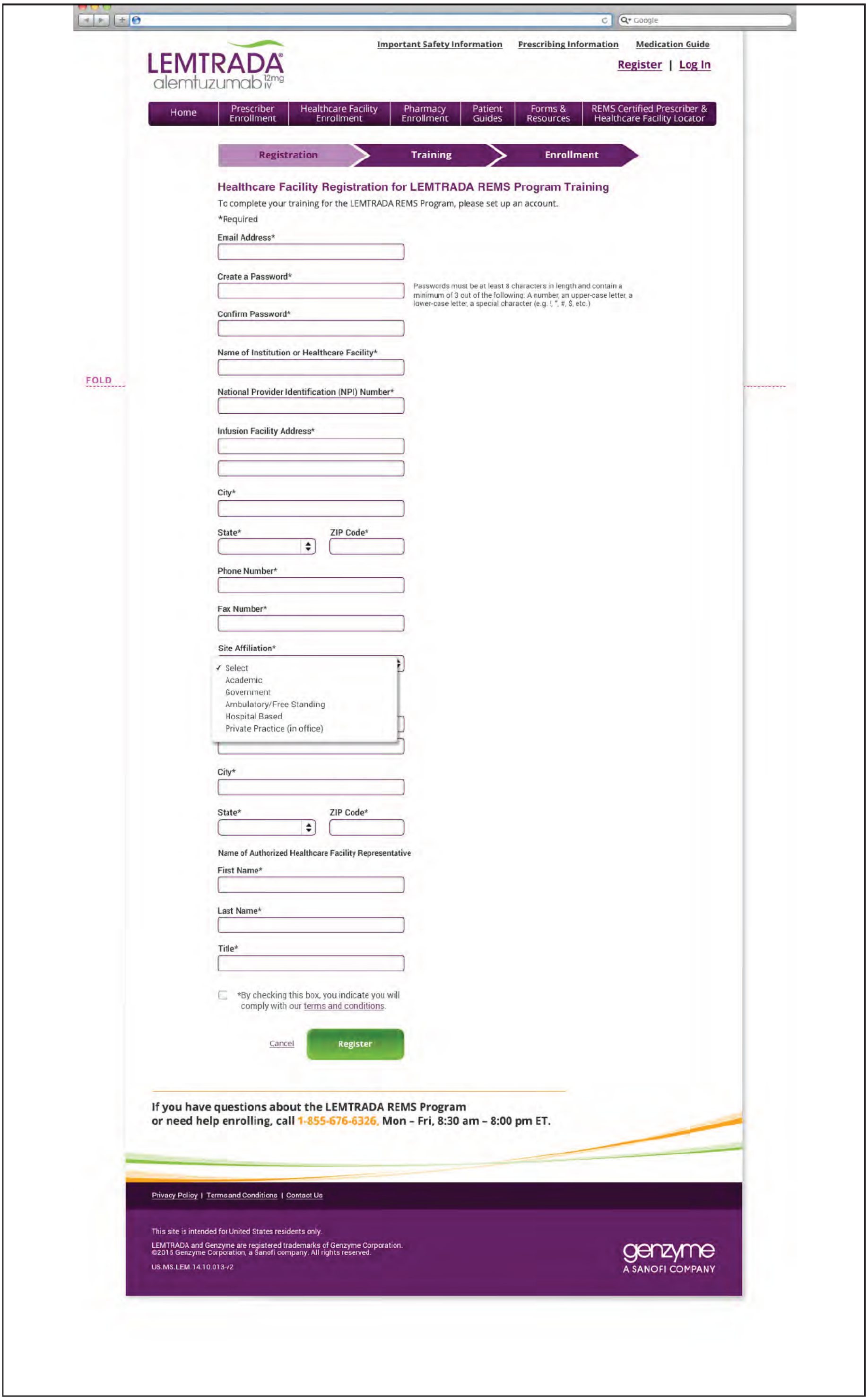
LEMTRADA REMS Desktop - HCF Training - Facility Registration



LEMTRADA REMS Desktop - HCF Training - Facility Registration, State Dropdown 1



LEMTRADA REMS Desktop - HCF Training - Facility Registration, Site Affiliation Dropdown



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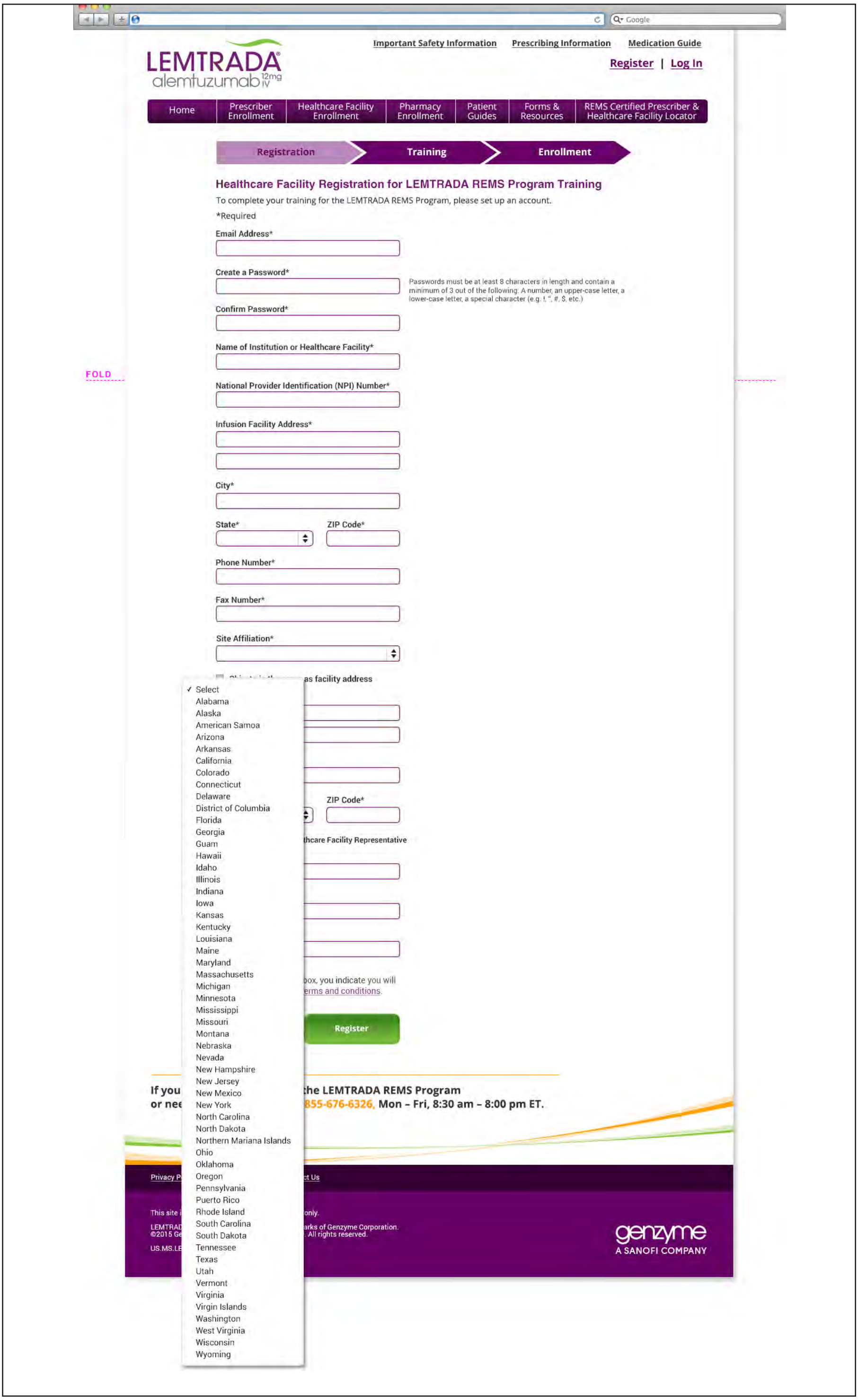
LEMTRADA REMS Desktop - HCF Training - Facility Registration, State Dropdown 2



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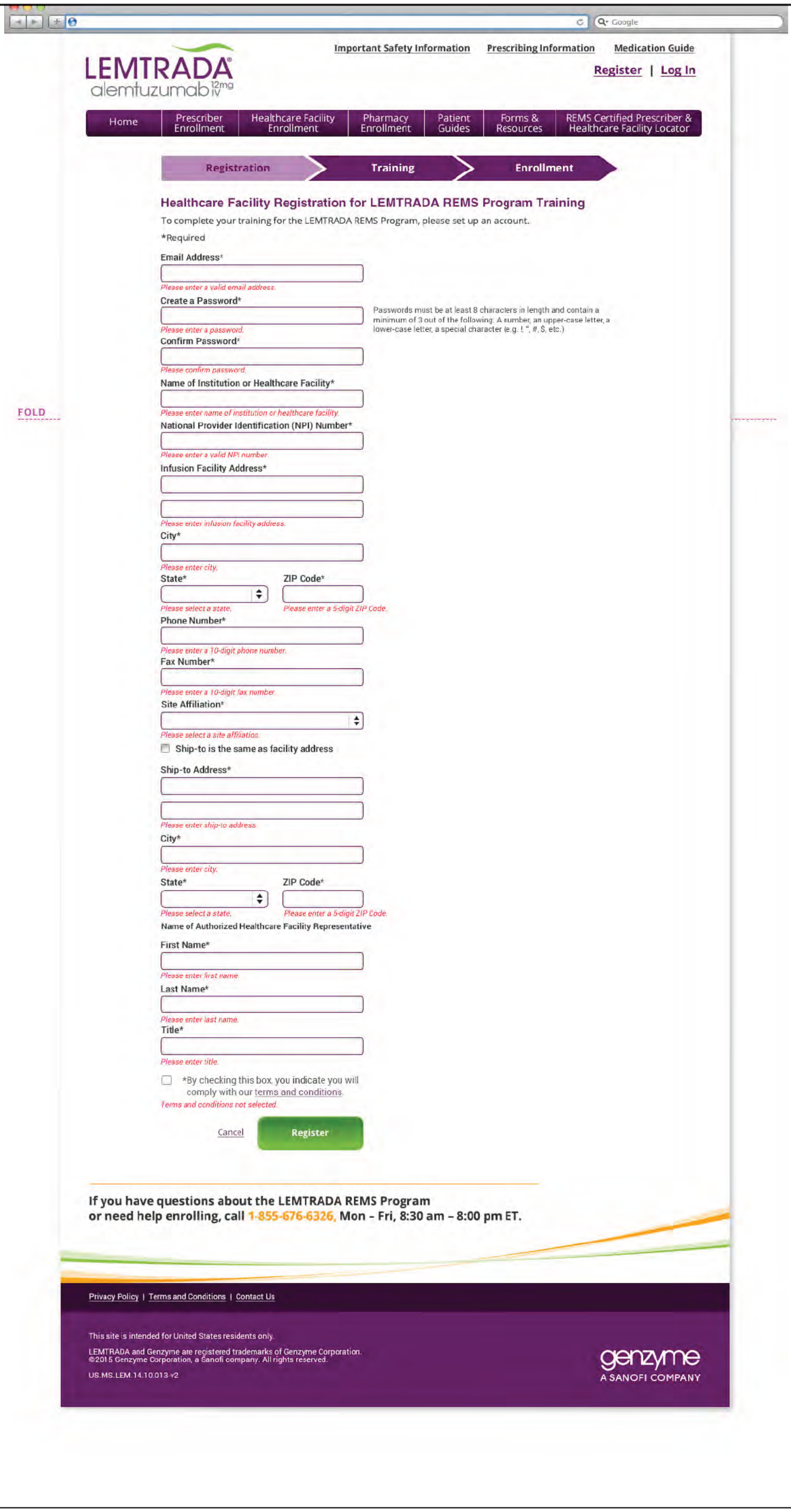
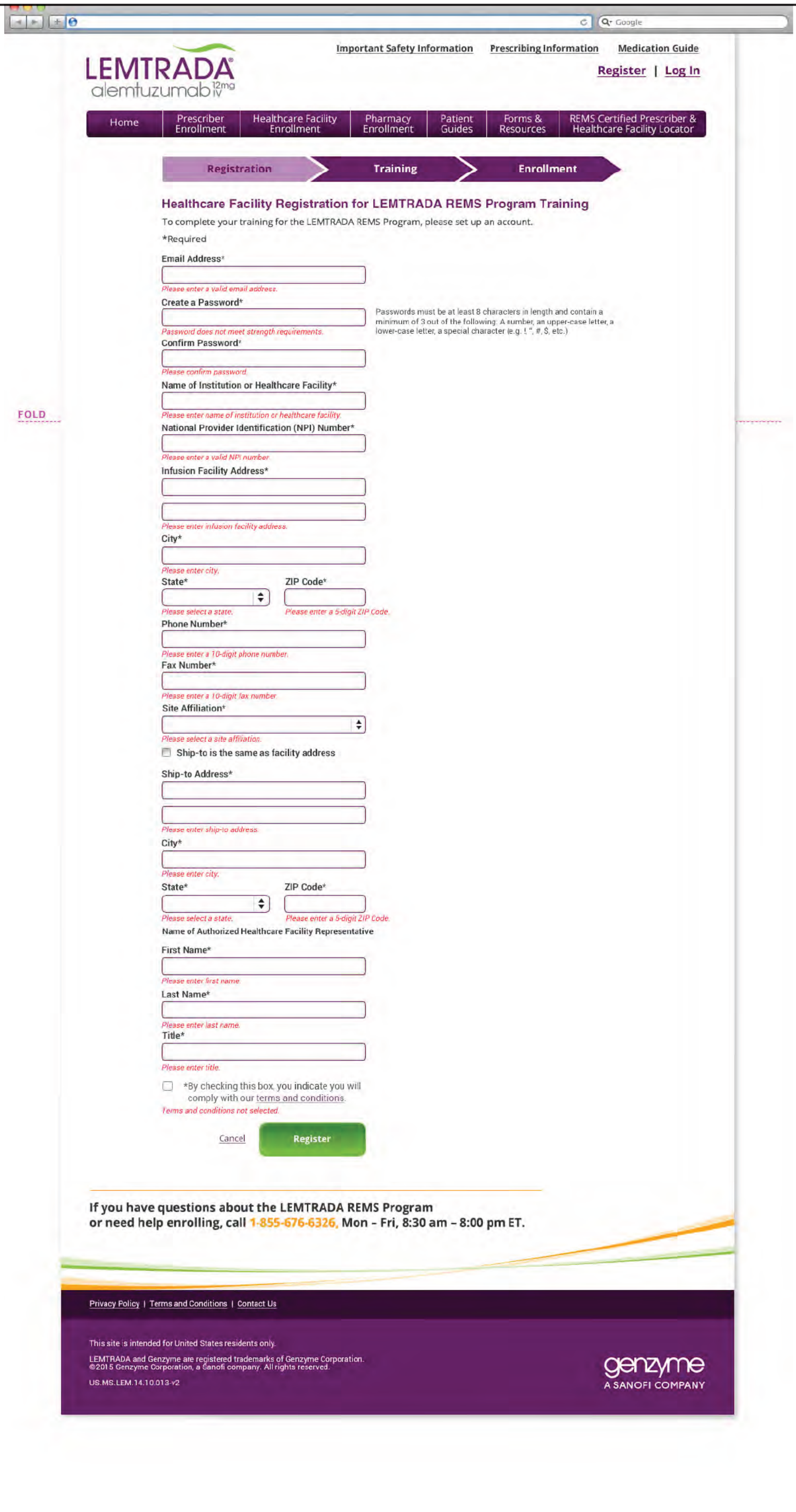
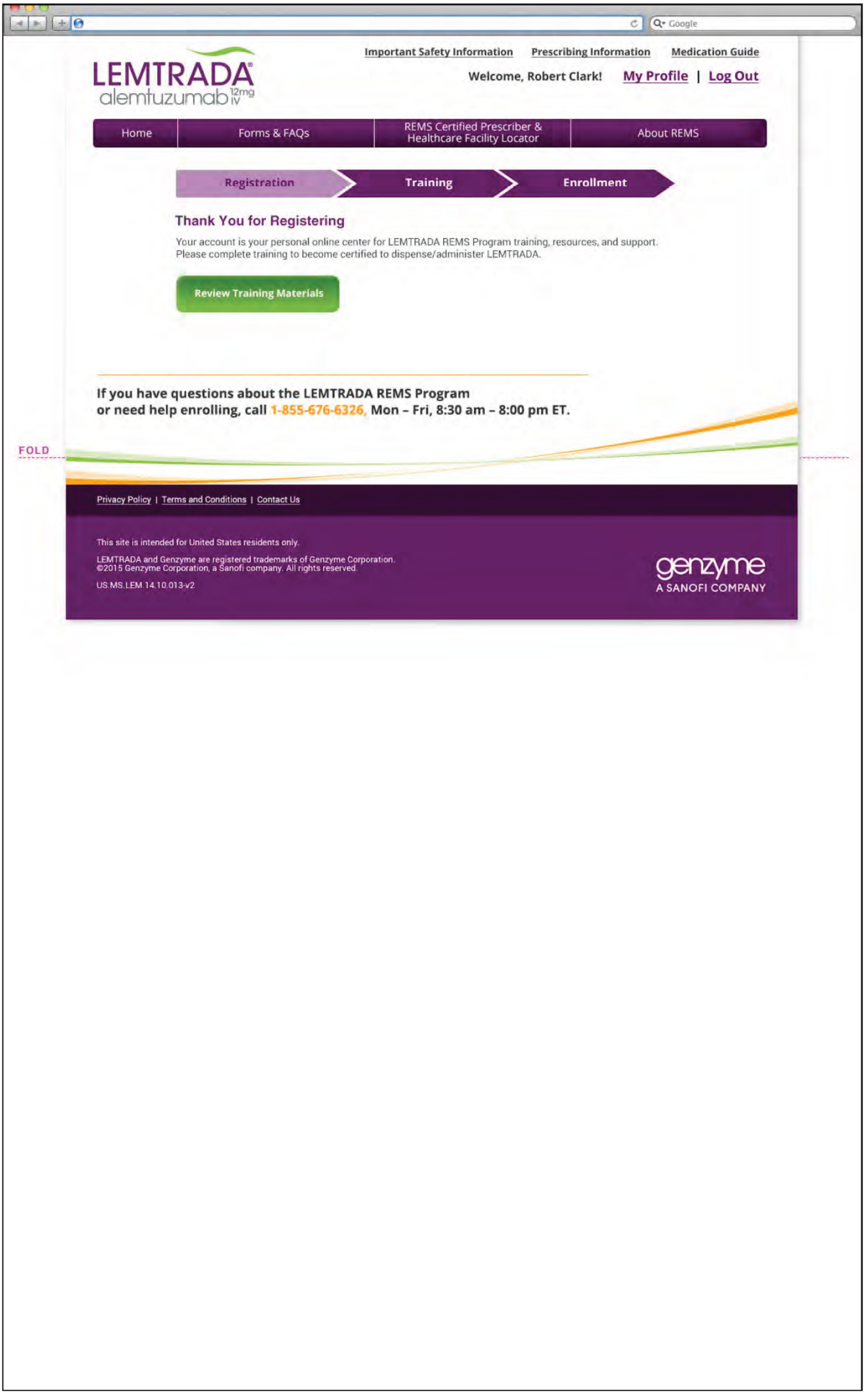
LEMTRADA REMS Desktop - HCF Training - Facility Registration, Error



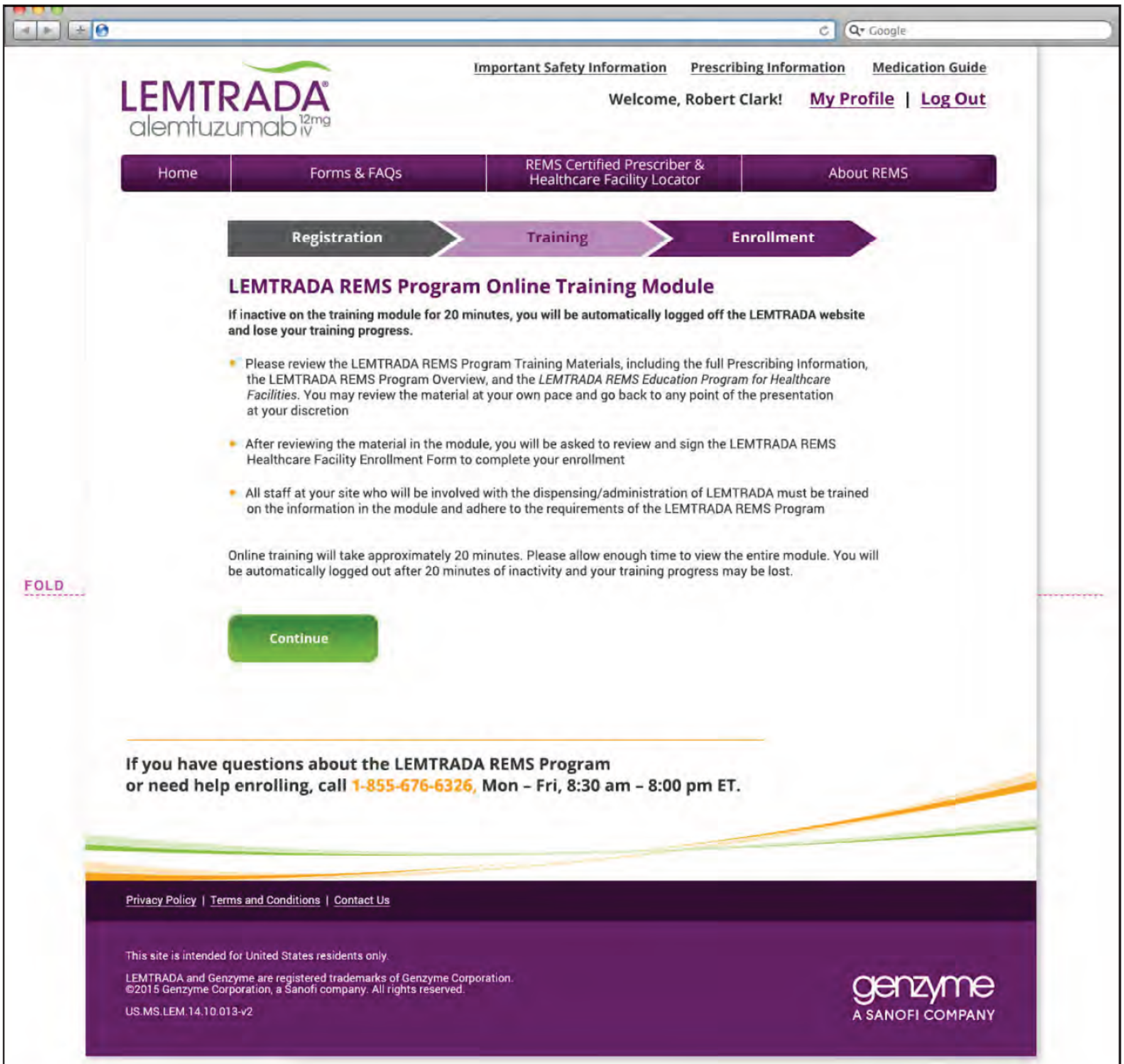
LEMTRADA REMS Desktop - HCF Training - Facility Registration, Password Strength Error



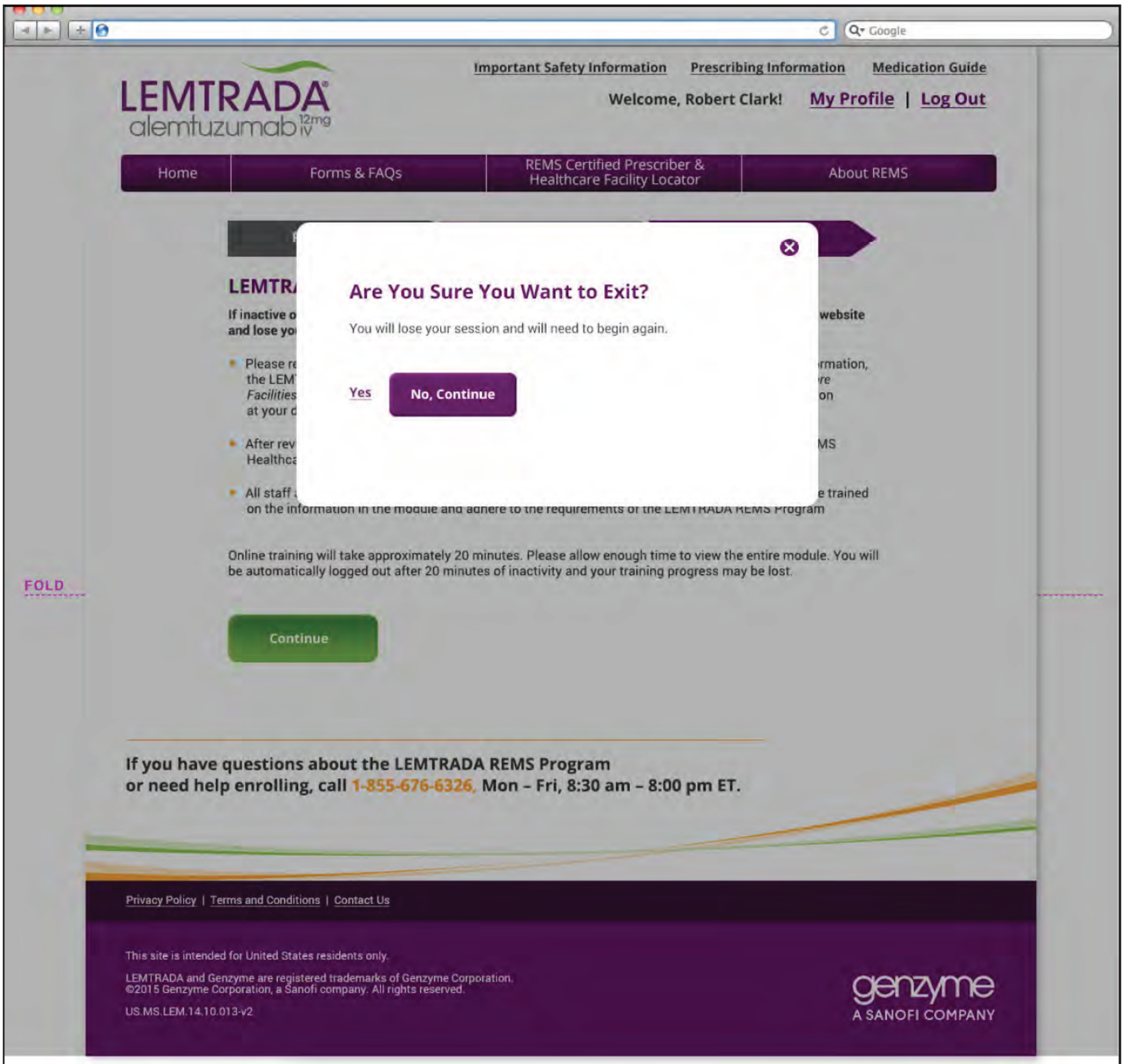
LEMTRADA REMS Desktop - HCF Training - Registration Confirmation



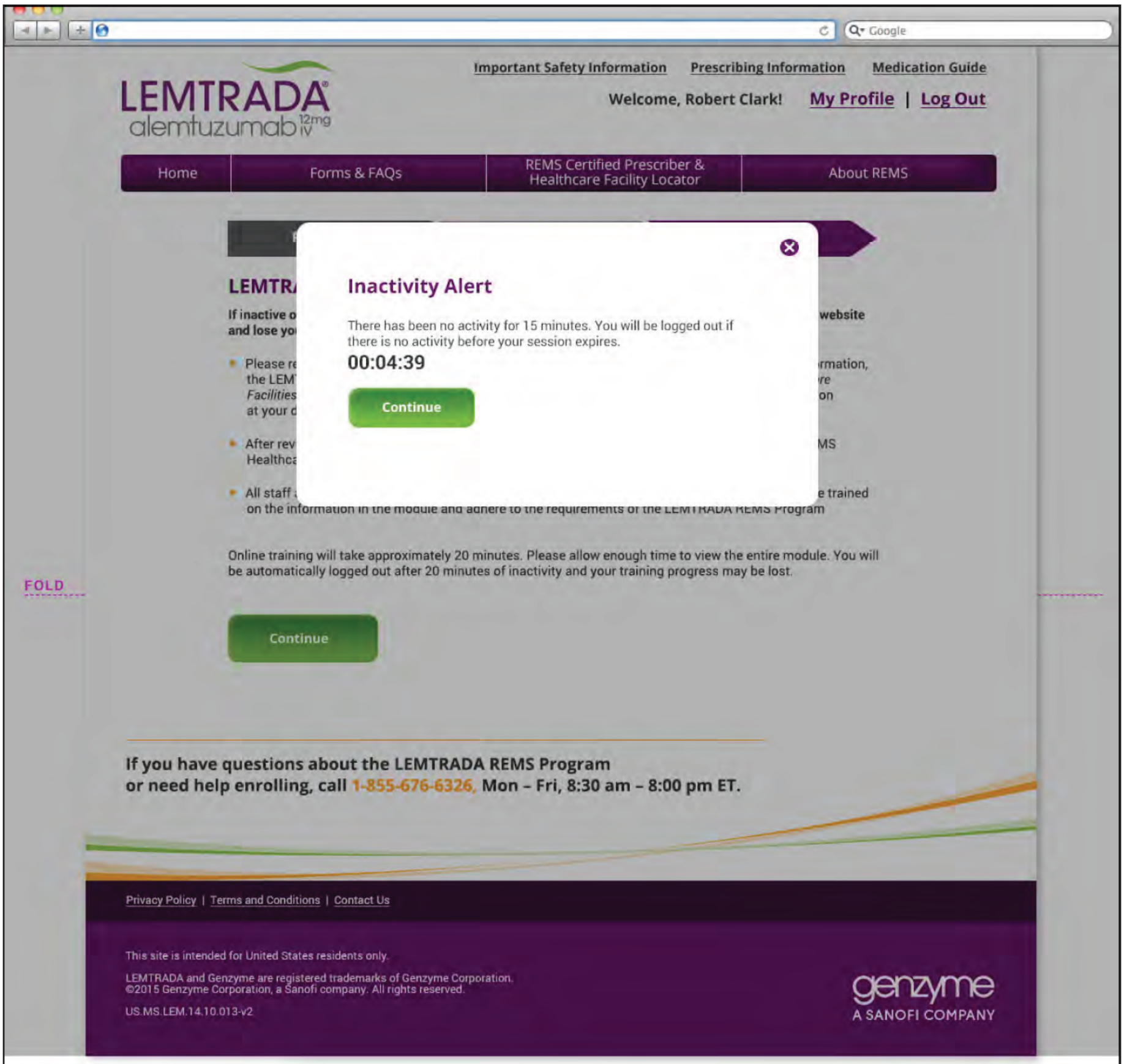
LEMTRADA REMS Desktop - HCF Training - Training Module



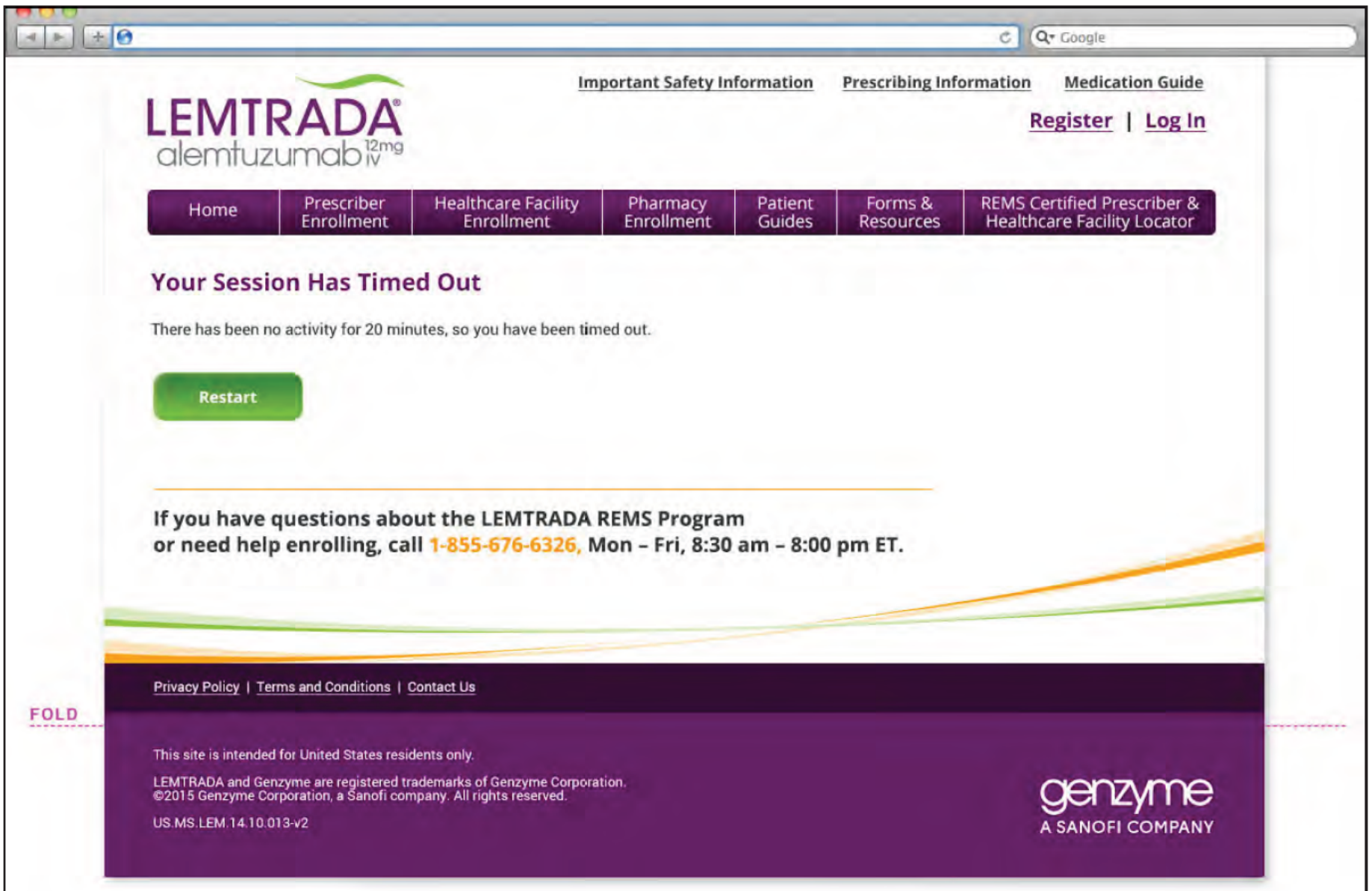
LEMTRADA REMS Desktop - HCF Training - Training Module, Exit



LEMTRADA REMS Desktop - HCF Training - Training Module, Timer



LEMTRADA REMS Desktop - HCF Training - Training Module, Timed Out



LEMTRADA REMS Program Training

Full Prescribing Information (1 of 8)

Total Training Screens: 1 of 18

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- LEMTRADA is available only through a restricted distribution program. (5.4)

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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2.3 Recommended Premedication and Concomitant Medication
2.4 Preparation Instructions
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LEMTRADA® alemtuzumab 12mg IV

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LEMTRADA REMS Program Training

Full Prescribing Information (2 of 8)

Total Training Screens: 2 of 18

FULL PRESCRIBING INFORMATION

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA *[see Warnings and Precautions (5.1)]*.
- LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period *[see Warnings and Precautions (5.2)]*.
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams *[see Warnings and Precautions (5.3)]*.
- Because of the risk of autoimmunity, infusion reactions, and malignancies, LEMTRADA is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS program *[see Warnings and Precautions (5.4)]*.

1 INDICATIONS AND USAGE

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Information

The recommended dosage of LEMTRADA is 12 mg/day administered by intravenous infusion for 2 treatment courses:

- First Treatment Course: 12 mg/day on 5 consecutive days (60 mg total dose)
- Second Treatment Course: 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course.

2.2 Vaccinations

Patients should complete any necessary immunizations at least 6 weeks prior to treatment with LEMTRADA *[see Warnings and Precautions (5.4)]*.

Prior to LEMTRADA treatment determine whether patients have a history of varicella or have been vaccinated for varicella zoster virus (VZV). If not, test the patient for antibodies to VZV and consider vaccination for those who are antibody-negative. Postpone treatment with LEMTRADA until 6 weeks after VZV vaccination.

2.3 Recommended Premedication and Concomitant Medication

Corticosteroids

Premedicate patients with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course *[see Warnings and Precautions (5.2)]*.

Herpes Prophylaxis

Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later *[see Warnings and Precautions (5.9)]*.

2.4 Preparation Instructions

Follow the steps below to prepare the diluted solution of LEMTRADA for intravenous infusion:

- Inspect LEMTRADA visually for particulate matter and discoloration prior to administration. Do not use if particulate matter is present or the solution is discolored. Do not freeze or shake vials prior to use.
- Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique and inject into a 100 mL bag of sterile 0.9% Sodium Chloride, USP or 5% Dextrose in Water, USP.
- Gently invert the bag to mix the solution. Ensure the sterility of the prepared solution, because it contains no antimicrobial preservatives. Each vial is for single use only.

Prior to administration, protect diluted LEMTRADA solution from light and store for as long as 8 hours either at room temperature 15°C to 25°C (59°F to 77°F) or keep refrigerated at conditions 2°C to 8°C (36°F to 46°F).

2.5 Infusion Instructions

Infuse LEMTRADA over 4 hours starting within 8 hours after dilution. Extend the duration of the infusion if clinically indicated.

Administer LEMTRADA in a setting in which equipment and personnel to appropriately manage anaphylaxis or serious infusion reactions are available *[see Warnings and Precautions (5.4)]*.

Do not add or simultaneously infuse other drug substances through the same intravenous line. Do not administer as an intravenous push or bolus.

Monitor vital signs before the infusion and periodically during the infusion. Provide appropriate symptomatic treatment for infusion reactions as needed. Consider immediate discontinuation of the intravenous infusion if severe infusion reactions occur.

Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Inform patients that they should report symptoms that occur during and after each infusion because they may indicate a need for prompt medical intervention *[see Warnings and Precautions (5.2)]*.

2.6 Laboratory Testing and Monitoring to Assess Safety

Conduct the following laboratory tests at baseline and at periodic intervals for 48 months following the last treatment course of LEMTRADA in order to monitor for early signs of potentially serious adverse effects:

- Complete blood count (CBC) with differential (prior to treatment initiation and at monthly intervals thereafter)
- Serum creatinine levels (prior to treatment initiation and at monthly intervals thereafter)
- Urinalysis with urine cell counts (prior to treatment initiation and at monthly intervals thereafter)
- A test of thyroid function, such as thyroid stimulating hormone (TSH) level (prior to treatment initiation and every 3 months thereafter)

Conduct baseline and yearly skin exams to monitor for melanoma *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. LEMTRADA is a clear and colorless to slightly yellow solution that requires dilution prior to intravenous infusion.

4 CONTRAINDICATIONS

LEMTRADA is contraindicated in patients who are infected with Human Immunodeficiency Virus (HIV) because LEMTRADA causes prolonged reductions of CD4+ lymphocyte counts.

5 WARNINGS AND PRECAUTIONS

5.1 Autoimmunity

Treatment with LEMTRADA can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions. In clinical studies LEMTRADA-treated patients experienced thyroid disorders (34%), immune thrombocytopenia (2%), and glomerular nephropathies (0.3%) *[see Warnings and Precautions (5.5, 5.6, 5.7)]*. Autoimmune hemolytic anemia and autoimmune pancytopenia *[see Warnings and Precautions (5.8)]*, undifferentiated connective tissue disorders, and acquired hemophilia A (anti-Factor VIII antibodies) each occurred in 0.2% of patients. Rheumatoid arthritis, type I diabetes, vitiligo, and retinal pigment epitheliopathy occurred in 0.1% of patients. During postmarketing use, additional autoimmune events including Guillain-Barré syndrome and chronic inflammatory demyelinating polyradiculoneuropathy have been reported in the treatment of patients with B-cell chronic lymphocytic leukemia (B-CLL), as well as other disorders, generally at higher and more frequent doses than recommended in MS. An oncology patient treated with alemtuzumab had fatal transfusion-associated graft-versus-host disease.

Autoantibodies may be transferred from the mother to the fetus during pregnancy. A case of transplacental transfer of anti-thyrotropin receptor antibodies resulting in neonatal Graves' disease occurred after alemtuzumab treatment in the mother *[see Use in Specific Populations (8.1)]*.

LEMTRADA may increase the risk of other autoimmune conditions because of the broad range of autoantibody formation with LEMTRADA.

Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts before starting treatment and then at monthly intervals for 48 months after the last dose of LEMTRADA to allow for early detection and treatment of autoimmune adverse reactions *[see Dosage and Administration (2.6)]*. After 48 months, testing should be performed based on clinical findings suggestive of autoimmunity.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.2 Infusion Reactions

LEMTRADA causes cytokine release syndrome resulting in infusion reactions, some of which may be serious and life threatening. In clinical studies, 92% of LEMTRADA-treated patients experienced infusion reactions. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients and included anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

During postmarketing use, other serious and sometimes fatal infusion reactions included hypotension, syncope, acute respiratory distress syndrome, respiratory arrest, myocardial infarction, acute cardiac insufficiency and cardiac arrest have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Premedicate patients with corticosteroids immediately prior to LEMTRADA infusion for the first 3 days of each treatment course. In clinical trials, patients received 1,000 mg of methylprednisolone for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment.

Consider additional monitoring in patients with medical conditions which predispose them to cardiovascular or pulmonary compromise.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.3 Malignancies

Thyroid cancer

LEMTRADA may increase the risk of thyroid cancer. In controlled clinical studies, 3 of 918 (0.3%) LEMTRADA-treated patients developed thyroid cancer, compared to none in the interferon beta-1a-treated group. However, screening for thyroid cancer was performed more frequently in the LEMTRADA-treated group, because of the higher incidence of autoimmune thyroid disorders in those patients. Two additional cases of thyroid cancer in LEMTRADA-treated patients occurred in uncontrolled studies.

Patients and healthcare providers should monitor for symptoms of thyroid cancer including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

Melanoma

LEMTRADA may increase the risk of melanoma. In uncontrolled studies, 4 of 1498 (0.3%) LEMTRADA-treated patients developed melanoma or melanoma *in situ*. One of those patients had evidence of locally advanced disease.

Perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.

Lymphoproliferative disorders and lymphoma

Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS, including a MALT lymphoma, Castleman's Disease, and a fatality following treatment of non-Epstein Barr Virus-associated Burkitt's lymphoma. There are postmarketing reports of Epstein Barr Virus-associated lymphoproliferative disorders in non-MS patients.

Because LEMTRADA is an immunomodulatory therapy, caution should also be exercised in initiating LEMTRADA in patients with pre-existing or ongoing malignancies.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.4 LEMTRADA REMS Program

LEMTRADA is available only through a restricted program under a REMS called the LEMTRADA REMS Program, because of the risks of autoimmunity, infusion reactions, and malignancies *[see Warnings and Precautions (5.1, 5.2, 5.3)]*.

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

Full Prescribing Information (3 of 8)

Total Training Screens: 3 of 18

Notable requirements of the LEMTRADA REMS Program include the following:
- Prescribers must be certified with the program by enrolling and completing training.
- Patients must enroll in the program and comply with ongoing monitoring requirements [see Dosage and Administration (2.6)].
- Pharmacies must be certified with the program and must only dispense to certified healthcare facilities that are authorized to receive LEMTRADA.
- Healthcare facilities must enroll in the program and verify that patients are authorized before infusing LEMTRADA. Healthcare facilities must have on-site access to equipment and personnel trained to manage infusion reactions.

Further information, including a list of qualified healthcare facilities, is available at 1-855-676-6326.

5.5 Immune Thrombocytopenia

Immune thrombocytopenia (ITP) occurred in 2% of LEMTRADA-treated patients in clinical studies in MS.

In a controlled clinical trial in patients with MS, one LEMTRADA-treated patient developed ITP that went unrecognized prior to the implementation of monthly blood monitoring requirements, and died from intracerebral hemorrhage. Nadir platelet counts <20,000 cells per microliter as a result of ITP occurred in 2% of all LEMTRADA-treated patients in clinical studies in MS. Anti-platelet antibodies did not precede ITP onset. ITP has been diagnosed more than 3 years after the last LEMTRADA dose.

Symptoms of ITP include easy bruising, petechiae, spontaneous mucocutaneous bleeding (e.g., epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. Hemoptysis may also be indicative of anti-glomerular basement membrane (GBM) disease [see Warnings and Precautions (5.6)], and an appropriate differential diagnosis has to be undertaken. Remind the patient to remain vigilant for symptoms they may experience and to seek immediate medical help if they have any concerns.

Obtain complete blood counts (CBCs) with differential prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion [see Dosage and Administration (2.6)]. After this period of time, testing should be performed based on clinical findings suggestive of ITP. If ITP is suspected, a complete blood count should be obtained immediately. If ITP onset is confirmed, promptly initiate appropriate medical intervention.

5.6 Glomerular Nephropathies

Glomerular nephropathies occurred in 0.3% of LEMTRADA-treated patients in MS clinical trials. There were 3 cases of membranous glomerulonephritis and 2 cases of anti-glomerular basement membrane (anti-GBM) disease. There are published and post-marketing cases of MS patients treated with alemtuzumab who developed anti-GBM disease and subsequently developed end stage renal disease requiring renal transplantation. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA. Urgent evaluation and treatment is required because anti-GBM disease can lead to renal failure requiring dialysis or transplantation and can be life-threatening if left untreated. Clinical manifestations of nephropathy may include elevated serum creatinine levels, hematuria, or proteinuria. Alveolar hemorrhage manifested as hemoptysis is a common component of anti-GBM disease but did not occur in clinical trials.

Obtain serum creatinine levels and urinalysis with cell counts prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

If clinically significant changes from baseline in serum creatinine, unexplained hematuria, or proteinuria are observed, perform further evaluation for nephropathies. Early detection and treatment of nephropathies may decrease the risk of poor outcomes.

5.7 Thyroid Disorders

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Autoimmune thyroid disorders included Graves' disease, hyperthyroidism and hypothyroidism. Graves' ophthalmopathy with decreased vision, eye pain, and exophthalmos occurred in 1% of LEMTRADA-treated patients. Two patients required surgical orbital decompression. Serious thyroid events occurred in about 2% of LEMTRADA-treated patients in clinical studies and included cardiac and psychiatric events associated with thyroid disease. Of all LEMTRADA-treated patients, 3% underwent thyroidectomy.

Thyroid disease poses special risks in women who are pregnant [see Use in Specific Populations (8.1)].

Obtain thyroid function tests, such as TSH levels, prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

In patients with ongoing thyroid disorder, LEMTRADA should be administered only if the potential benefit justifies the potential risks.

5.8 Other Autoimmune Cytopenias

Autoimmune cytopenias such as neutropenia (0.1%), hemolytic anemia (0.2%), and pancytopenia (0.2%) occurred in LEMTRADA-treated patients in clinical studies in MS. In cases of autoimmune hemolytic anemia, patients tested positive for direct antiglobulin antibodies, and nadir hemoglobin levels ranged from 2.9–8.6 g/dL. Symptoms of autoimmune hemolytic anemia include weakness, chest pain, jaundice, dark urine, and tachycardia. One LEMTRADA-treated patient with autoimmune pancytopenia died from sepsis.

During postmarketing use, additional autoimmune cytopenias including fatal autoimmune hemolytic anemia and aplastic anemia have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Use CBC results to monitor for cytopenias. Prompt medical intervention is indicated if a cytopenia is confirmed.

5.9 Infections

Infections occurred in 71% of LEMTRADA-treated patients compared to 53% of patients treated with interferon beta-1a in controlled clinical trials in MS up to 2 years in duration. Infections that occurred more often in LEMTRADA-treated patients than interferon beta-1a patients included nasopharyngitis, urinary tract infection, upper respiratory tract infection, sinusitis, herpetic infections, influenza, and bronchitis. Serious infections occurred in 3% of patients treated with LEMTRADA as compared to 1% of patients treated with interferon beta-1a. Serious infections in the LEMTRADA group included appendicitis, gastroenteritis, pneumonia, herpes zoster, and tooth infection.

Do not administer live viral vaccines following a course of LEMTRADA. Patients treated with LEMTRADA have altered immunity and may be at increased risk of infection following administration of live viral vaccines.

Consider delaying LEMTRADA administration in patients with active infection until the infection is fully controlled.

Concomitant use of LEMTRADA with antineoplastic or immunosuppressive therapies could increase the risk of immunosuppression.

Herpes Viral Infections

In controlled clinical trials, 16% of LEMTRADA-treated patients developed a herpes viral infection compared to 3% of interferon beta-1a patients. These events included oral herpes (8.8%), herpes zoster (4.2%), herpes simplex (1.8%), and genital herpes (1.3%). Serious herpetic infections in LEMTRADA-treated patients included primary varicella (0.1%), herpes zoster (0.2%), and herpes meningitis (0.1%). Administer antiviral agents for herpetic prophylaxis at appropriate suppressive dosing regimens. Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later [see Dosage and Administration (2.3)].

Human Papilloma Virus

Cervical human papilloma virus (HPV) infection, including cervical dysplasia, occurred in 2% of LEMTRADA-treated patients. Annual HPV screening is recommended for female patients.

Tuberculosis

Tuberculosis occurred in patients treated with LEMTRADA and interferon beta-1a in controlled clinical trials. Active and latent tuberculosis cases occurred in 0.3% of LEMTRADA-treated patients, most often in endemic regions. Perform tuberculosis screening according to local guidelines prior to initiation of LEMTRADA. For patients testing positive in tuberculosis screening, treat by standard medical practice prior to therapy with LEMTRADA.

Fungal Infections

Fungal infections, especially oral and vaginal candidiasis, occurred more commonly in LEMTRADA-treated patients (12%) than in patients treated with interferon beta-1a (3%) in controlled clinical trials in MS.

Listeria Infections

Listeria meningitis has been reported in LEMTRADA-treated patients. Cases of listeria meningitis occurred within 1 month of alemtuzumab dosing. The duration of increased risk for listeria meningitis is unclear. Patients should avoid or adequately heat foods that are potential sources of *Listeria monocytogenes*.

Infections in non-MS patients

During postmarketing use, serious and sometimes fatal viral, bacterial, protozoan, and fungal infections, including some due to reactivation of latent infections, have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Hepatitis

No data are available on the association of LEMTRADA with Hepatitis B virus (HBV) or Hepatitis C virus (HCV) reactivation because patients with evidence of active or chronic infections were excluded from the clinical trials. Consider screening patients at high risk of HBV and/or HCV infection before initiation of LEMTRADA and exercise caution in prescribing LEMTRADA to patients identified as carriers of HBV and/or HCV as these patients may be at risk of irreversible liver damage relative to a potential virus reactivation as a consequence of their pre-existing status.

5.10 Pneumonitis

In clinical studies, 6 of 1217 (0.5%) LEMTRADA-treated patients had pneumonitis of varying severity. Cases of hypersensitivity pneumonitis and pneumonitis with fibrosis occurred in clinical studies. Patients should be advised to report symptoms of pneumonitis, which include shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

5.11 Drug Products with Same Active Ingredient

LEMTRADA contains the same active ingredient (alemtuzumab) found in CAMPATH®. If LEMTRADA is considered for use in a patient who has previously received CAMPATH, exercise increased vigilance for additive and long-lasting effects on the immune system.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling:
- Autoimmunity [see Boxed Warning and Warnings and Precautions (5.1)]
- Infusion reactions [see Boxed Warning and Warnings and Precautions (5.2)]
- Malignancies [see Warnings and Precautions (5.3)]
- Immune Thrombocytopenia [see Warnings and Precautions (5.5)]
- Glomerular Nephropathies [see Warnings and Precautions (5.6)]
- Thyroid Disorder [see Warnings and Precautions (5.7)]
- Other Autoimmune Cytopenias [see Warnings and Precautions (5.8)]
- Infections [see Warnings and Precautions (5.9)]
- Pneumonitis [see Warnings and Precautions (5.10)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In controlled clinical trials (Study 1 and Study 2), a total of 811 patients with relapsing forms of MS received LEMTRADA. A total of 811 patients received 1 course of therapy, and 789 patients received a second course of therapy at 12 months. The overall follow-up in the controlled trials was equivalent to 1622 patient years, with an additional 3411 person-years of follow-up in an open label extension study. The population was 18-55 years of age, 65% were female, and 92% were Caucasian.

Most Common Adverse Reactions

In clinical trials, the most common adverse reactions with LEMTRADA [in at least 10% of patients and more frequently than in interferon beta-1a] were rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting.

Table 1 lists adverse reactions occurring in ≥5% of LEMTRADA-treated patients in Study 1 and 2 and at the same or at a higher rate than interferon beta-1a.

Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=386) %
Rash	53	6
Headache	52	25
Pyrexia	29	9

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LEMTRADA REMS Program Training

Full Prescribing Information (4 of 8)

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Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis (continued)

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=389) %
Nasopharyngitis	25	19
Nausea	21	9
Urinary tract infection	19	8
Fatigue	18	13
Insomnia	16	15
Upper respiratory tract infection	16	13
Herpes viral infection	16	3
Urticaria	16	2
Pruritus	14	2
Thyroid gland disorders	13	3
Fungal infection	13	4
Arthralgia	12	9
Pain in extremity	12	9
Back pain	12	8
Diarrhea	12	6
Sinusitis	11	8
Oropharyngeal pain	11	8
Paresthesia	10	8
Dizziness	10	5
Abdominal pain	10	5
Flushing	10	4
Vomiting	10	3
Cough	9	4
Chills	9	3
Dysgeusia	8	7
Influenza	8	6
Dermatitis	8	5
Dyspepsia	8	4
Blood in urine	8	3
Dyspnea	8	1
Tachycardia	8	1
Anxiety	7	6
Muscular weakness	7	6
Bronchitis	7	4
Chest discomfort	7	2
Muscle spasms	6	5
Myalgia	6	5
Decrease in CD4 lymphocytes	6	2
Decrease in CD8 lymphocytes	6	2
Asthenia	5	4
Decrease in T-lymphocyte count	5	3
Erythema	5	2
Peripheral edema	5	2
Epistaxis	5	2
Neck Pain	5	2
Abnormal uterine bleeding	5	1

6.2 Lymphopenia

Nearly all (99.9%) patients treated with LEMTRADA in MS clinical trials experienced lymphopenia. The lowest lymphocyte counts occurred approximately by 1 month after each course of treatment. The mean lymphocyte count at 1 month after LEMTRADA treatment was 0.25 x 10^9/L (range: 0.03-0.230 x 10^9/L) and 0.32 (0.03-1.81 x 10^9/L) for treatment courses 1 and 2, respectively. Total lymphocyte counts increased to reach the lower limit of normal in approximately 40% of patients by 6 months after each LEMTRADA treatment course and approximately 80% of patients by 12 months after each course [see *Clinical Pharmacology (12.2)*].

6.3 Suicidal Behavior or Ideation

In clinical studies, 0.6% of patients in both the LEMTRADA and interferon beta-1a groups had events of attempted suicide or suicidal ideation. There were no completed suicides in either clinical study treatment group. Suicidal behavior or ideation occurred in patients with or without a history of a psychiatric or thyroid disorder. Advise patients to report immediately any symptoms of depression or suicidal ideation to the prescribing physician.

6.4 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Using an enzyme-linked immunosorbent assay (ELISA) and a competitive binding assay, anti-alemtuzumab binding antibodies were detected in 62%, 67%, and 29% of LEMTRADA-treated patients, at months 1, 3, 12 (Course 1) as well as 63%, 83%, and 75% of LEMTRADA-treated patients at months 13, 15, and 24 (Course 2). Samples that tested positive for binding antibodies were further evaluated for evidence of *in vitro* inhibition using a flow cytometry assay. Neutralizing antibodies were detected in 87%, 46%, and 8% of positive binding antibody patients at months 1, 3, 12 (Course 1) as well as 94%, 89%, and 42% of positive binding antibody patients at months 13, 15, and 24 (Course 2). Anti-alemtuzumab antibodies were associated with decreased alemtuzumab concentration during Course 2 but not Course 1. There was no evidence from clinical trials that the presence of binding or inhibitory anti-alemtuzumab antibodies had a significant effect on clinical outcomes, total lymphocyte count, or adverse events. The incidence of antibodies is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including inhibitory antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to LEMTRADA with the incidence of antibodies to other products may be misleading.

6.5 Postmarketing Experience

The following adverse reactions, not described elsewhere, were identified during post-approval use of alemtuzumab (CAMPATH) for the treatment of B-cell chronic lymphocytic leukemia (B-CLL), as well as for the treatment of other disorders, generally at higher and more frequent doses (e.g., 30 mg) than that recommended in the treatment of MS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac Disorders

Congestive heart failure, cardiomyopathy, and decreased ejection fraction in non-MS patients previously treated with potentially cardiotoxic agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. LEMTRADA was embryolethal in pregnant huCD52 transgenic mice when administered during organogenesis. Auto-antibodies may develop after administration of LEMTRADA. Placental transfer of anti-thyroid antibodies resulting in neonatal Graves' disease has been reported. LEMTRADA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

When LEMTRADA was administered to pregnant huCD52 transgenic mice during organogenesis (gestation days [GD] 9-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, no teratogenic effects were observed. However, there was an increase in embryolethality (increased post-implantation loss and the number of dams with all fetuses dead or resorbed) in pregnant animals dosed during GD 11-15.

In a separate study in pregnant huCD52 transgenic mice, administration of LEMTRADA during organogenesis (GD 9-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, decreases in B lymphocytes and T-lymphocyte populations were observed in the offspring at both doses tested. The effects of LEMTRADA, administered during organogenesis, on postnatal development have not been adequately assessed.

Clinical Considerations

To avoid in utero exposure to LEMTRADA, women of child bearing potential should use effective contraceptive measures when receiving a course of treatment with LEMTRADA and for 4 months following that course of treatment.

LEMTRADA induces persistent thyroid disorders [see *Warnings and Precautions (5.7)*]. Untreated hypothyroidism in pregnant women increases the risk for miscarriage and may have effects on the fetus including mental retardation and dwarfism. In mothers with Graves' disease, maternal thyroid stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause neonatal Graves' disease. In a patient who developed Graves' disease after treatment with alemtuzumab, placental transfer of anti-thyrotropin receptor antibodies resulted in neonatal Graves' Disease with thyroid storm in her infant who was born 1 year after alemtuzumab dosing [see *Warnings and Precautions (5.15)*].

8.3 Nursing Mothers

Alemtuzumab was detected in the milk of lactating mice administered 10 mg/kg LEMTRADA on Days 9 through 12 postpartum. Serum levels of alemtuzumab were similar in lactating mice and offspring on Day 13 postpartum, and were associated with evidence of pharmacological activity (decrease in lymphocyte counts) in the offspring.

It is not known whether alemtuzumab is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from LEMTRADA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients less than 17 years of age have not been established. Use of LEMTRADA is not recommended in pediatric patients due to the risks of autoimmunity, infusion reactions, and because it may increase the risk of malignancies (thyroid, melanoma, lymphoproliferative disorders, and lymphoma) [see *Warnings and Precautions (5.1, 5.2, 5.3)*].

8.5 Geriatric Use

Clinical studies of LEMTRADA did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

10 OVERDOSAGE

Two MS patients experienced serious reactions (headache, rash, and either hypotension or sinus tachycardia) after a single accidental infusion up to 60 mg of LEMTRADA. Doses of LEMTRADA greater than those recommended may increase the intensity and/or duration of infusion reactions or its immune effects. There is no known antidote for alemtuzumab overdosage.

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LEMTRADA REMS Program Training

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11 DESCRIPTION

LEMTRADA (alemtuzumab) is a recombinant humanized IgG1 kappa monoclonal antibody directed against the cell surface glycoprotein, CD52. Alemtuzumab has an approximate molecular weight of 150kD. LEMTRADA is produced in mammalian cell (Chinese hamster ovary) suspension culture in a nutrient medium containing neomycin. Neomycin is not detectable in the final product. LEMTRADA is a sterile, clear and colorless to slightly yellow, solution (pH 7.2±0.2) for infusion.

Each 1 mL of solution contains alemtuzumab 10 mg, dibasic sodium phosphate (1.15 mg), disodium edetate dihydrate (0.0187 mg), polysorbate 80 (0.1 mg), potassium chloride (0.2 mg), potassium dihydrogen phosphate (0.2 mg), sodium chloride (8 mg), and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which alemtuzumab exerts its therapeutic effects in multiple sclerosis is unknown but is presumed to involve binding to CD52, a cell surface antigen present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

12.2 Pharmacodynamics

Effects of LEMTRADA on the Lymphocyte Population

LEMTRADA depletes circulating T and B lymphocytes after each treatment course. In clinical trials, the lowest cell counts occurred 1 month after a course of treatment at the time of the first post-treatment blood count. Lymphocyte counts then increased over time: B cell counts usually recovered within 6 months; T cell counts increased more slowly and usually remained below baseline 12 months after treatment. Approximately 60% of patients had total lymphocyte counts below the lower limit of normal 6 months after each treatment course and 20% had counts below the lower limit of normal after 12 months.

Reconstitution of the lymphocyte population varies for the different lymphocyte subtypes. At Month 1 in clinical trials, the mean CD4+ lymphocyte count was 40 cells per microliter, and, at Month 12, 270 cells per microliter. At 30 months, approximately half of patients had CD4+ lymphocyte counts that remained below the lower limit of normal.

Cardiac Electrophysiology

In a study of 53 MS patients, alemtuzumab 12 mg per day for 5 days caused no changes in the QTc interval greater than 20ms. An average 22 to 26 beats-per-minute increase in heart rate was observed for at least 2 hours after the first but not subsequent infusions.

12.3 Pharmacokinetics

The pharmacokinetics of LEMTRADA were evaluated in a total of 148 patients with relapsing forms of MS who received 12 mg/day on 5 consecutive days, followed by 12 mg/day on 3 consecutive days 12 months following the first treatment course.

Absorption

Serum concentrations increased with each consecutive dose within a treatment course, with the highest observed concentrations occurring following the last infusion of a treatment course. The mean maximum concentration was 3014 ng/mL on Day 5 of the first treatment course, and 2221 ng/mL on Day 3 of the second treatment course.

Distribution

LEMTRADA is largely confined to the blood and interstitial space with a central volume of distribution of 14.1 L.

Elimination

The elimination half-life was approximately 2 weeks and was comparable between courses. The serum concentrations were generally undetectable (< 50 ng/mL) within approximately 30 days following each treatment course.

Specific Populations

Age, race, or gender had no effect on the pharmacokinetics of LEMTRADA.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to assess the carcinogenic or genotoxic potential of LEMTRADA have not been conducted.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic male mice on 5 consecutive days prior to cohabitation with untreated wild-type females, no effect on fertility or reproductive performance was observed. However, adverse effects on sperm parameters (including abnormal morphology [detached mo head] and reduced total count and mobility) were observed at both doses tested.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic female mice for 5 consecutive days prior to cohabitation with untreated wild-type males, there was a decrease in the average number of corpora lutea and implantation sites and an increase in post-implantation loss, resulting in fewer viable embryos at the higher dose tested.

14 CLINICAL STUDIES

The efficacy of LEMTRADA was demonstrated in two studies (Study 1 and 2) that evaluated LEMTRADA 12 mg in patients with relapsing-remitting multiple sclerosis (RRMS). LEMTRADA was administered by intravenous infusion once daily over a 5-day course, followed one year later by intravenous infusion once daily over a 3-day course. Both studies included patients who had experienced at least 2 relapses during the 2 years prior to trial entry and at least 1 relapse during the year prior to trial entry. Neurological examinations were performed every 12 weeks and at the time of suspected relapse. Magnetic resonance imaging (MRI) evaluations were performed annually.

Study 1

Study 1 was a 2 year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 1 had Expanded Disability Status Scale (EDSS) scores of 5 or less and had to have experienced at least one relapse while on interferon beta or glatiramer acetate therapy.

Patients were randomized to receive LEMTRADA (n=426) or interferon beta-1a (n=202). At baseline, the mean age was 36 years, the mean disease duration was 4.6 years, and the mean EDSS score was 2.7.

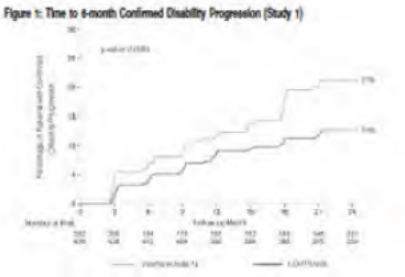
The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression. Confirmed disability progression was defined as at least a 1 point increase above baseline EDSS (1.5 point increase for patients with baseline EDSS of 0) sustained for 6 months. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. Time to onset of 6-month confirmed disability progression was significantly delayed with LEMTRADA treatment compared to interferon beta-1a. There was no significant difference between the treatment groups for the change in T2 lesion volume. The results of Study 1 are shown in Table 2 and Figure 1.

Table 2: Clinical and MRI Results of Study 1

	LEMTRADA (N=426)	Interferon beta-1a 44 mcg (N=202)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.26 49%	0.52	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	13% 42%	21%	0.0094
Percent of patients remaining relapse-free at Year 2	65%	47%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-1.3	-1.2	0.14

Figure 1: Time to 6-month Confirmed Disability Progression (Study 1)



Study 2

Study 2 was a 2-year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 2 had EDSS scores of 3 or less and no prior treatment for multiple sclerosis. Patients were randomized to receive LEMTRADA (n=376) or interferon beta-1a (n=187). At baseline, the mean age was 33 years, the mean disease duration was 2 years, and the mean EDSS score was 2.

The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression, as defined in Study 1. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. There was no significant difference between the treatment groups for the time to confirmed disability progression and for the primary MRI endpoint (change in T2 lesion volume). The results for Study 2 are shown in Table 3.

Table 3: Clinical and MRI Results of Study 2

	LEMTRADA (N=376)	Interferon beta-1a 44 mcg (N=187)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.18 55%	0.39	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	8% 30%	11%	0.22
Percent of patients remaining relapse-free at Year 2	78%	59%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-6.3	-6.5	0.31

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each LEMTRADA carton (NDC: 58468-0200-1) contains 1 single-use vial that delivers 12 mg/1.2 mL (10 mg/mL). The vial stopper is not made with natural rubber latex.

LEMTRADA is a sterile, clear and colorless to slightly yellow solution for infusion, containing no antimicrobial preservatives.

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16.2 Storage and Handling
Store LEMTRADA vials at 2°C to 8°C (36°F to 46°F). Do not freeze or shake. Store in original carton to protect from light.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Autoimmunity
- Advise patients to contact their healthcare provider promptly if they experience any symptoms of potential autoimmune disease. Give examples of important symptoms such as bleeding, easy bruising, petechiae, purpura, hematuria, edema, jaundice, or hemoptysis [see Warnings and Precautions (5.1)].
- Advise patients of the importance of monthly blood and urine tests for 48 months following the last course of LEMTRADA to monitor for signs of autoimmunity because early detection and prompt treatment can help prevent serious and potentially fatal outcomes associated with these events. Advise patients that monitoring may need to continue past 48 months if they have signs or symptoms of autoimmunity.
- Advise patients that LEMTRADA may cause hyperthyroid or hypothyroid disorders.
- Advise patients to contact their healthcare provider if they experience symptoms reflective of a potential thyroid disorder such as unexplained weight loss or gain, fast heartbeat or palpitations, eye swelling, constipation, or feeling cold.
- Advise women of childbearing potential of the risks of pregnancy with concomitant thyroid disease. Advise women of childbearing potential to discuss pregnancy planning with their doctor.

Infusion Reactions
- Advise patients that infusion reactions can occur after they leave the infusion center [see Warnings and Precautions (5.2)].
- Instruct the patient to remain at the infusion center for 2 hours after each LEMTRADA infusion, or longer at the discretion of the physician. Advise patients that symptoms of infusion reactions may occur after they leave the infusion center and to report these symptoms to their doctor.
- Advise patients to contact their healthcare provider promptly if they experience infusion reactions, which include swelling in the mouth or throat, difficulty breathing, weakness, abnormal heart rate (fast, slow, or irregular), chest pain, and rash.

Malignancies
- Advise patients that LEMTRADA may increase their risk of malignancies including thyroid cancer and melanoma [see Warnings and Precautions (5.3)].
- Advise patients to report symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, hoarseness or other voice changes that do not go away, trouble swallowing or breathing, or a constant cough not due to a cold.
- Advise patients that they should have baseline and yearly skin examinations.

LEMTRADA REMS Program
- LEMTRADA is available only through a restricted program called the LEMTRADA REMS Program [see Warnings and Precautions (5.4)]. Inform the patient of the following notable requirements:
  - Patients and providers must be enrolled in the program.
  - Patients must comply with the ongoing monitoring requirements.
  - Patients must report any side effects or symptoms to their doctor.
- LEMTRADA is available only at certified infusion centers participating in the program. Therefore, provide patients with information on the LEMTRADA REMS Program in order to locate an infusion center.
- Advise patients to read the LEMTRADA REMS material for patients, *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*.
- Instruct patients to carry the LEMTRADA REMS Patient Safety Information Card with them in case of an emergency.

Infections
- Advise patients to contact their healthcare provider if they develop symptoms of serious infection such as fever or swollen glands [see Warnings and Precautions (5.6)].
- Advise patients to complete any necessary immunizations at least 6 weeks prior to treatment with LEMTRADA [see Dosage and Administration (2.2)]. Advise patients that they should talk to their healthcare provider before taking any vaccine after recent treatment with LEMTRADA [see Warnings and Precautions (5.9)].
- Advise patients to take their prescribed medication for herpes prophylaxis as directed by their healthcare provider [see Warnings and Precautions (5.6)].
- Advise patients that yearly HPV screening is recommended [see Warnings and Precautions (5.9)].
- Advise patients to avoid or adequately heat foods that are potential sources of *Listeria monocytogenes* if they have had a recent course of LEMTRADA. The duration of increased risk for listeria infection after LEMTRADA administration is not known [see Warnings and Precautions (5.6)].

Pneumonitis
- Advise patients that pneumonitis has been reported in patients treated with LEMTRADA [see Warnings and Precautions (5.10)]. Advise patients to report symptoms of lung disease such as shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

Concomitant Use of Campath
- Advise patients that alemtuzumab is the same drug as Campath for use in B-CLL. Patients should inform their healthcare provider if they have taken Campath [see Warnings and Precautions (5.11)].

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Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142

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MEDICATION GUIDE
LEMTRADA™ (lem-TRA-da)
(alemtuzumab)
injection for intravenous infusion

Read this Medication Guide before you start receiving LEMTRADA and before you begin each treatment course. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is the most important information I should know about LEMTRADA?
LEMTRADA can cause serious side effects, including:

1. **Serious autoimmune problems.** Some people receiving LEMTRADA develop a condition where the immune cells in your body attack other cells or organs in the body (autoimmunity) which can be serious and may cause death. Serious autoimmune problems may include:
   - **Immune thrombocytopenic purpura (ITP).** LEMTRADA may cause the number of platelets in your blood to be reduced (ITP). ITP can cause severe bleeding that, if not treated, may cause life-threatening problems. Call your healthcare provider right away if you have any of the following symptoms:
     - easy bruising
     - bleeding from a cut that is hard to stop
     - heavier menstrual periods than normal
     - bleeding from your gums or nose that is new or takes longer than usual to stop
     - small, scattered spots on your skin that are red, pink, or purple
   - **kidney problems.** LEMTRADA may cause a serious kidney problem, called anti-glomerular basement membrane disease. If this happens and you do not get treated, anti-glomerular basement membrane disease can lead to severe kidney damage, kidney failure that needs dialysis, a kidney transplant, or death. Call your healthcare provider right away if you have any of the following symptoms:
     - blood in the urine (red or tea-colored urine)
     - swelling in your legs or feet
     - coughing up blood

   Side effects may happen while you receive LEMTRADA and for 4 years after you stop receiving LEMTRADA. Your healthcare provider will order blood and urine tests before you receive, while you are receiving, and every month for 4 years after you receive your last LEMTRADA infusion. You may need to continue these blood and urine tests after 4 years if you have any autoimmune signs or symptoms. The blood and urine tests will help your healthcare provider watch for signs and symptoms of serious autoimmune problems.
   It is important to have your blood and urine tested, even if you are feeling well and do not have any symptoms from LEMTRADA and your multiple sclerosis. This may help your healthcare provider find any problems early and will increase your chances of getting better.
2. **Serious infusion reactions.** LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.
   You will receive your infusion at a healthcare facility with equipment and staff trained to manage infusion reactions. You will be watched while you receive and for 2 hours after you receive LEMTRADA. It **is important** that you stay at the infusion center for 2 hours after your infusion is finished or longer if your healthcare provider decides you need to stay longer. If a serious infusion reaction happens while you are receiving LEMTRADA, your infusion may be stopped.
   Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion, and after you have left the healthcare facility:
   - swelling in your mouth or throat
   - trouble breathing
   - weakness
   - fast, slow, or irregular heart beat
   - chest pain
   - rash

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LEMTRADA REMS Program Training

Full Prescribing Information (7 of 8) Total Training Screens: 7 of 18

To lower your chances of getting a serious infusion reaction, your healthcare provider will give you a medicine called corticosteroids before your first 3 infusions of a treatment course. You may also be given other medicines before or after the infusion to try reduce your chances of these reactions or to treat them after they happen.

3. **Certain cancers.** Receiving LEMTRADA may increase your chance of getting some kinds of cancers, including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:

- new lump
- swelling in your neck
- pain in the front of your neck
- hoarseness or other voice changes that do not go away
- trouble swallowing or breathing
- cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA and each year while you are receiving treatment to monitor symptoms of skin cancer.

Because of your risk of autoimmunity, infusion reactions and the risk of some kinds of cancers, LEMTRADA is only available through a restricted program called the LEMTRADA Risk Evaluation and Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS Program.

- You and your healthcare provider must be enrolled in the LEMTRADA REMS Program.
- LEMTRADA can only be given at a certified healthcare facility that participates in the LEMTRADA REMS Program. Your healthcare provider can give you information on how to find a certified healthcare facility.
- Read the LEMTRADA REMS "What You Need to Know About LEMTRADA Treatment: A Patient Guide" and "What you Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide" after you are enrolled in the program.
- Carry your LEMTRADA REMS Patient Safety Information Card with you in case of an emergency.

What is LEMTRADA?

LEMTRADA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). Because of its risks, LEMTRADA is generally used in people who have tried 2 or more MS medicines that have not worked well enough. It is not known if LEMTRADA is safe and effective for use in children under 17 years of age.

Who should not receive LEMTRADA?

Do not receive LEMTRADA if you are infected with human immunodeficiency virus (HIV).

What should I tell my healthcare provider before receiving LEMTRADA?

Before receiving LEMTRADA, tell your healthcare provider if you:

- are taking a medicine called Campath®. Alemtuzumab the active ingredient in LEMTRADA is the same drug as Campath.
- have bleeding problems
- have thyroid problems
- have kidney problems
- have a recent history of infection
- have HIV
- have received a live vaccine in the past 6 weeks before receiving LEMTRADA or plan to receive any live vaccines. Ask your healthcare provider if you are not sure if your vaccine is a live vaccine.
- are pregnant or plan to become pregnant. LEMTRADA may harm your unborn baby. You should use birth control while receiving LEMTRADA and for 4 months after your course of treatment.
- are breastfeeding or plan to breastfeed. It is not known if LEMTRADA passes into your breast milk. You and your healthcare provider should decide if you should receive LEMTRADA or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

LEMTRADA and other medicines may affect each other causing side effects. Especially tell your healthcare provider if you take medicines that increase your chance of getting infections, including medicines used to treat cancer or to control your immune system.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How will I receive LEMTRADA?

- LEMTRADA is given through a needle placed in your vein (IV infusion).
- It takes about 4 hours to receive a full dose of LEMTRADA each day.
- You will receive LEMTRADA over 2 treatment courses.
- You will receive LEMTRADA for 5 days in a row (consecutive) for the first treatment course and then for 3 days in a row (consecutive) about 1 year later for your second treatment course.

What are the possible side effects of LEMTRADA?

LEMTRADA may cause serious side effects including:

- See **"What is the most important information I should know about LEMTRADA?"**
- **thyroid problems.** Some people who receive LEMTRADA may get thyroid problems including an overactive thyroid (hyperthyroidism) or an underactive thyroid (hypothyroidism). Your healthcare provider will do blood tests to check how your thyroid is working. Call your healthcare provider if you have any of the symptoms of thyroid problems.

Symptoms of **hyperthyroidism** may include:

- excessive sweating
- unexplained weight loss
- eye swelling
- nervousness
- fast heartbeat

Symptoms of **hypothyroidism** may include:

- unexplained weight gain
- feeling cold
- worsening tiredness
- constipation

- **low blood counts (cytopenias).** LEMTRADA may cause a decrease in some types of blood cells. Some people with these low blood counts have increased infections. Symptoms of cytopenias may include:

- weakness
- chest pain
- yellowing of the skin or whites of eyes (jaundice)
- dark urine
- fast heartbeat

Your healthcare provider will do blood tests to check for cytopenias. Call your healthcare provider right away if you have symptoms listed above.

- **serious infections.** LEMTRADA may cause you to have serious infections while you receive and after receiving a treatment course. Serious infections may include:
  - **herpes viral infections.** Some people taking LEMTRADA have an increased chance of getting herpes viral infections. Your healthcare provider will prescribe medicines to reduce your chances of getting these infections. Take these medicines exactly as your healthcare provider tells you to.
  - **human papilloma virus (HPV).** Females have an increased chance of getting a cervical HPV infection. If you are a female, you should have an HPV screening each year.
  - **tuberculosis.** Your healthcare provider should check you for tuberculosis before you receive LEMTRADA.
  - **fungal infections.**
  - **listeria.** People who receive LEMTRADA have an increased chance of getting an infection caused by the bacteria, listeria. Avoid foods that may be a source for listeria (for example, deli meat, unpasteurized milk and cheese products, or undercooked meat, seafood or poultry) or make sure that the food you eat which may contain listeria is heated well if you receive treatment with LEMTRADA.

Call your healthcare provider right away if you have symptoms of a serious infection, such as fever or swollen glands. You may need to go to the hospital for treatment if you get a serious infection. If is

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

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important to tell the healthcare providers that you have received LEMTRADA.
Talk to your healthcare provider before you get vaccinations after receiving LEMTRADA. Certain vaccinations may increase your chances of getting infections.

- **swelling of lung tissue (pneumonitis).** Some people have had swelling of the lung tissue while receiving LEMTRADA. Call your healthcare provider right away if you have the following symptoms:
  - shortness of breath
  - cough
  - wheezing
  - chest pain or tightness
  - coughing up blood

The most common side effects of LEMTRADA include:

- rash
- headache
- thyroid problems
- fever
- swelling of your nose and throat (nasopharyngitis)
- nausea
- urinary tract infection
- feeling tired
- trouble sleeping
- upper respiratory tract infection
- herpes viral infection
- hives
- itching
- fungal infection
- joint pain
- pain in your arms or legs
- back pain
- diarrhea
- sinus infection
- mouth pain or sore throat
- tingling sensation
- dizziness
- stomach pain
- sudden redness in face, neck, or chest
- vomiting

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.
These are not all the possible side effects of LEMTRADA. For more information, ask your healthcare provider or pharmacist.
Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

General information about the safe and effective use of LEMTRADA.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use LEMTRADA for a condition for which it was not prescribed. Do not give LEMTRADA to other people, even if they have the same symptoms that you have. It may harm them. This Medication Guide summarizes the most important information about LEMTRADA. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about LEMTRADA that is written for health professionals. For more information, go to www.LemtradaREMS.com or call Genzyme at 1-855-676-6326.

What are the ingredients in LEMTRADA?
Active ingredient: alemtuzumab
Inactive ingredients: sodium chloride, dibasic sodium phosphate, potassium chloride, potassium dihydrogen phosphate, polysorbate 80, disodium edetate dihydrate, and water for injection.
This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured and distributed by:

Genzyme Corporation

500 Kendall Street

Cambridge, MA 02142

US License Number: 1596

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LEMTRADA REMS Program Training

LEMTRADA REMS Program Overview (1 of 2) Total Training Screens: 9 of 18

LEMTRADA REMS PROGRAM OVERVIEW

What is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug. It is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions, and malignancies, LEMTRADA® (alemtuzumab) is only available through a restricted program called the LEMTRADA REMS Program.

LEMTRADA REMS Program Requirements

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

PRESCRIBER ENROLLMENT INSTRUCTIONS

1. Complete the training program, which includes reviewing the following:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - *LEMTRADA REMS Education Program for Prescribers*
2. Successfully complete the 8-question LEMTRADA REMS Knowledge Assessment.
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form.
4. Submit the completed and signed forms to the LEMTRADA REMS Program.

PHARMACY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the pharmacy by reviewing the LEMTRADA REMS Program Overview and completing the LEMTRADA REMS Pharmacy Enrollment Form, which acknowledges that the pharmacy agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All relevant staff at the pharmacy who will be involved with the dispensing of LEMTRADA must be educated and trained.
   - The pharmacy will verify that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
   - The pharmacy will verify that prescribers and healthcare facilities are certified and patients are authorized to receive LEMTRADA prior to dispensing LEMTRADA.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.
2. Submit the completed and signed LEMTRADA REMS Pharmacy Enrollment Form to the LEMTRADA REMS Program.

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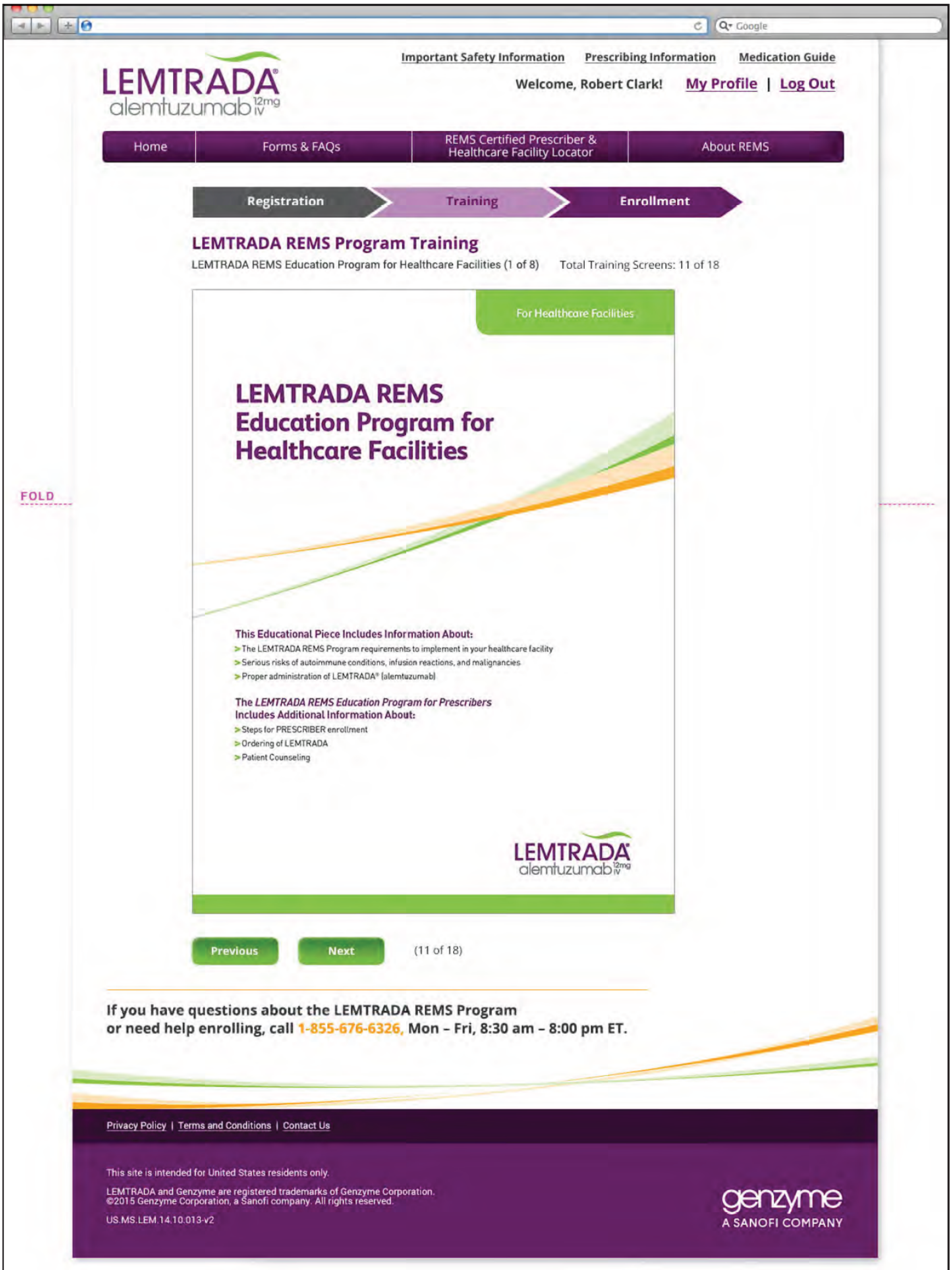
LEMTRADA REMS Desktop - HCF Training - Training Module, Overview Page 2



LEMTRADA REMS Desktop - HCF Training - Training Module, Training Page 1



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LEMTRADA REMS Program Training

LEMTRADA REMS Education Program for Healthcare Facilities (2 of 8) Total Training Screens: 12 of 18

What Is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS Program is a strategy to manage known or potential risks associated with a drug and is required by FDA to ensure that the benefits of the drug outweigh its risks. LEMTRADA is only available under a restricted program called the LEMTRADA REMS Program because of the risks of infusion reactions, autoimmune conditions, and malignancies. The *LEMTRADA REMS Education Program for Healthcare Facilities* is designed to educate and train healthcare facilities' authorized representatives on the serious risks associated with LEMTRADA, the LEMTRADA REMS Program requirements, and how to properly administer LEMTRADA.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

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Steps for Healthcare Facility Certification	
1	Designate an authorized representative.
2	Review the *LEMTRADA REMS Education Program for Healthcare Facilities*, including the Prescribing Information.
3	Complete and sign the LEMTRADA REMS Healthcare Facility Enrollment Form. This enrollment must be renewed every 2 years.
4	Implement the necessary staff training and processes to comply with the LEMTRADA REMS Program requirements.

The *LEMTRADA REMS Education Program for Healthcare Facilities*, LEMTRADA REMS Healthcare Facility Enrollment Form, and other LEMTRADA REMS Program tools are available online at www.LemtradaREMS.com or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program, call 1-855-676-6326 or enroll online at www.LemtradaREMS.com

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

LEMTRADA REMS Education Program for Healthcare Facilities (3 of 8) Total Training Screens: 13 of 18

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Who Can Be An Authorized Representative?

An authorized representative at the healthcare facility can be a:

- Pharmacist
- Director of infusion center
- Prescriber
- Nurse
- Or any responsible individual in the healthcare facility

Please check with your manager to ensure the appropriate person represents the healthcare facility and attests to the enrollment requirements as stated on the LEMTRADA REMS Healthcare Facility Enrollment Form.

- One representative needs to enroll per healthcare facility (the "authorized representative"). One authorized representative can manage more than one healthcare facility.
- Please note, there are no LEMTRADA REMS requirements for staff at a healthcare facility who will not be involved with dispensing or administering LEMTRADA.

Overview of Important Safety Information

INDICATION

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **boxed WARNING** for LEMTRADA.

Please see the Prescribing Information for complete safety information, including boxed WARNING.

SERIOUS RISKS ASSOCIATED WITH LEMTRADA

Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients, including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate patients with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

LEMTRADA REMS Education Program for Healthcare Facilities (4 of 8) Total Training Screens: 14 of 18

Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. If the infusion is not well tolerated, the duration of the infusion may be extended. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

Autoimmune Conditions

LEMTRADA has been associated with risk of autoimmune conditions, including immune thrombocytopenia, thyroid disorders, and glomerular nephropathies, which may occur many years after treatment and may be serious or life-threatening. Early detection can help to improve the outcomes of patients experiencing these events.

Please review the sections that follow to gain a better understanding of the risks of autoimmune conditions.

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Immune Thrombocytopenia (ITP)

Immune thrombocytopenia (ITP) is an autoimmune disorder usually associated with anti-platelet antibodies. Platelet depletion reduces the ability of the blood to clot.

ITP was reported in 2% of patients in clinical trials in MS. ITP can be a serious condition leading to morbidity and mortality, and may occur several years after dosing. Prescribers are required to monitor all patients for ITP by obtaining complete blood counts with differential ≤30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the patient's last infusion of LEMTRADA. After this period of time, testing should be performed based on clinical findings suggestive of ITP. Patients should also be monitored for clinical symptoms of ITP. Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. These clinical signs of ITP may be apparent before serious bleeding develops.

Potential Clinical Presentations of ITP

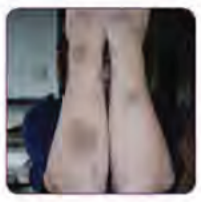
Note: These pictures are only a guide in order to show examples of bruises or petechiae. The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

Petechiae are small, scattered, "pinprick" spots under the skin that are red, pink, or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

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LEMTRADA REMS Program Training

LEMTRADA REMS Education Program for Healthcare Facilities (5 of 8) Total Training Screens: 15 of 18

Other Autoimmune Cytopenias (including neutropenia, hemolytic anemia, and pancytopenia)

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Monthly CBC results will also be used to monitor for cytopenias. If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

Glomerular Nephropathies

Glomerular nephropathies, including anti-glomerular basement membrane (anti-GBM) disease, have been reported after treatment with LEMTRADA in MS patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation, and this may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria. While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, prescribers are required to monitor patients by obtaining serum creatinine levels and urinalysis with microscopy ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

Thyroid Disorders

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention. Prescribers are required to monitor all patients for thyroid disorders by obtaining thyroid function tests, such as thyroid-stimulating hormone (TSH) levels ≤30 days prior to the first infusion of LEMTRADA, and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

Prescribers should also monitor for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness, and newly occurring constipation (hypothyroidism).

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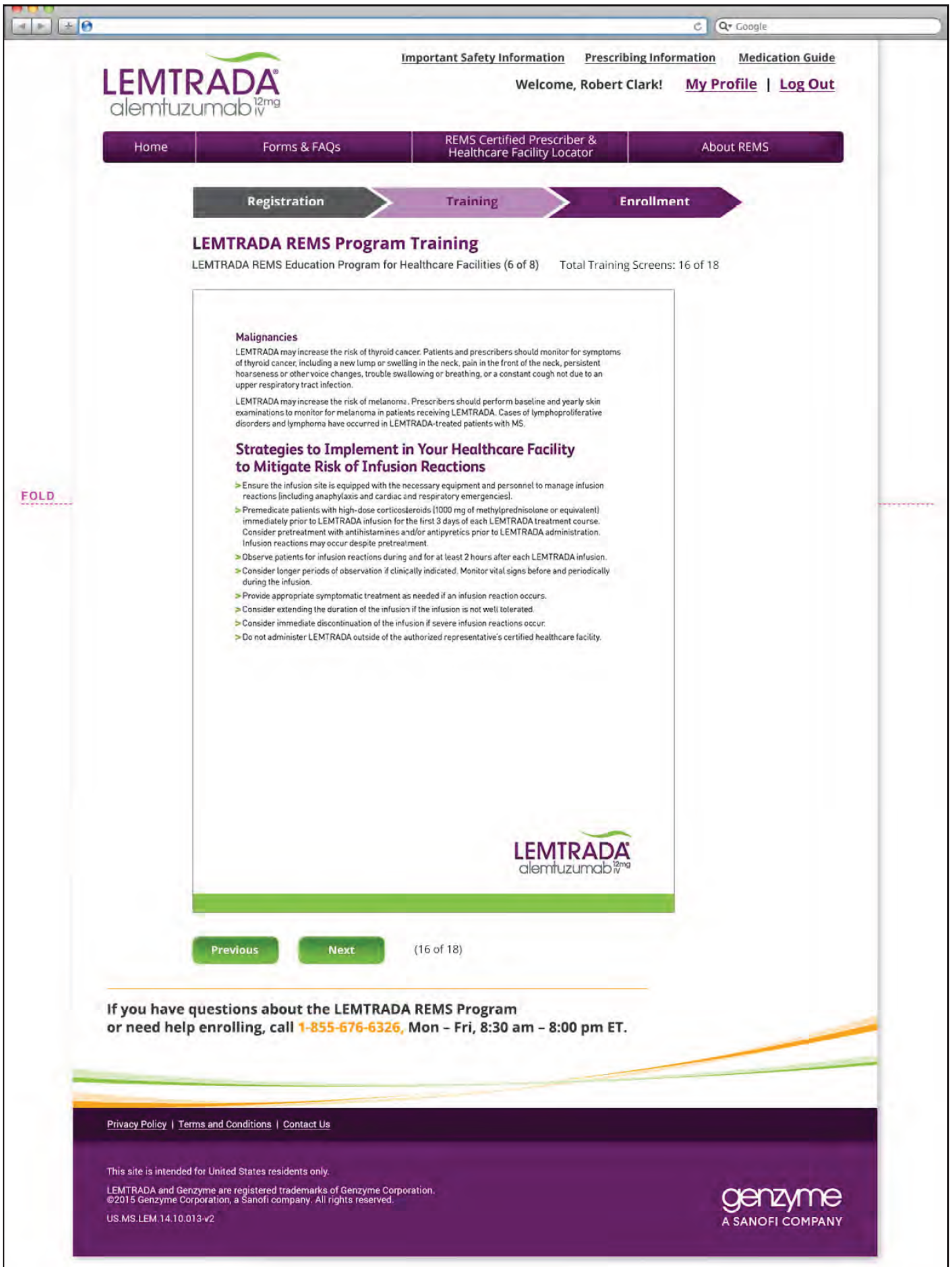
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Malignancies
LEMTRADA may increase the risk of thyroid cancer. Patients and prescribers should monitor for symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.
LEMTRADA may increase the risk of melanoma. Prescribers should perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA. Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS.
Strategies to Implement in Your Healthcare Facility to Mitigate Risk of Infusion Reactions
> Ensure the infusion site is equipped with the necessary equipment and personnel to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).
> Premedicate patients with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment.
> Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
> Consider longer periods of observation if clinically indicated. Monitor vital signs before and periodically during the infusion.
> Provide appropriate symptomatic treatment as needed if an infusion reaction occurs.
> Consider extending the duration of the infusion if the infusion is not well tolerated.
> Consider immediate discontinuation of the infusion if severe infusion reactions occur.
> Do not administer LEMTRADA outside of the authorized representative's certified healthcare facility.
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LEMTRADA REMS Program Training

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Proper Storage and Administration

STORAGE OF LEMTRADA

- LEMTRADA is packaged in 12 mg/1.2 mL (10 mg/mL) single-dose vials.
- LEMTRADA vials should be stored at 2° to 8°C (36° to 46°F). Do not freeze or shake. Protect from light

PRIOR TO EACH TREATMENT COURSE OF LEMTRADA

- Confirm prescriber is certified and patient is enrolled and authorized to receive LEMTRADA.
- Counsel each patient about the risk for infusion reactions.
- Provide the patient with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to dispensing LEMTRADA.
- Administer corticosteroids immediately prior to LEMTRADA administration for the first 3 days of each treatment course.
- Ensure oral prophylaxis for herpes infection is available or has been prescribed to start on the first day of each treatment course. Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed.
- Monitor vital signs before and periodically during the infusion.

ADMINISTRATION OF LEMTRADA

1. Inspect vial for particulate matter/discoloration prior to use.
2. Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique.
3. Inject into 100 mL sterile 0.9% Sodium Chloride USP or 5% Dextrose in Water USP. Gently invert the bag to mix the solution.
4. Cover IV solution bag to protect from light.
5. Administer 12 mg/day over approximately 4 hours.
6. Do not administer as IV push or bolus.
7. If infusion is not well tolerated, infusion duration may be extended.
8. Use the LEMTRADA diluted product within 8 hours after dilution. LEMTRADA diluted product may be stored at room temperature (15° to 25°C) or refrigerated conditions (2° to 8°C). Protect from light.
9. Monitor patient vital signs before and periodically during the infusion, and provide appropriate symptomatic treatment for infusion reactions as needed.
10. Monitor patients for at least 2 hours after each LEMTRADA infusion or longer if clinically indicated.

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FOLLOWING THE CONCLUSION OF EACH LEMTRADA TREATMENT COURSE

- Complete a LEMTRADA REMS Infusion Checklist for each patient at the conclusion of each treatment course and fax it to the LEMTRADA REMS Program (1-855-557-2478) or submit online at www.LemtradaREMS.com within 5 business days of the last infusion.
- Return unused vials of LEMTRADA to Genzyme within 50 days of receipt of the LEMTRADA REMS Patient Authorization and Baseline Lab Form.

Adverse Event Reporting

Report suspected adverse events to Genzyme at Medical Information at 1-800-745-4447 (option 2) or to FDA at 1-800-FDA-1088 or www.FDA.gov/medwatch

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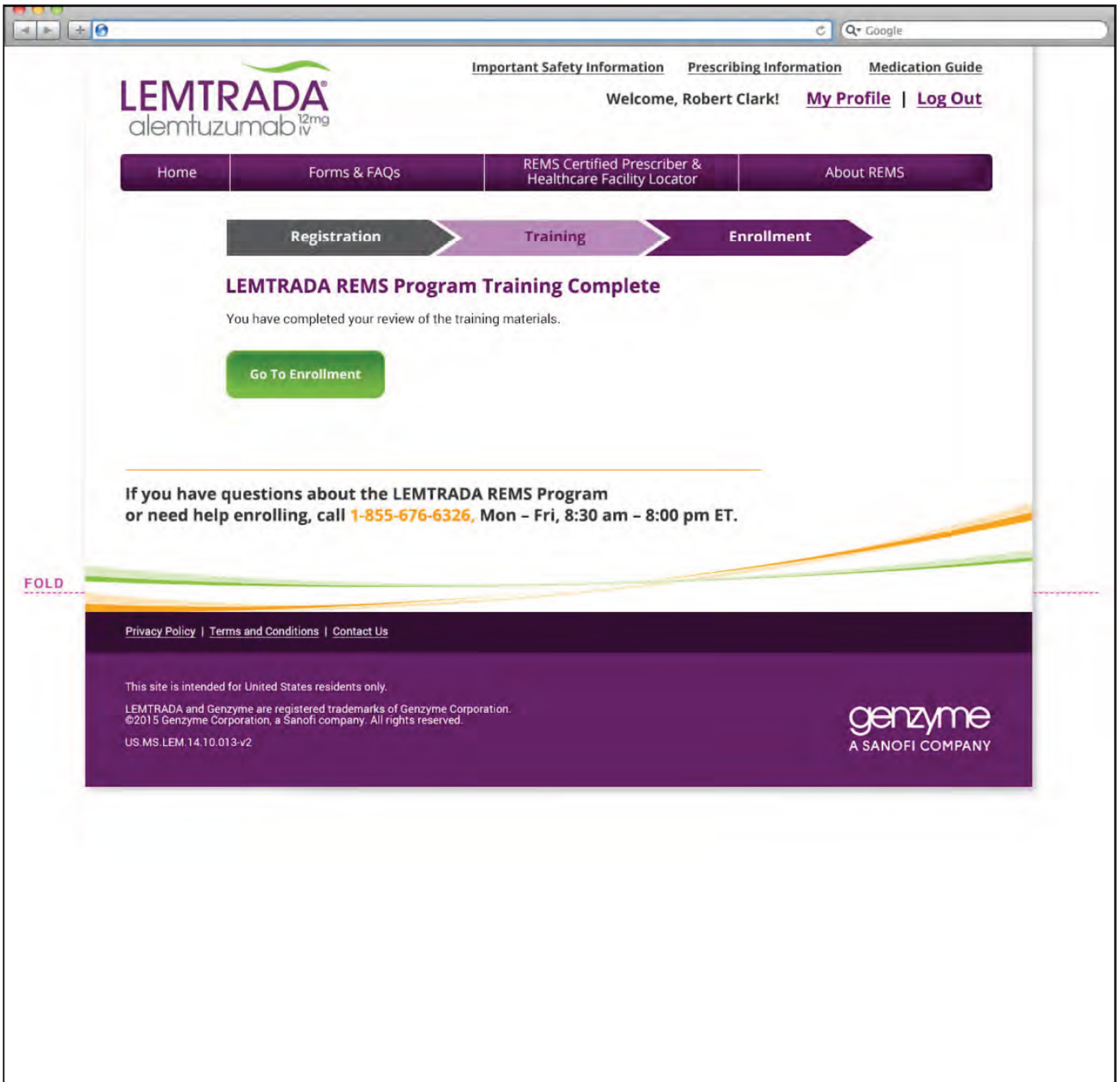

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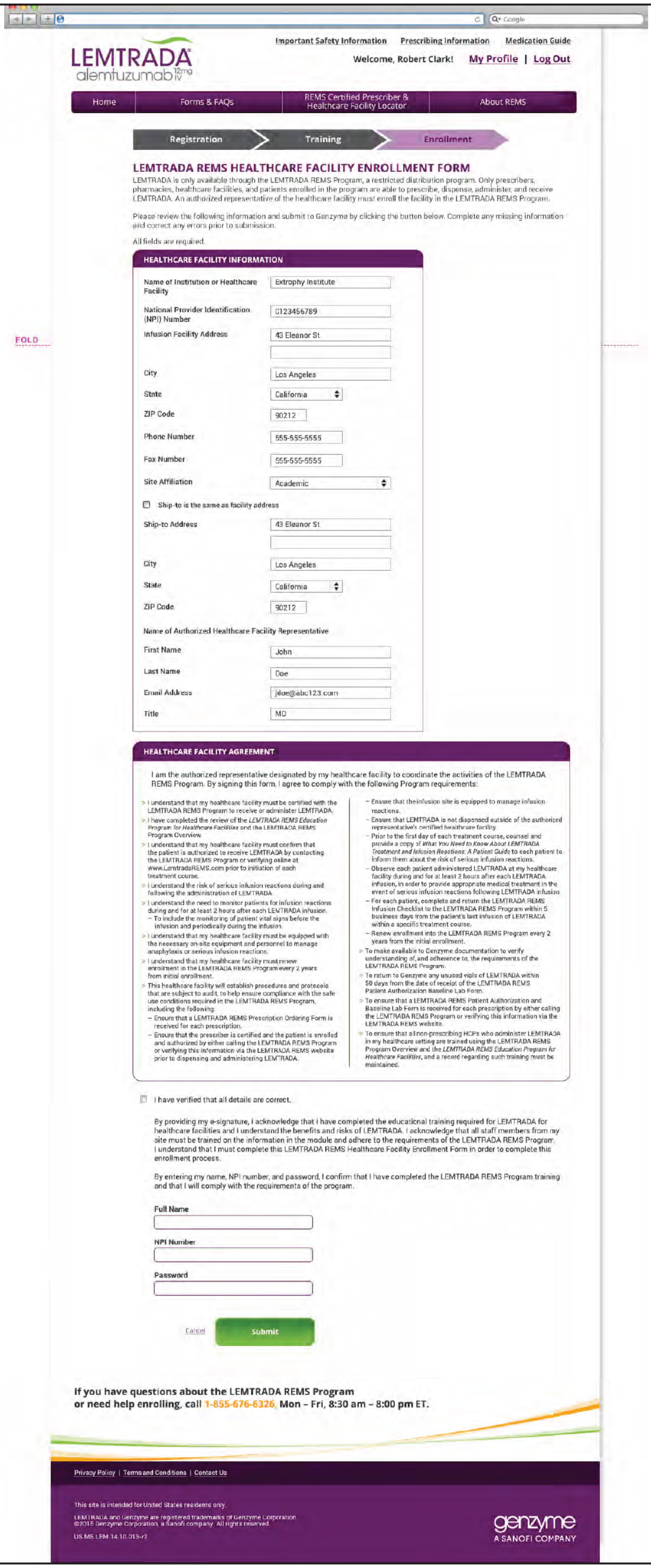
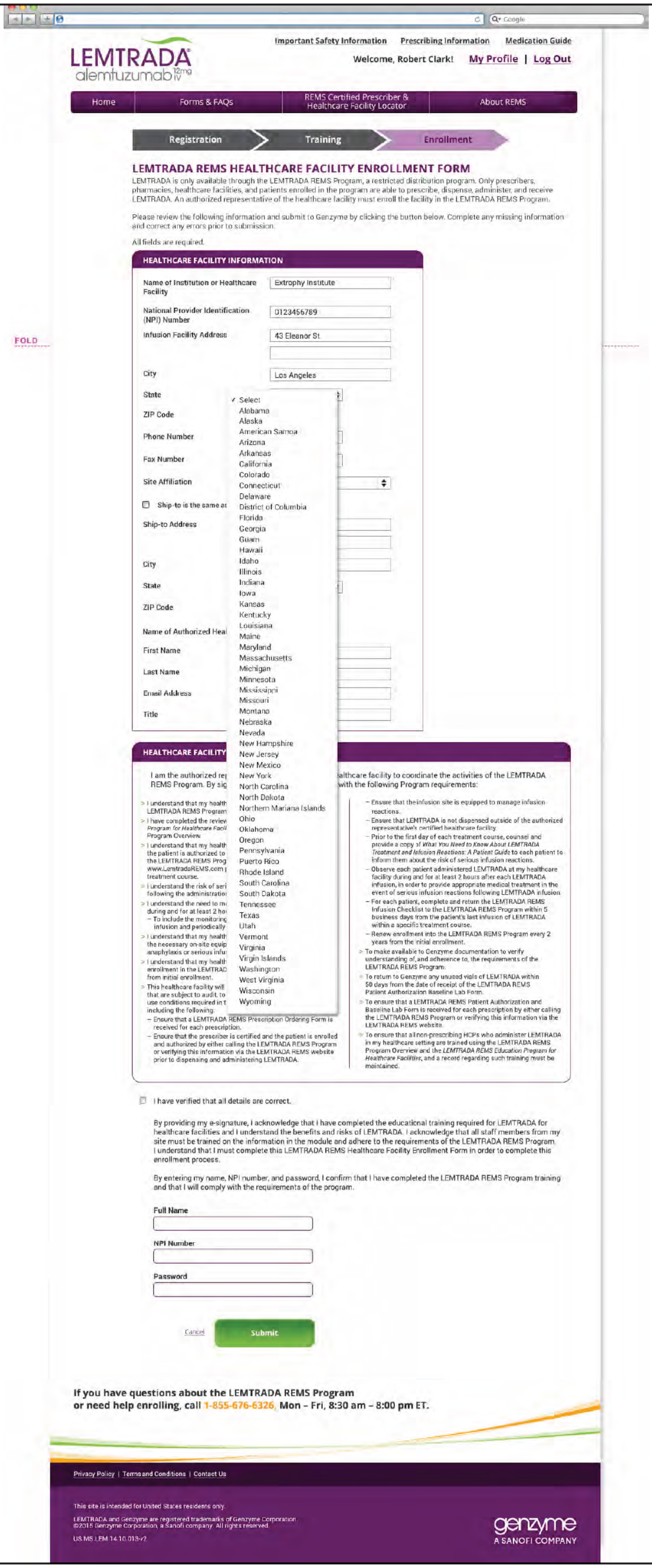


LEMTRADA REMS Desktop - HCF Training - Enrollment, State Dropdown 1



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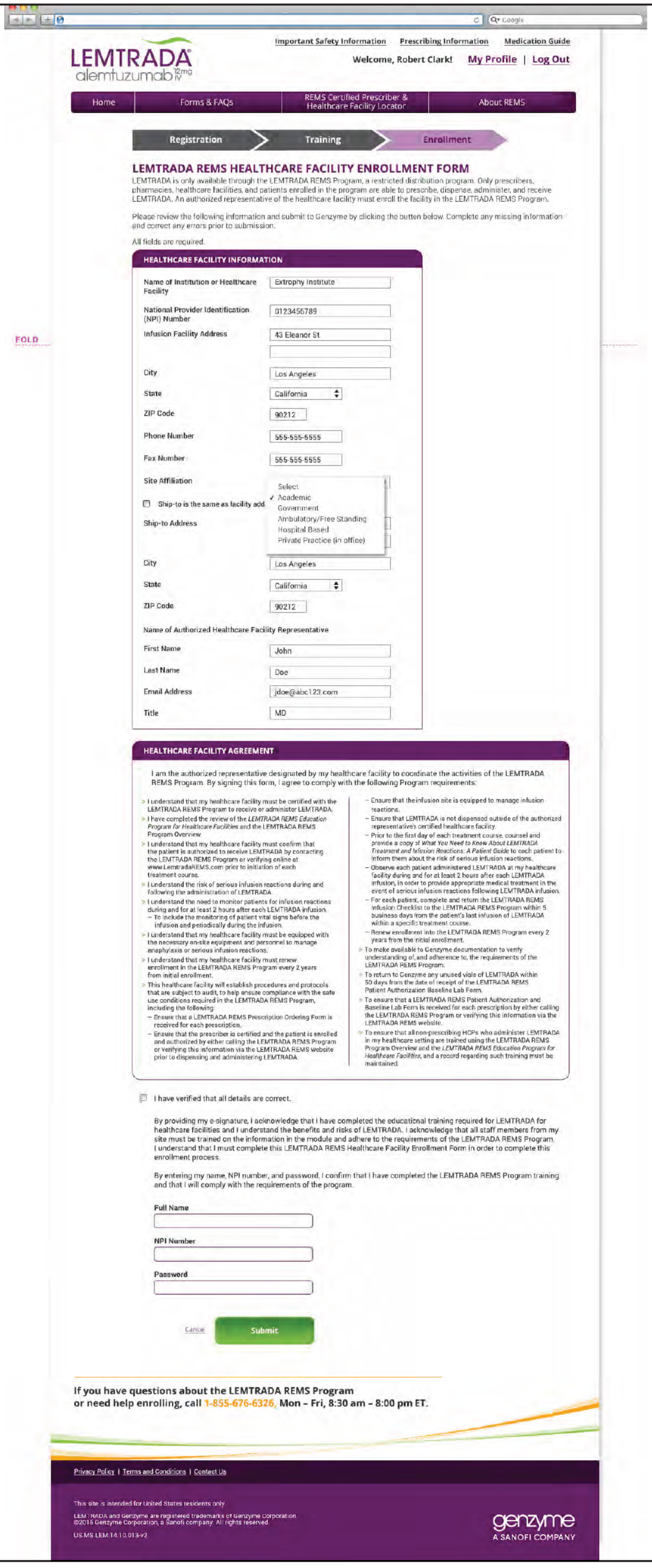

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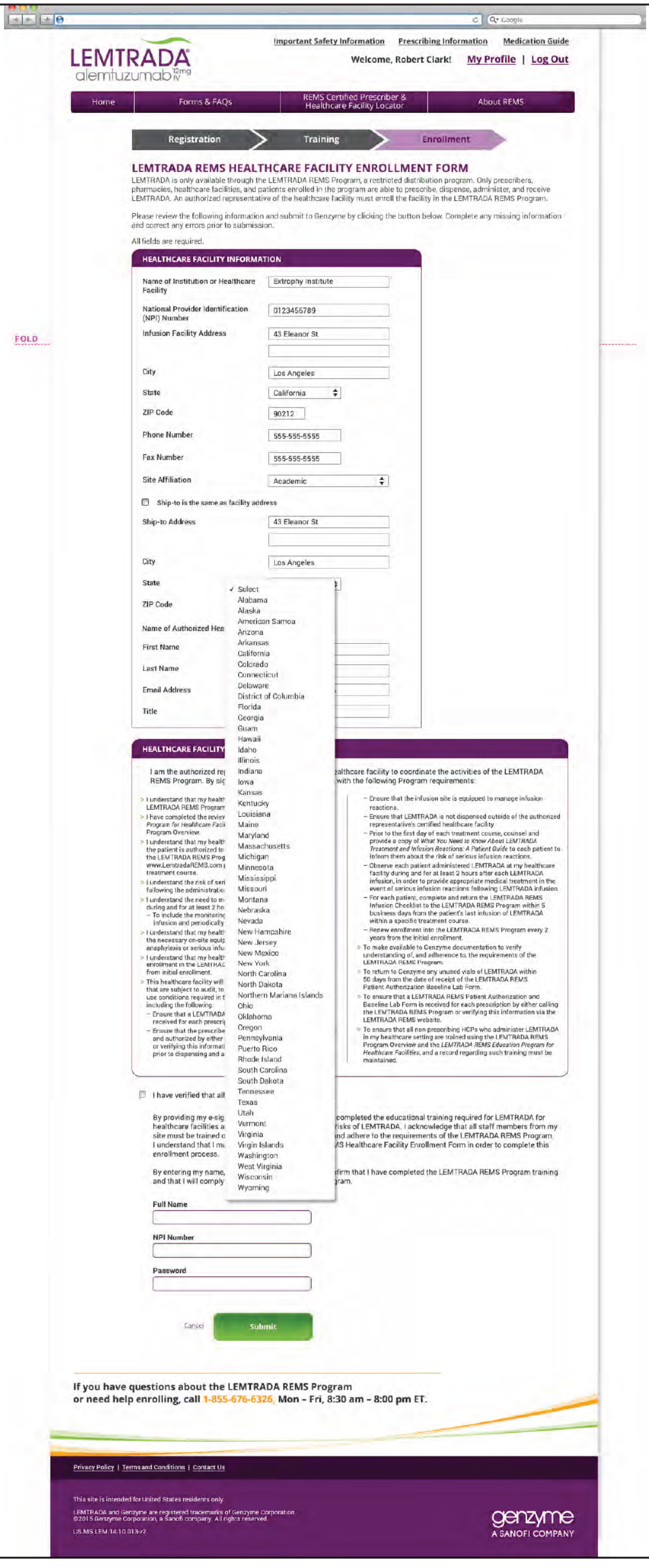

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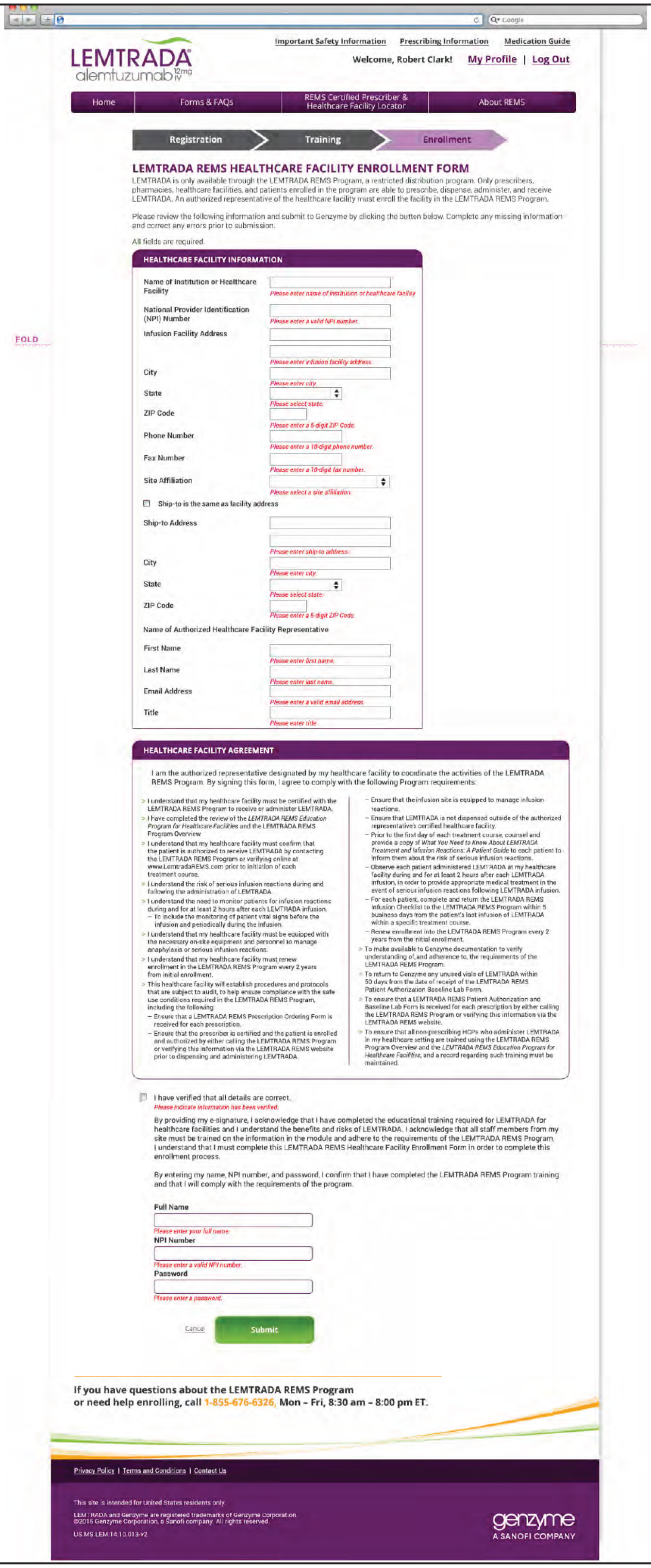

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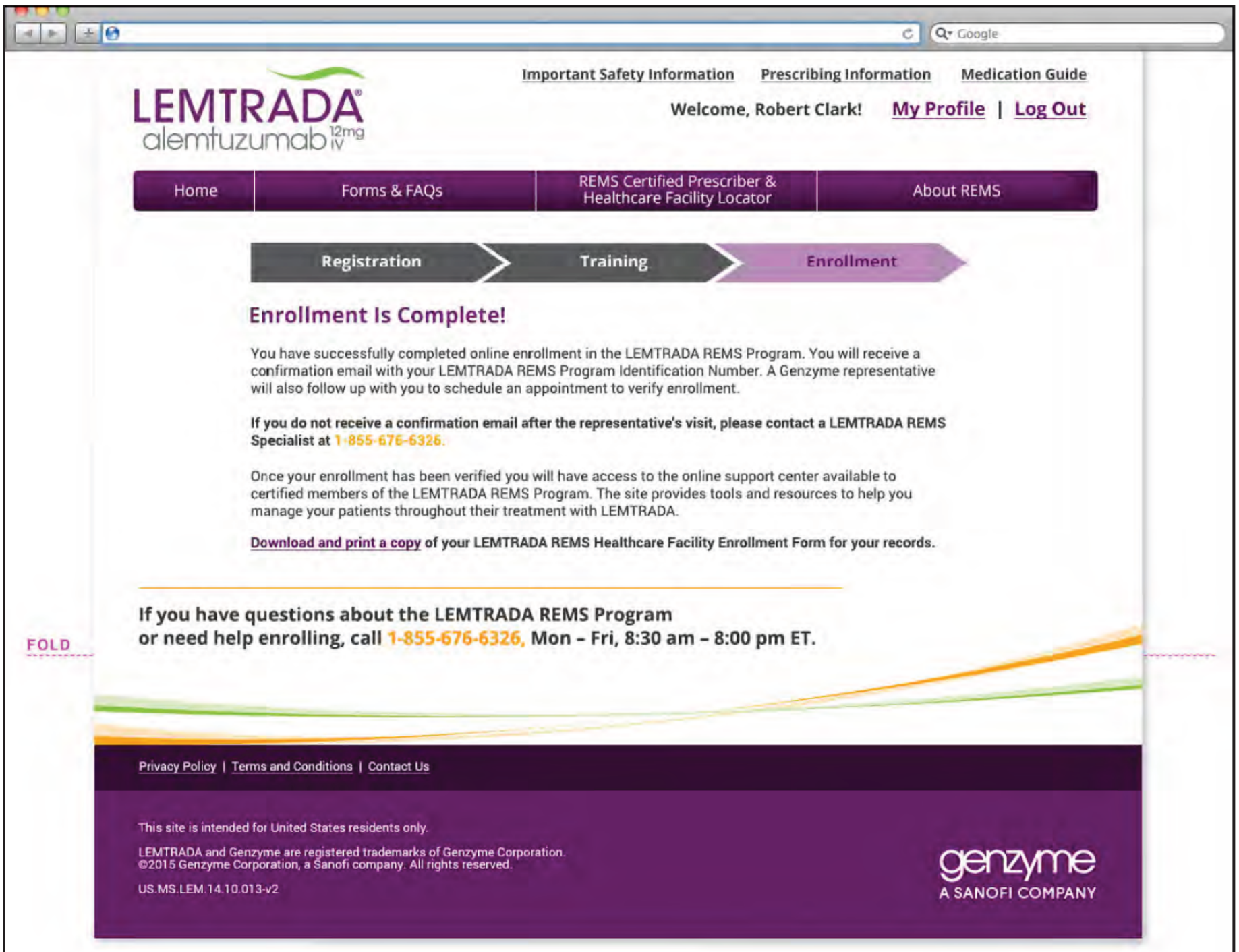
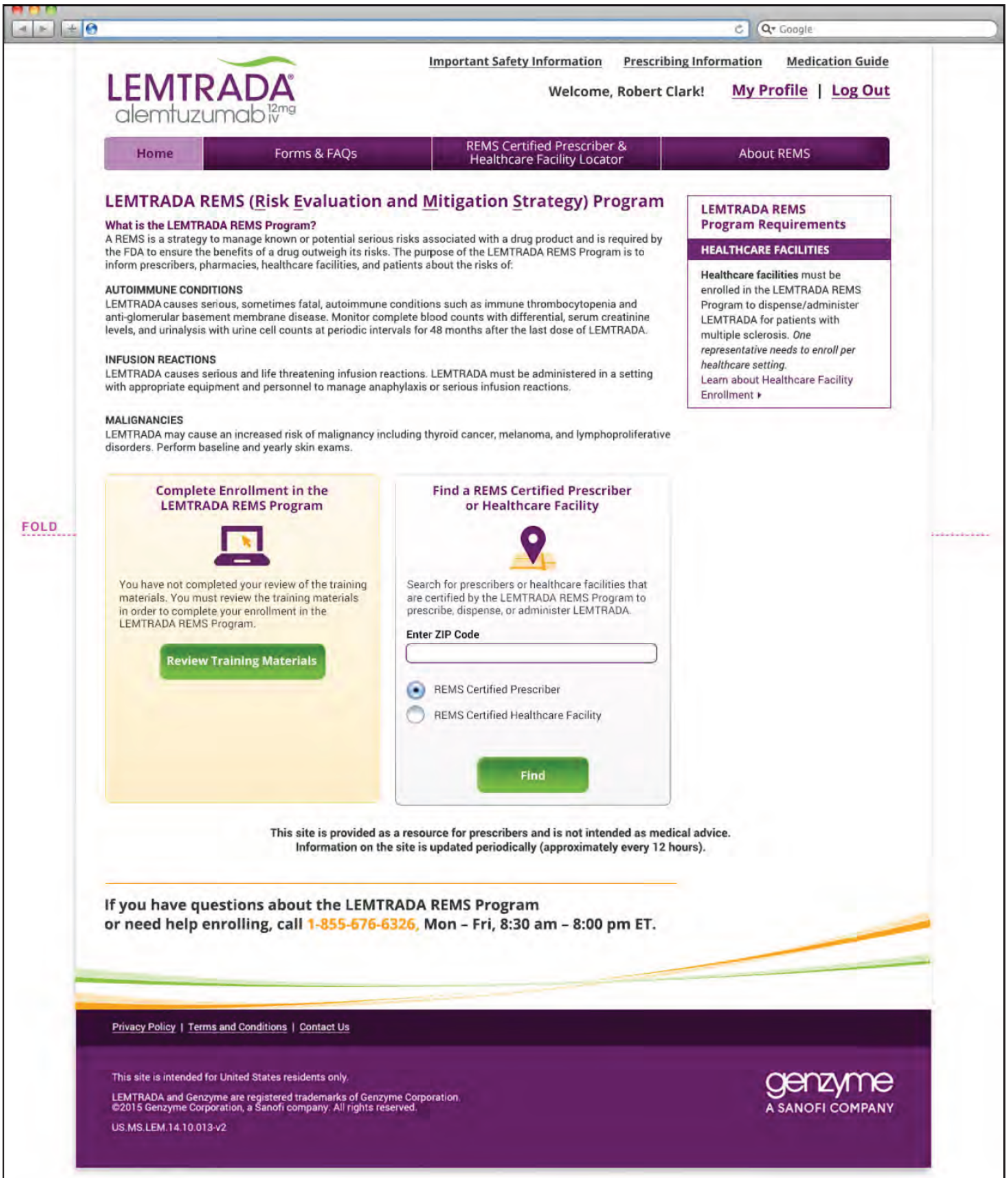


LEMTRADA REMS Desktop - HCF Training - Pre-REMS Cert, Training Incomplete



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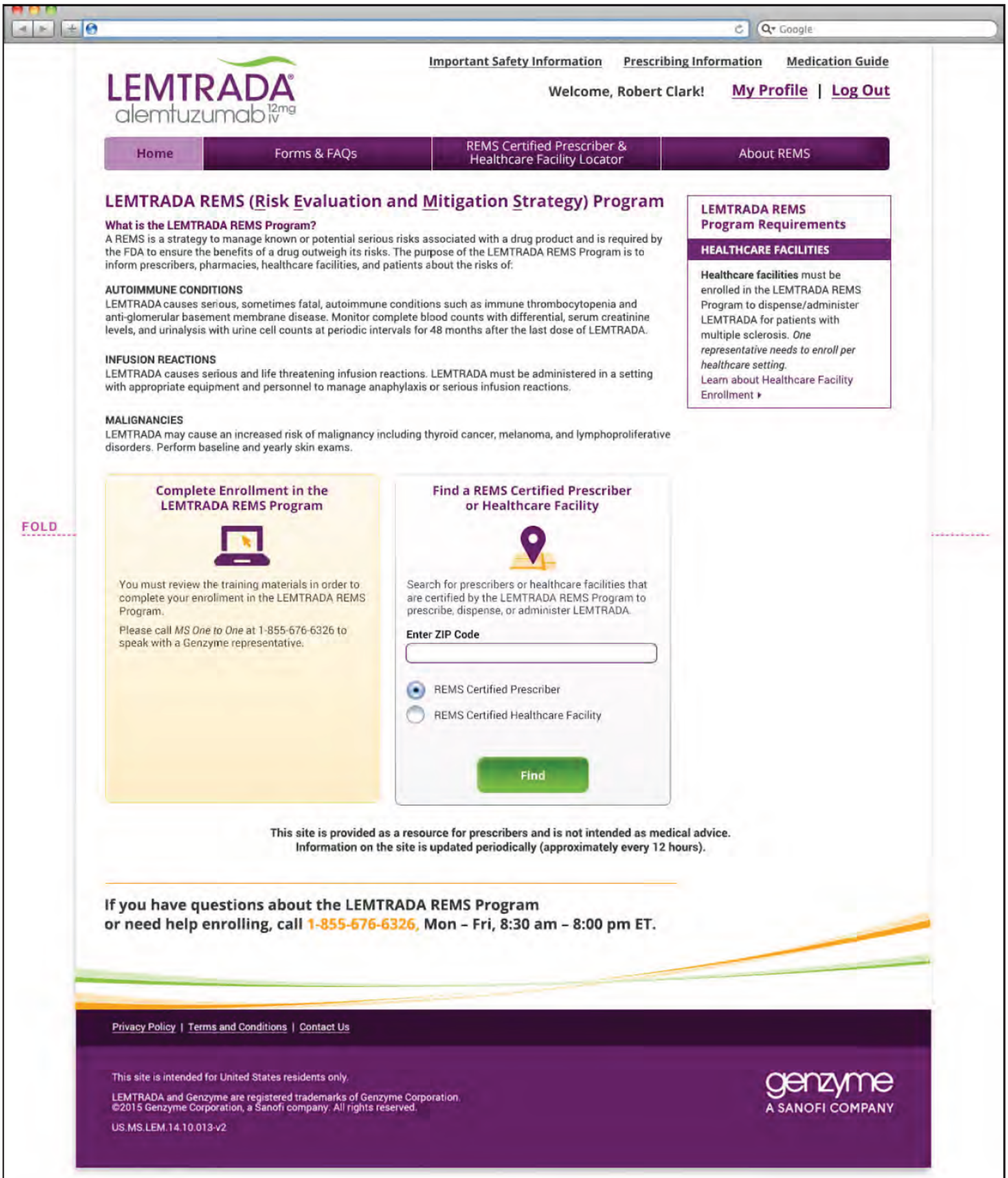

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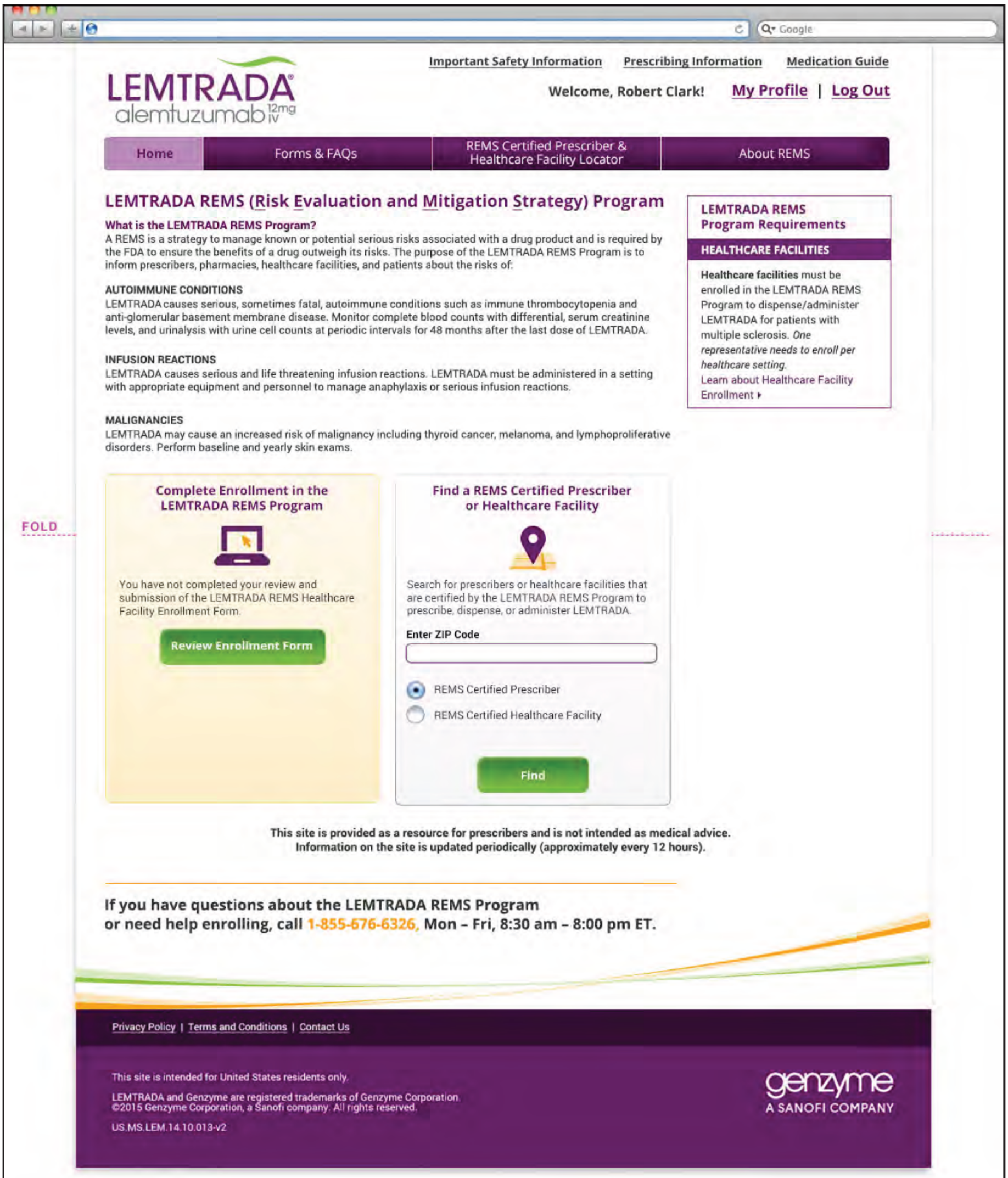

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- LEMTRADA is available only through a restricted distribution program. (5.4)

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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*Sections or subsections omitted from the full prescribing information are not listed

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REMS CERTIFIED HEALTHCARE FACILITY DASHBOARD PAGES

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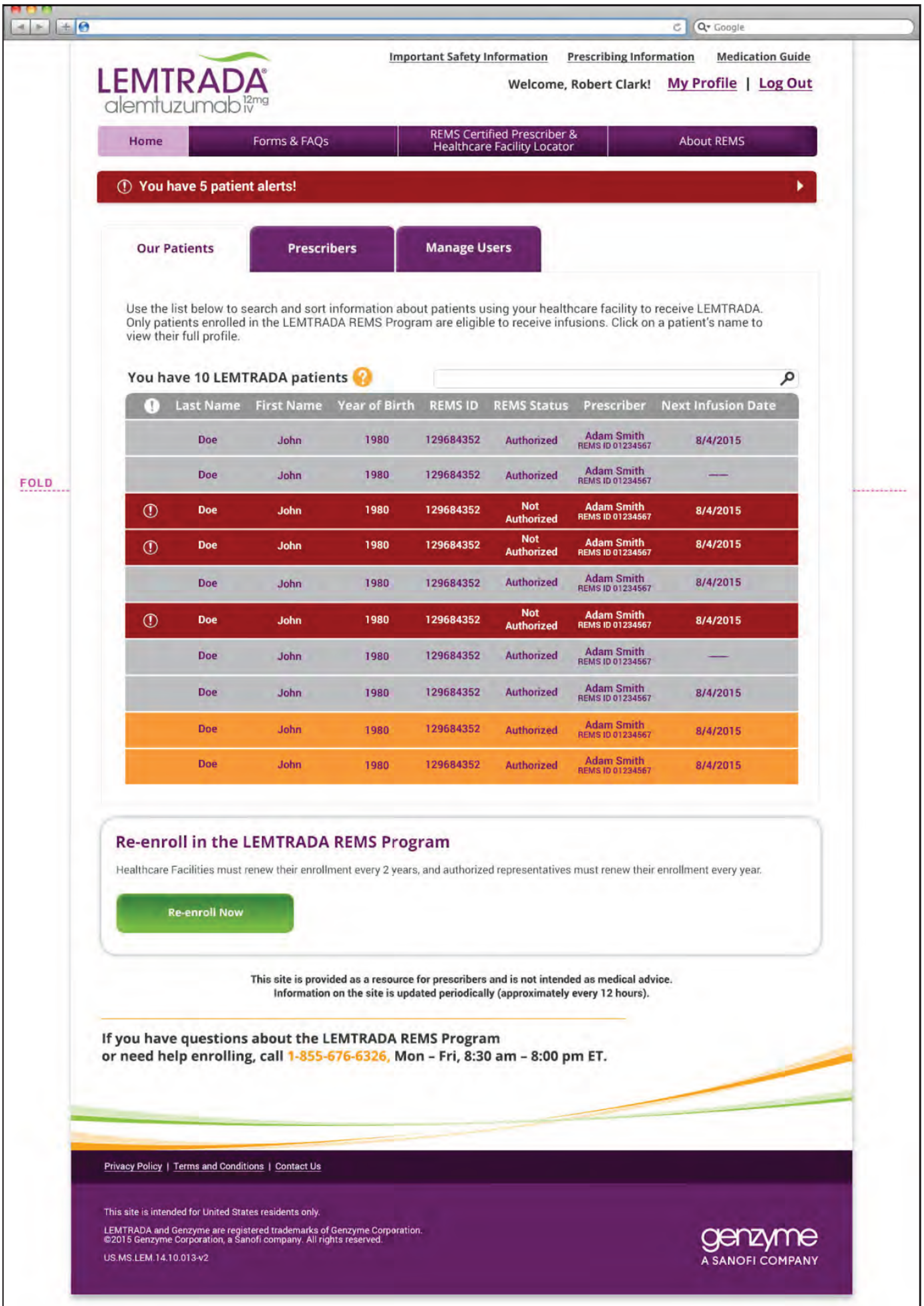

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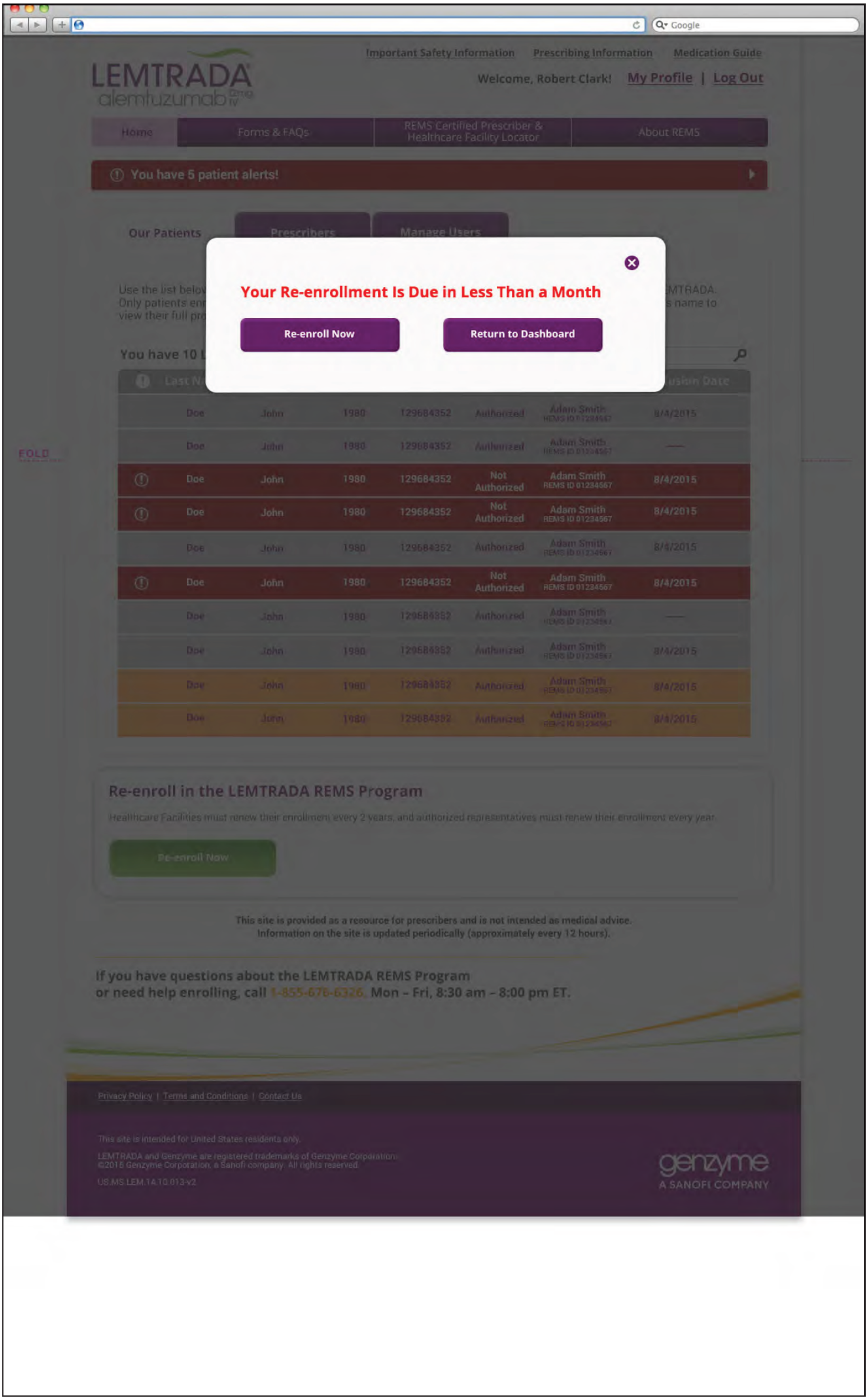
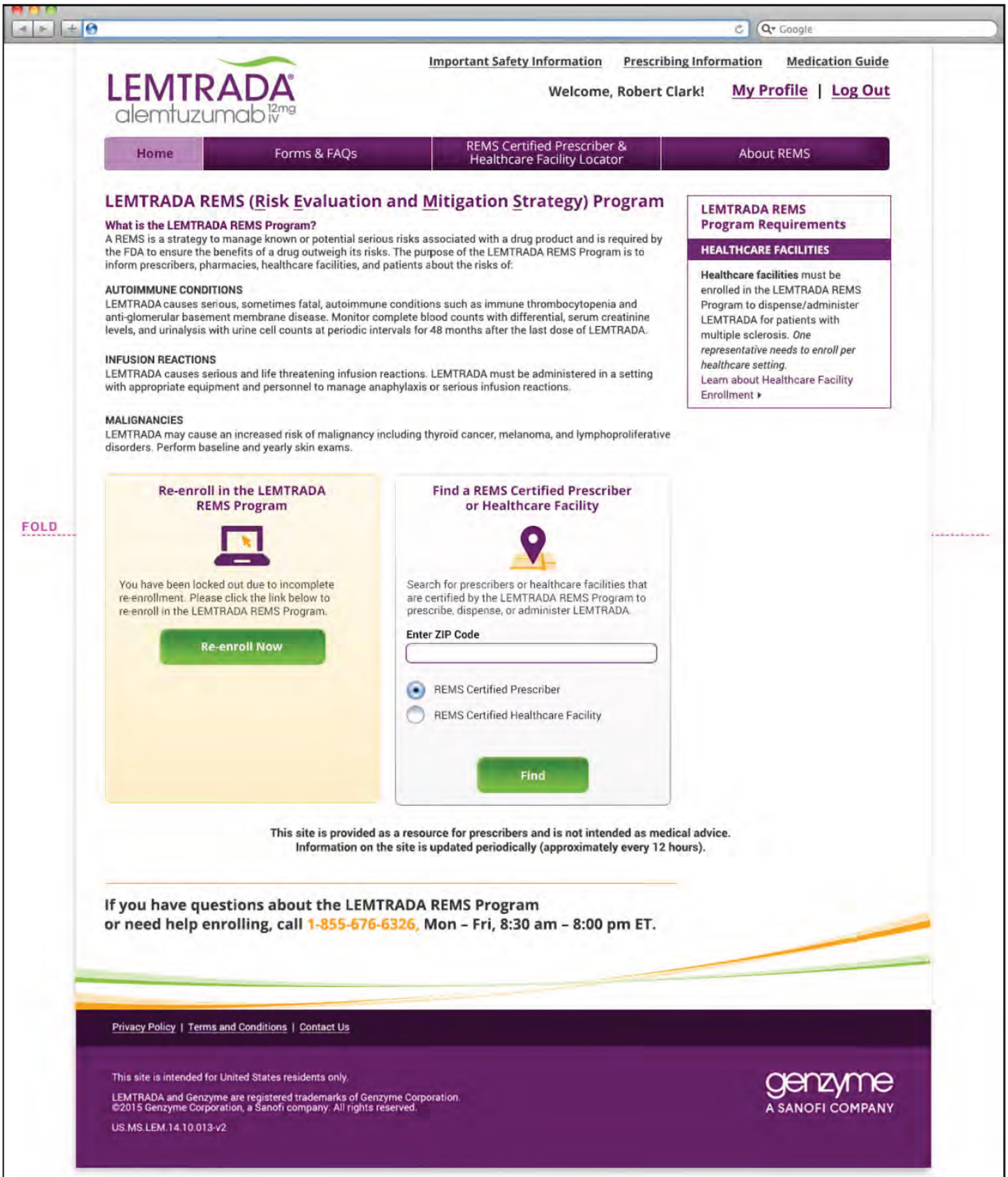
LEMTRADA REMS Desktop - HCF Dashboard - Patient List, Alert On PopUp Re-Enrollment Message



LEMTRADA REMS Desktop - HCF Dashboard - Re-enrollment Lockout



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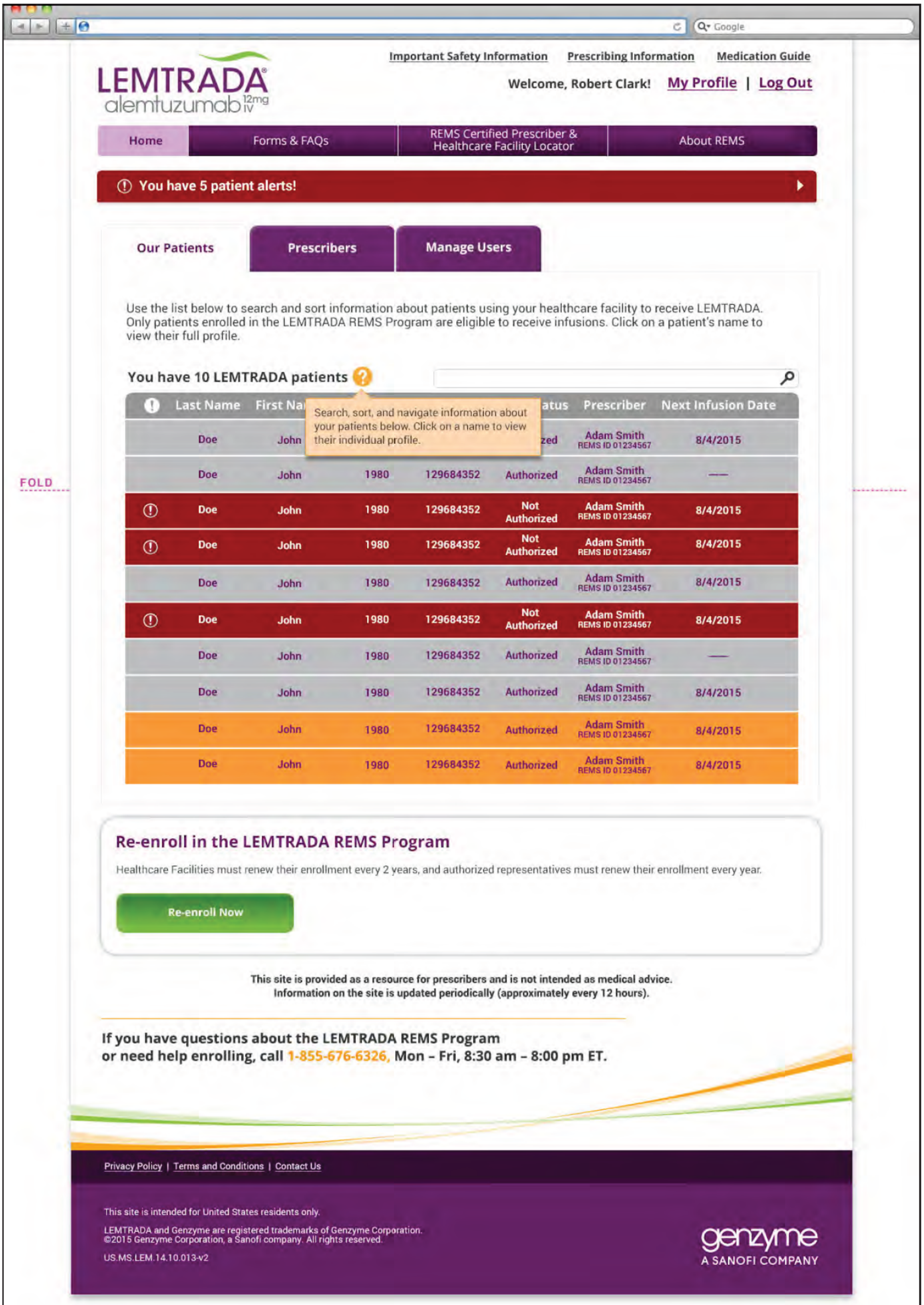
LEMTRADA REMS Desktop - HCF Dashboard - Patient List, Tool Tip Expanded



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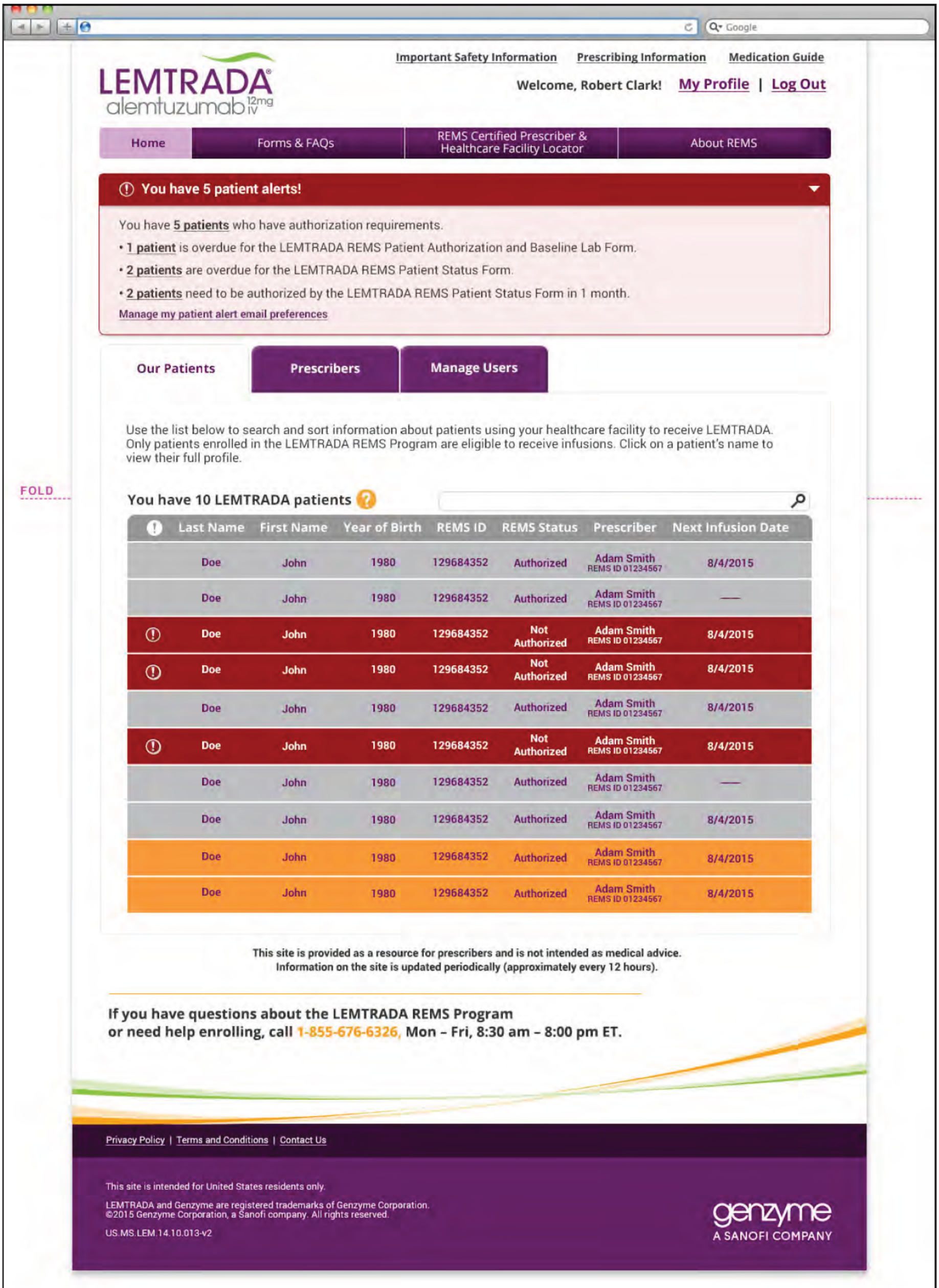
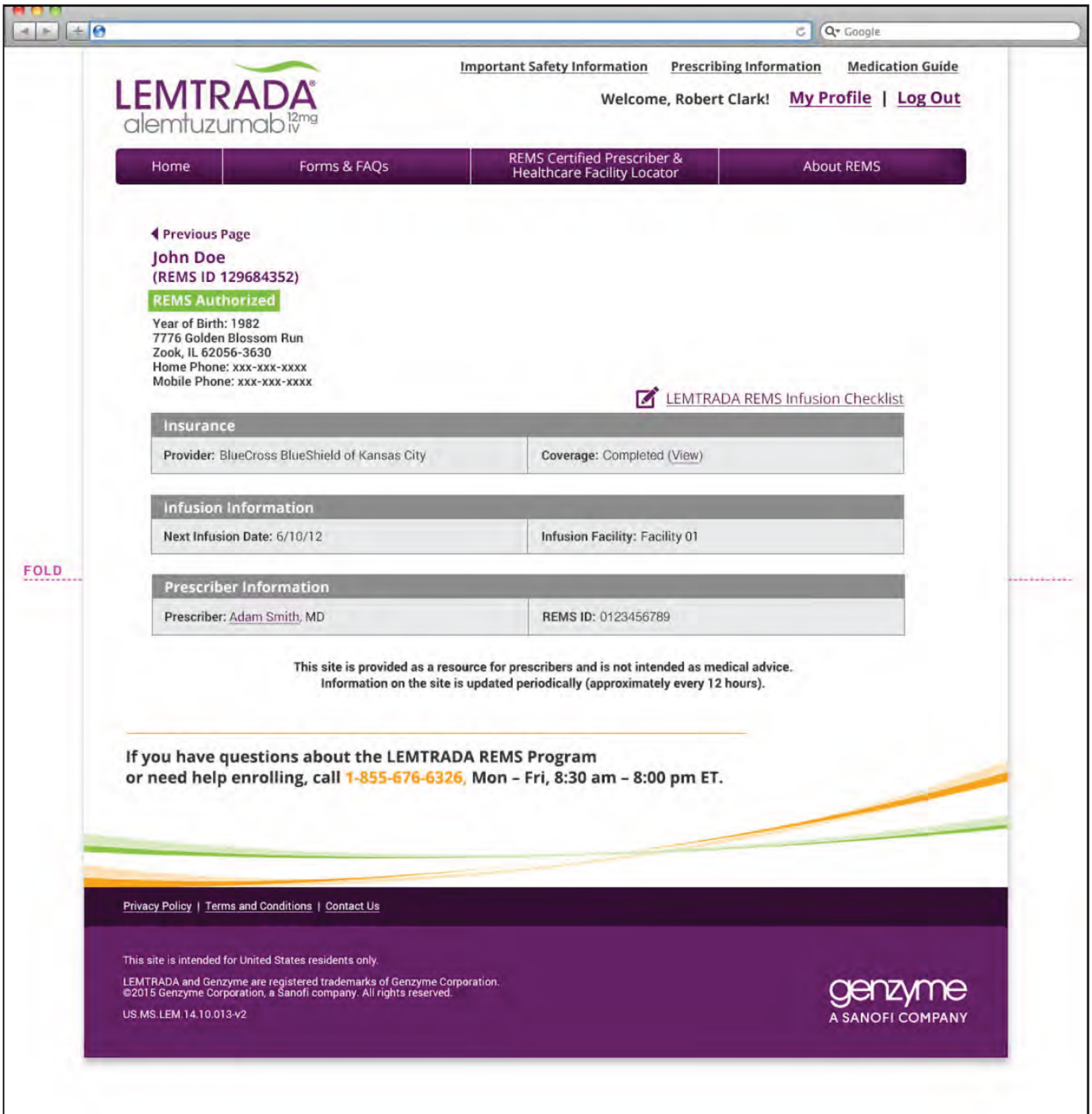
LEMTRADA REMS Desktop - HCF Dashboard - Patient List, Alert Expanded



LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, REMS Authorized, Before 1st Infusion



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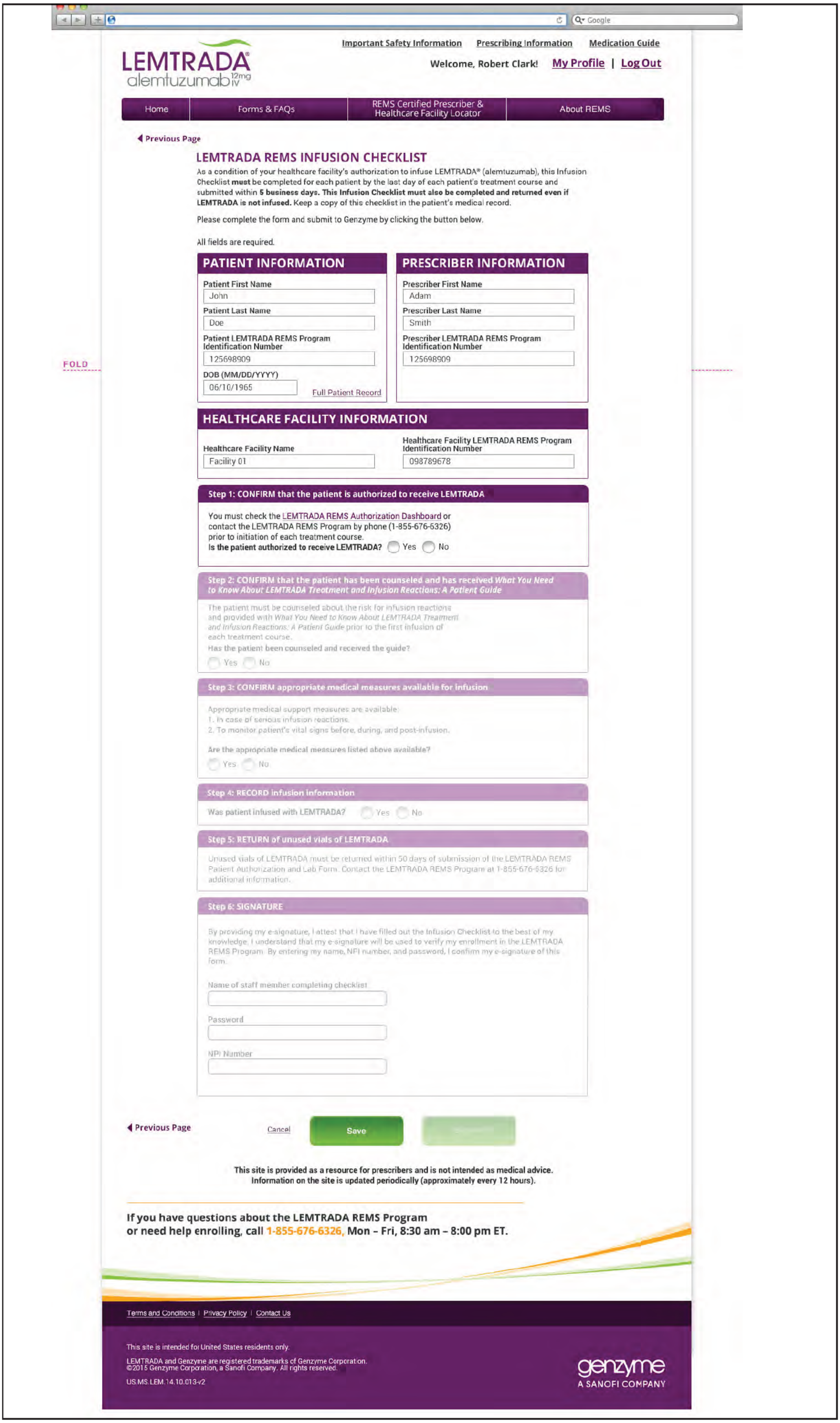
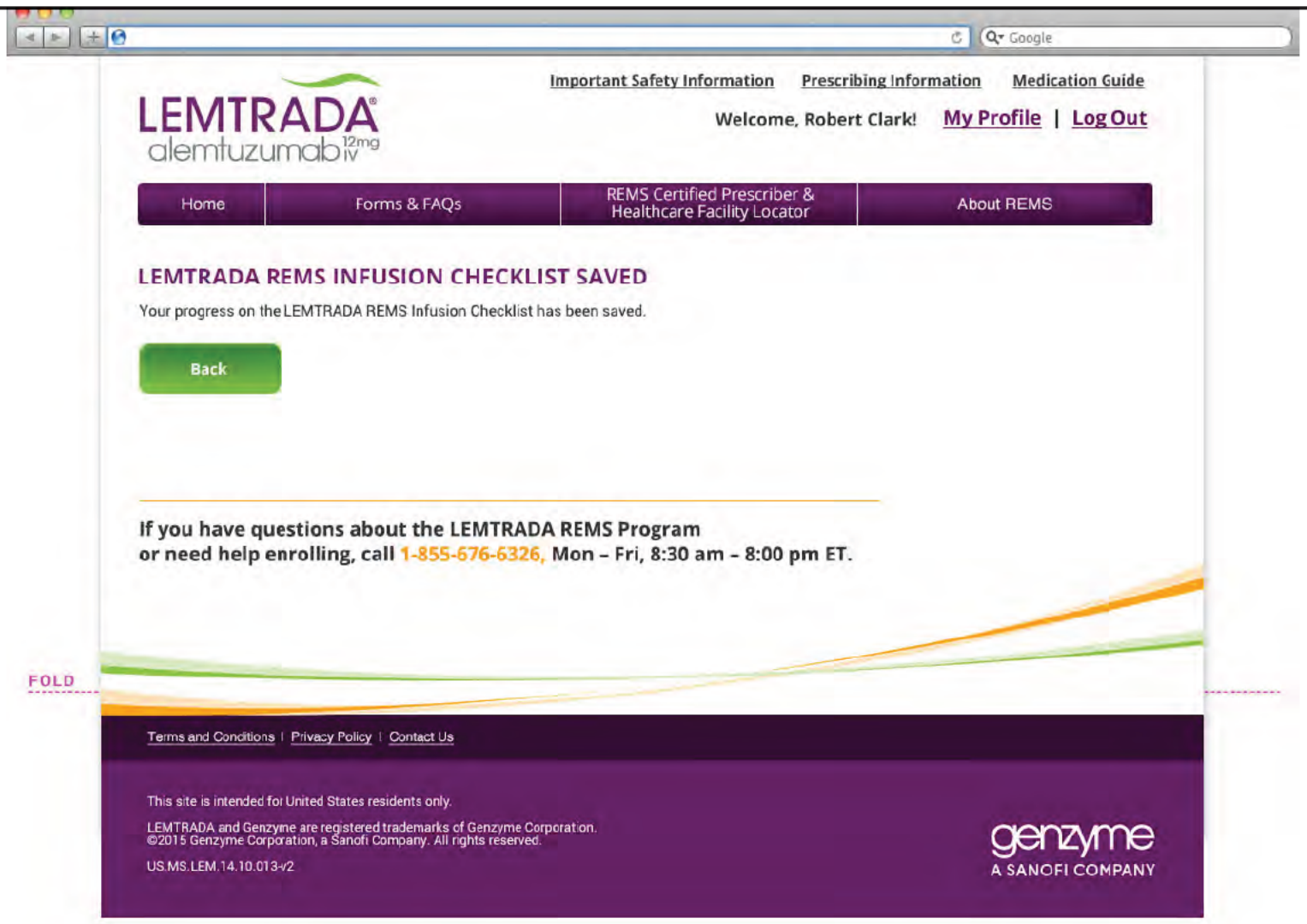


LEMTRADA REMS Desktop - Infusion Checklist Form - Save Confirmation



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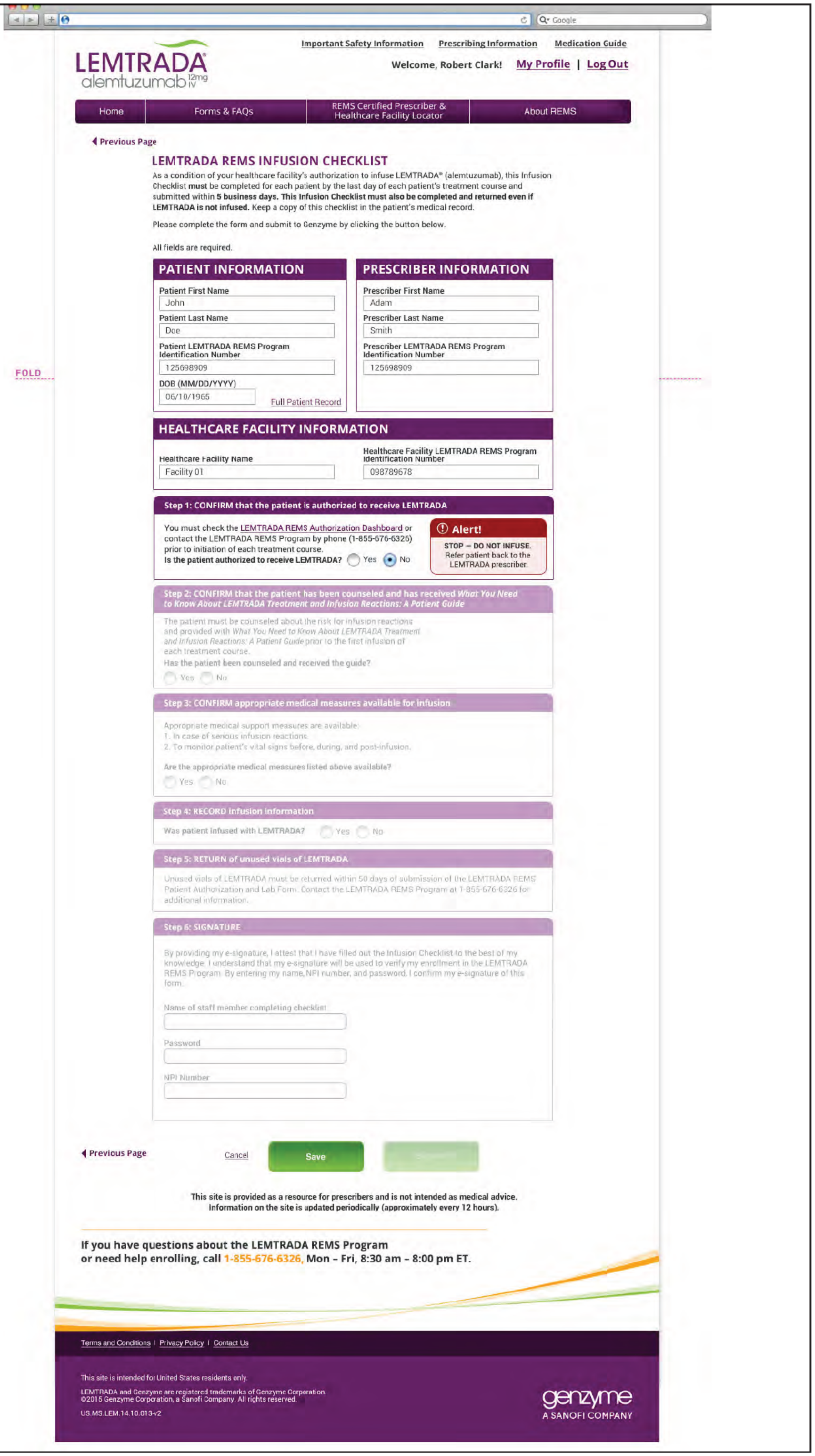

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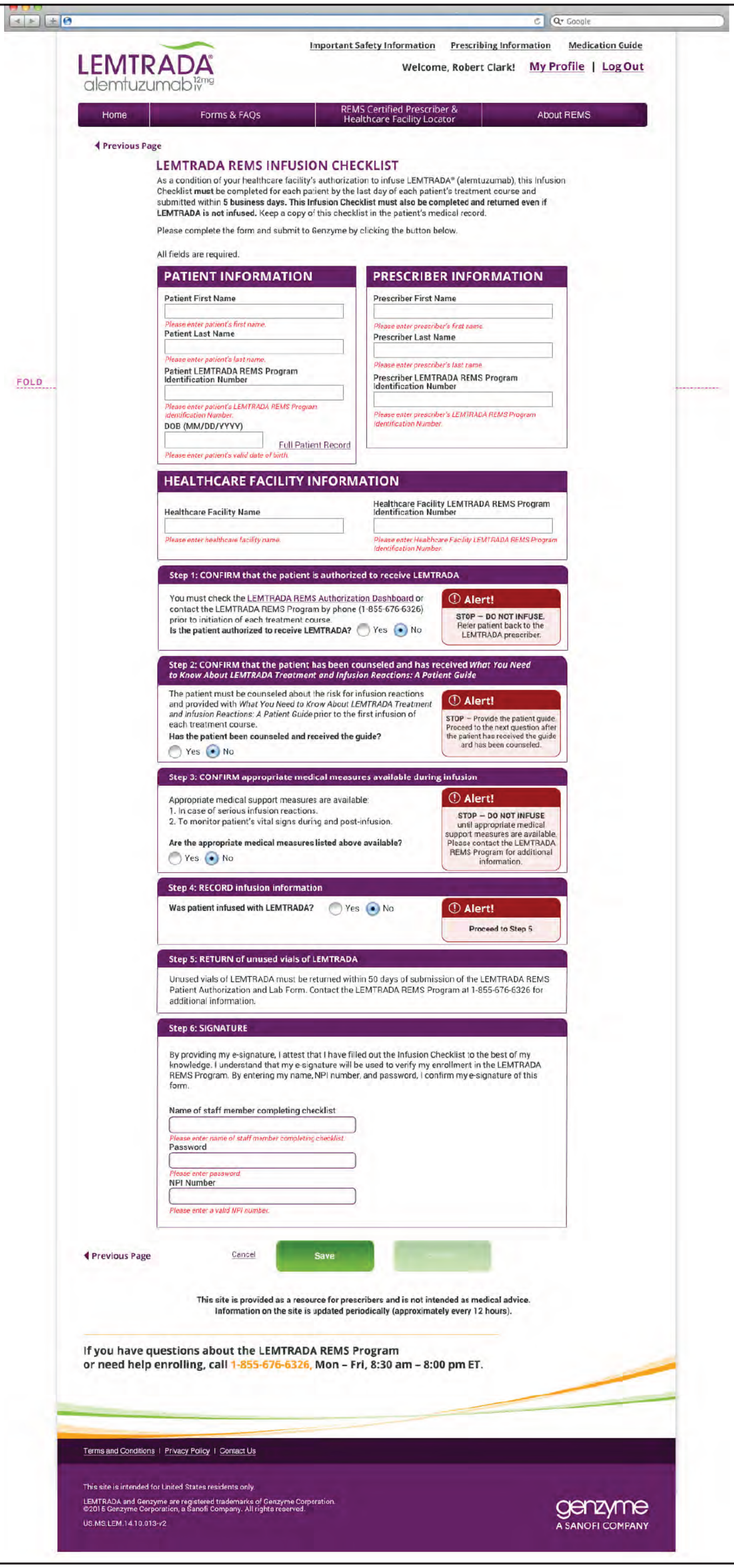
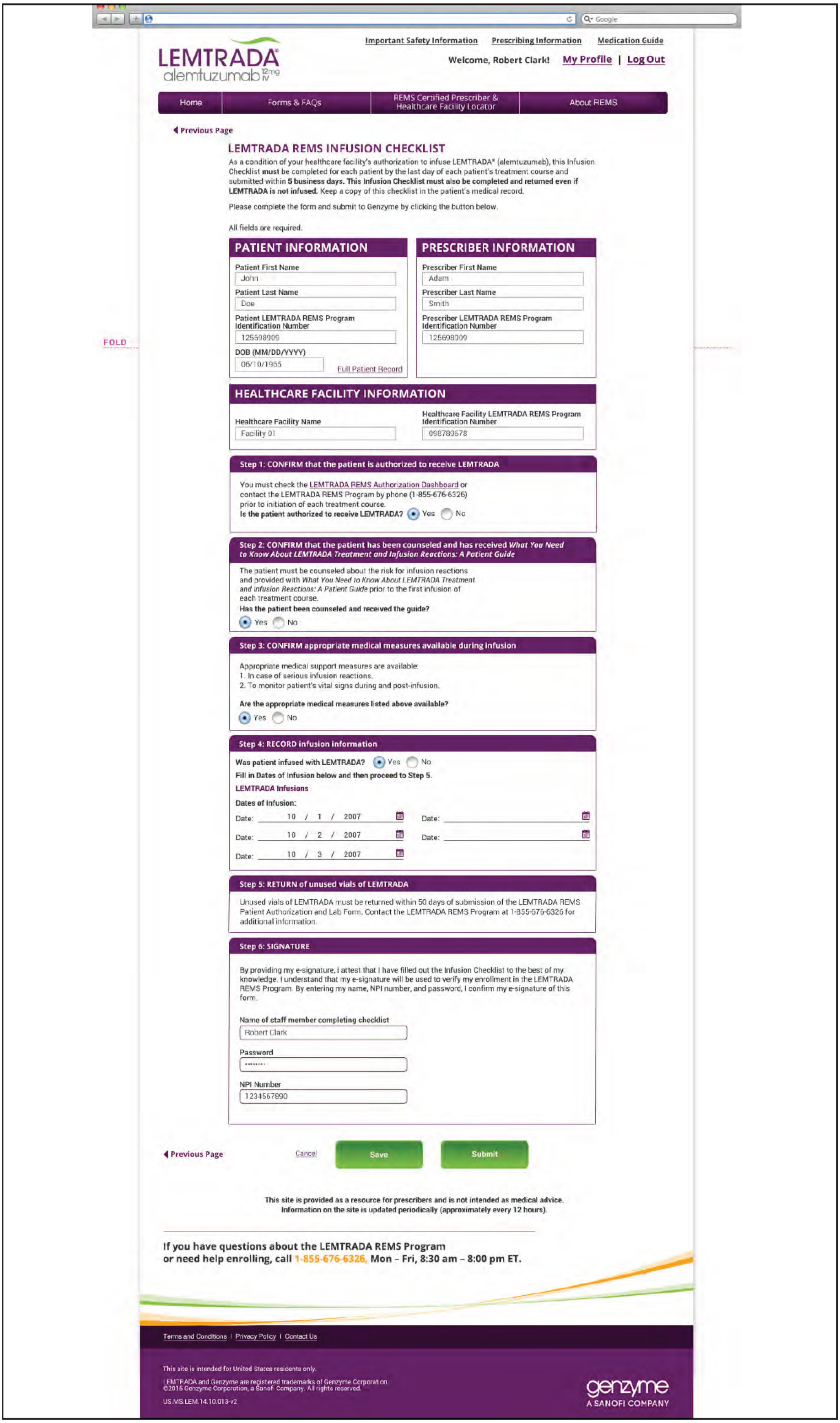
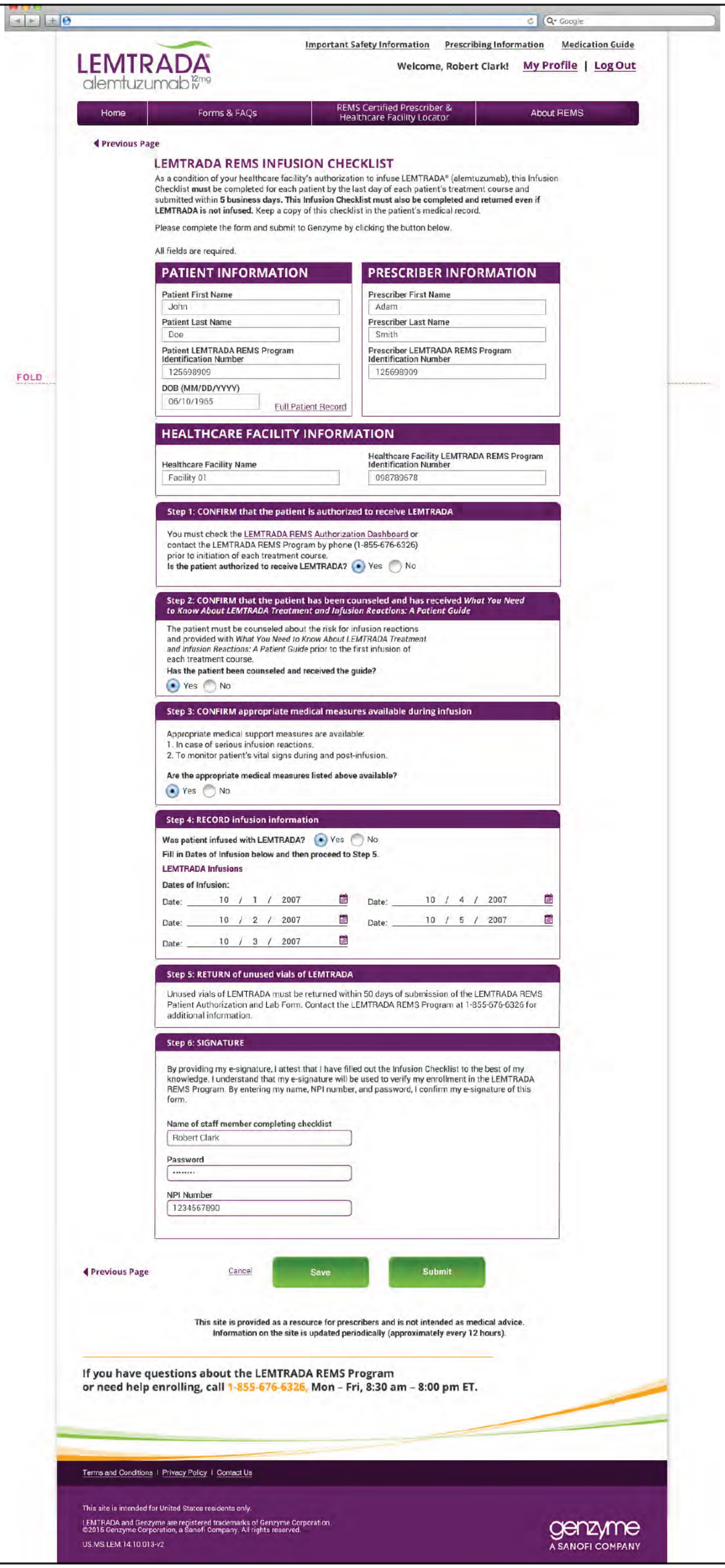


Reference ID: 3821900

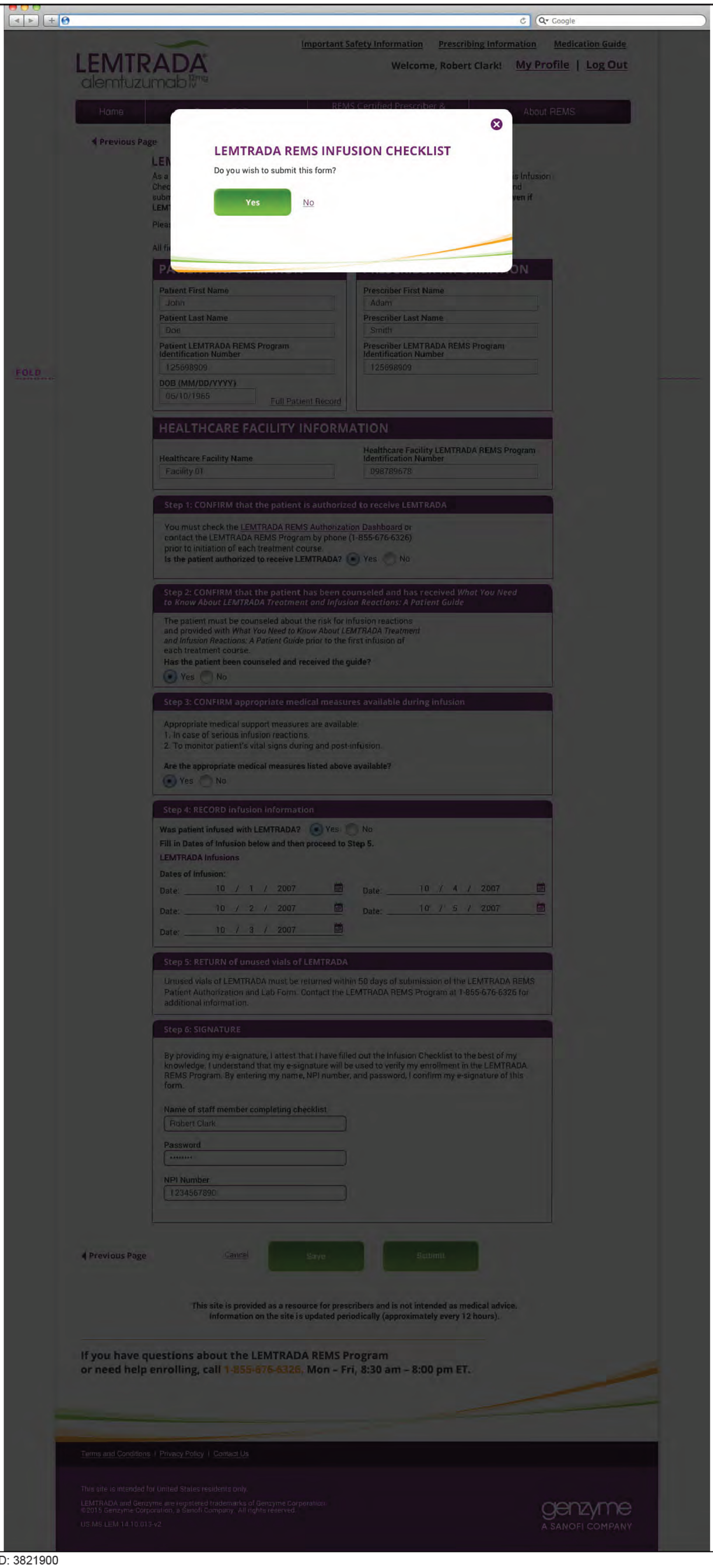
LEMTRADA REMS Desktop - Infusion Checklist Form - "Yes" Selected Save



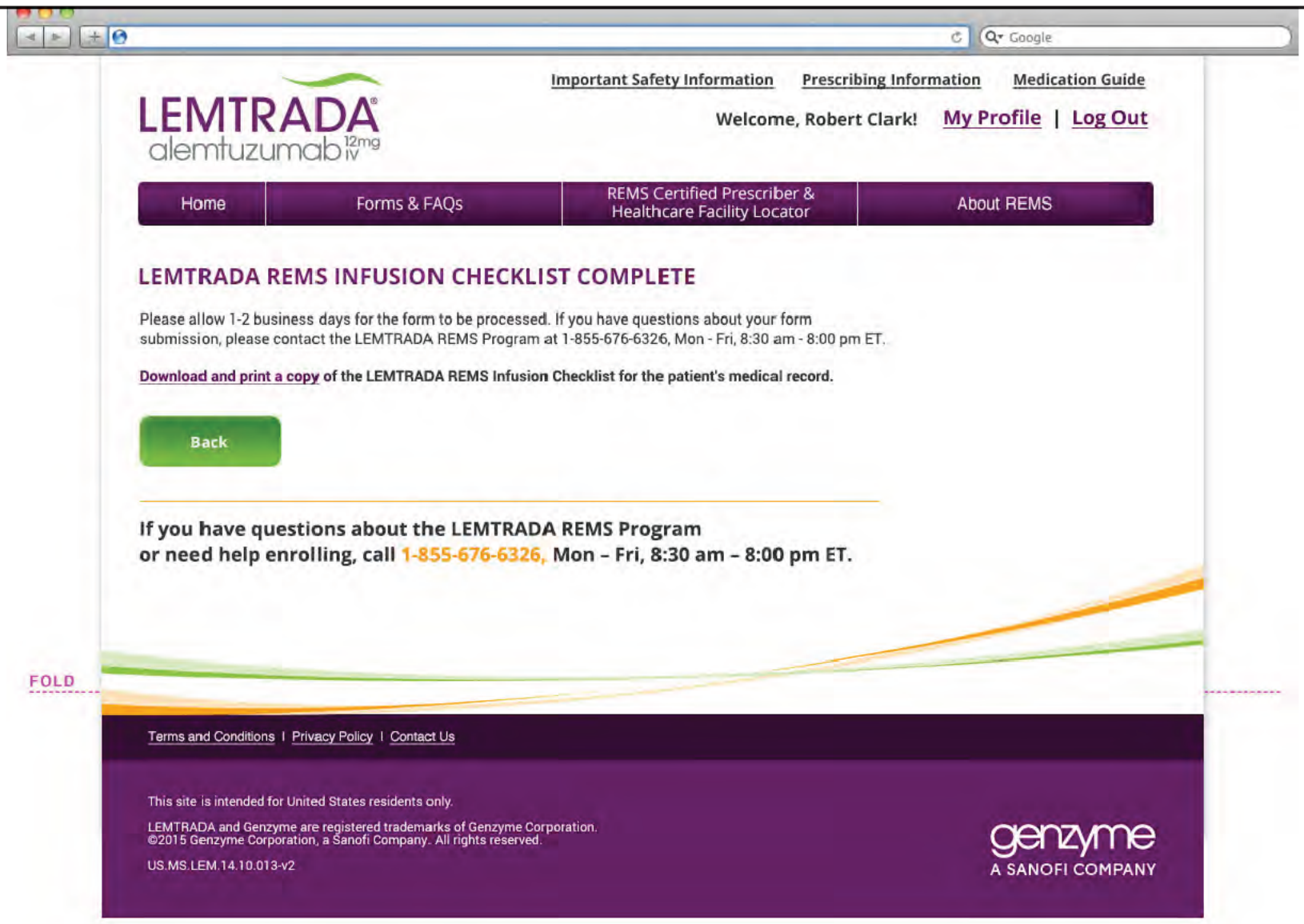
LEMTRADA REMS Desktop - Infusion Checklist Form - "Yes" Selected, Infusion Dates Added Save



LEMTRADA REMS Desktop - Infusion Checklist Form - Submit Confirmation



LEMTRADA REMS Desktop - Infusion Checklist Form - Confirmation

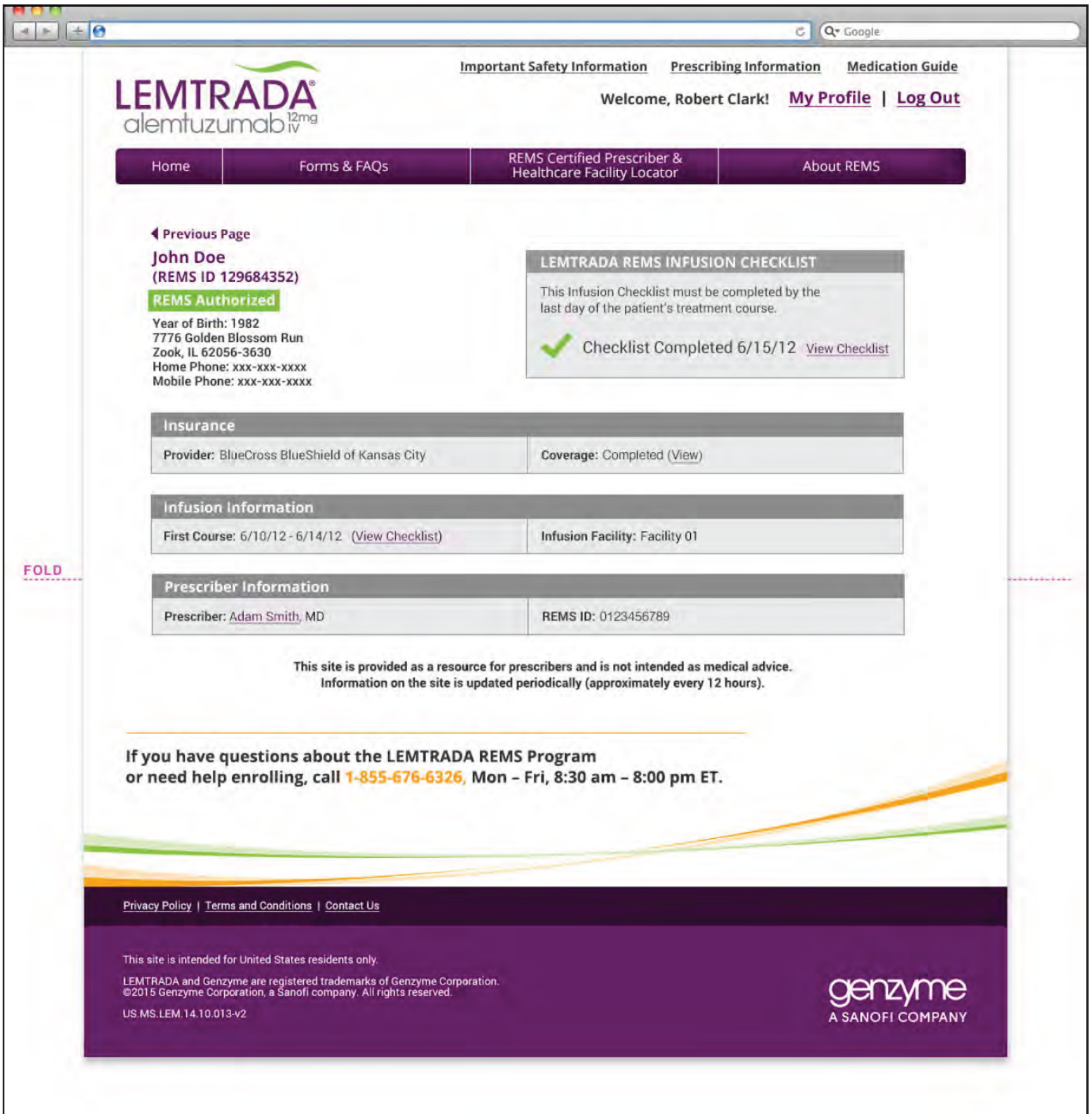


LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, Checklist Saved



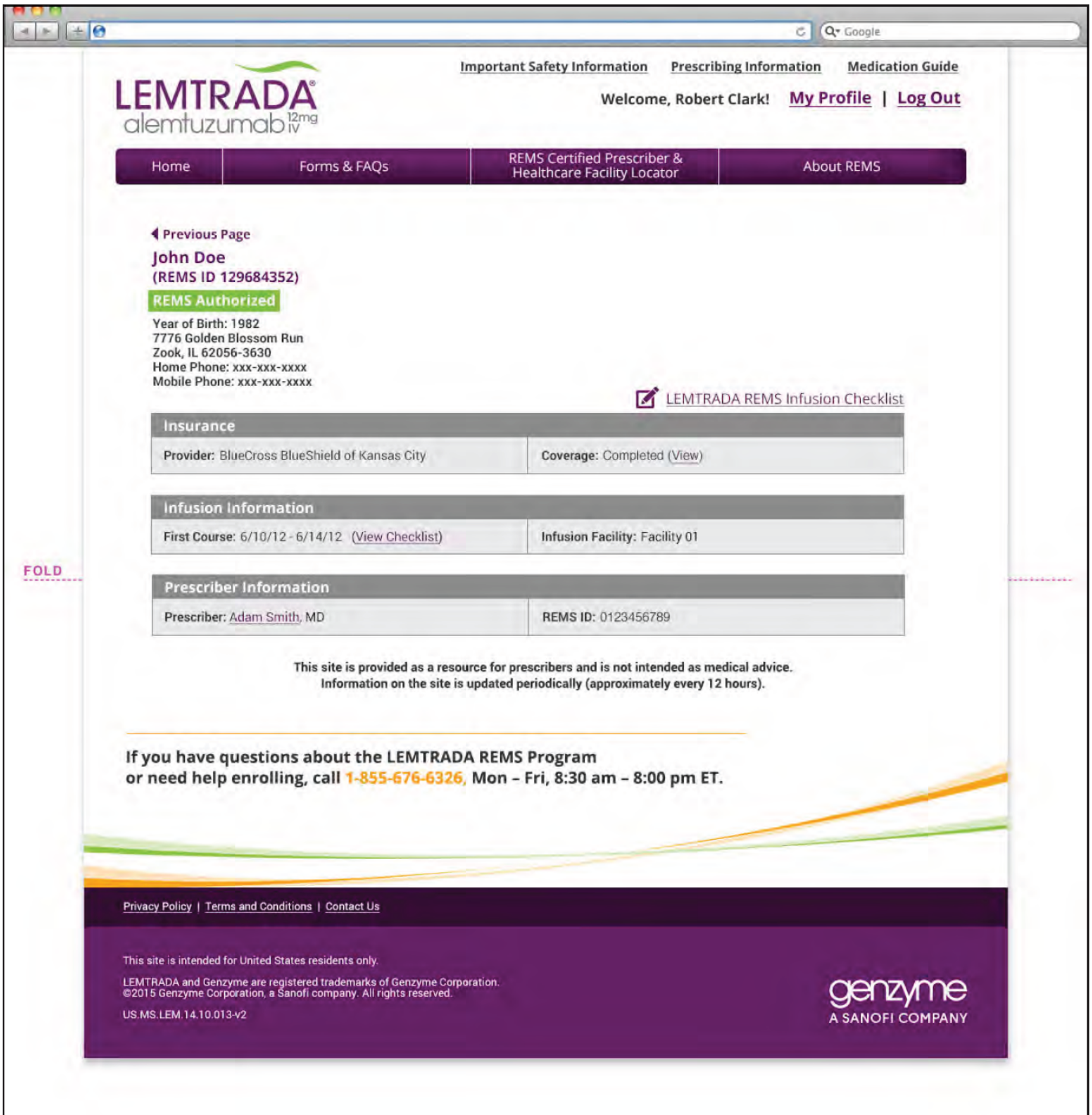
FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, 1st Infusion Checklist Completed



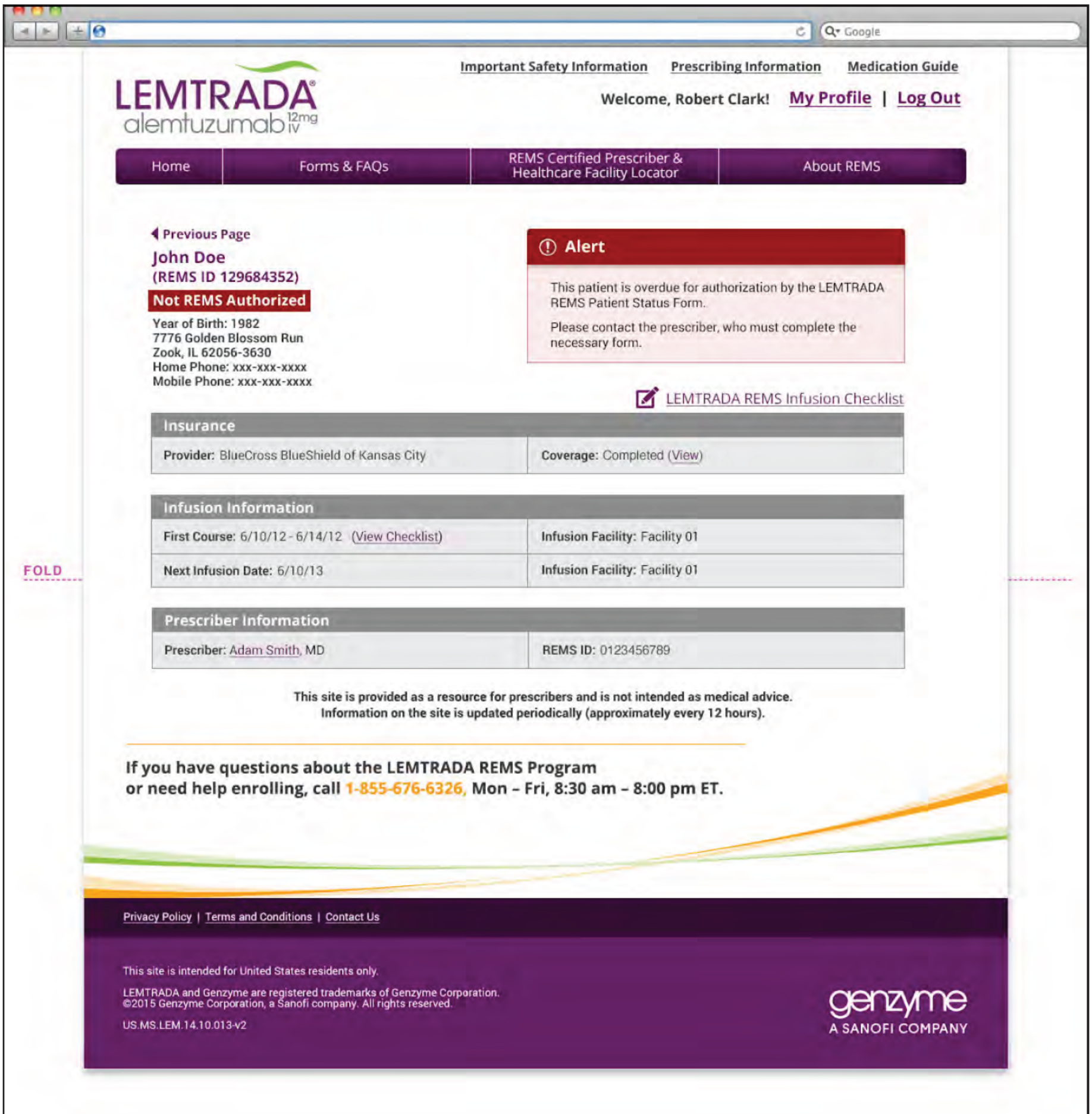
FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, After 1st Infusion



FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, Patient Status Form Alert



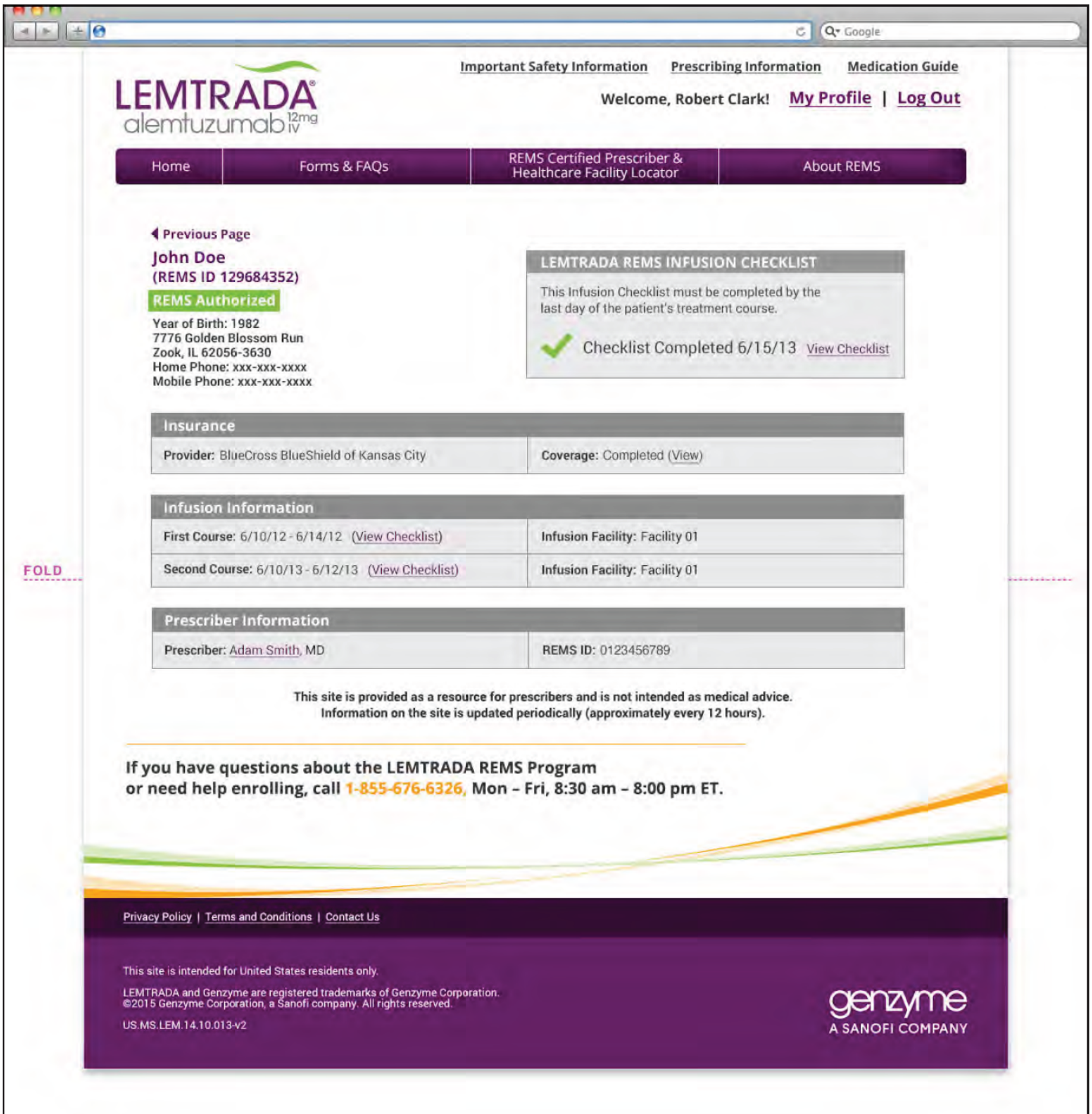
FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, Authorization and Baseline Lab Form Alert



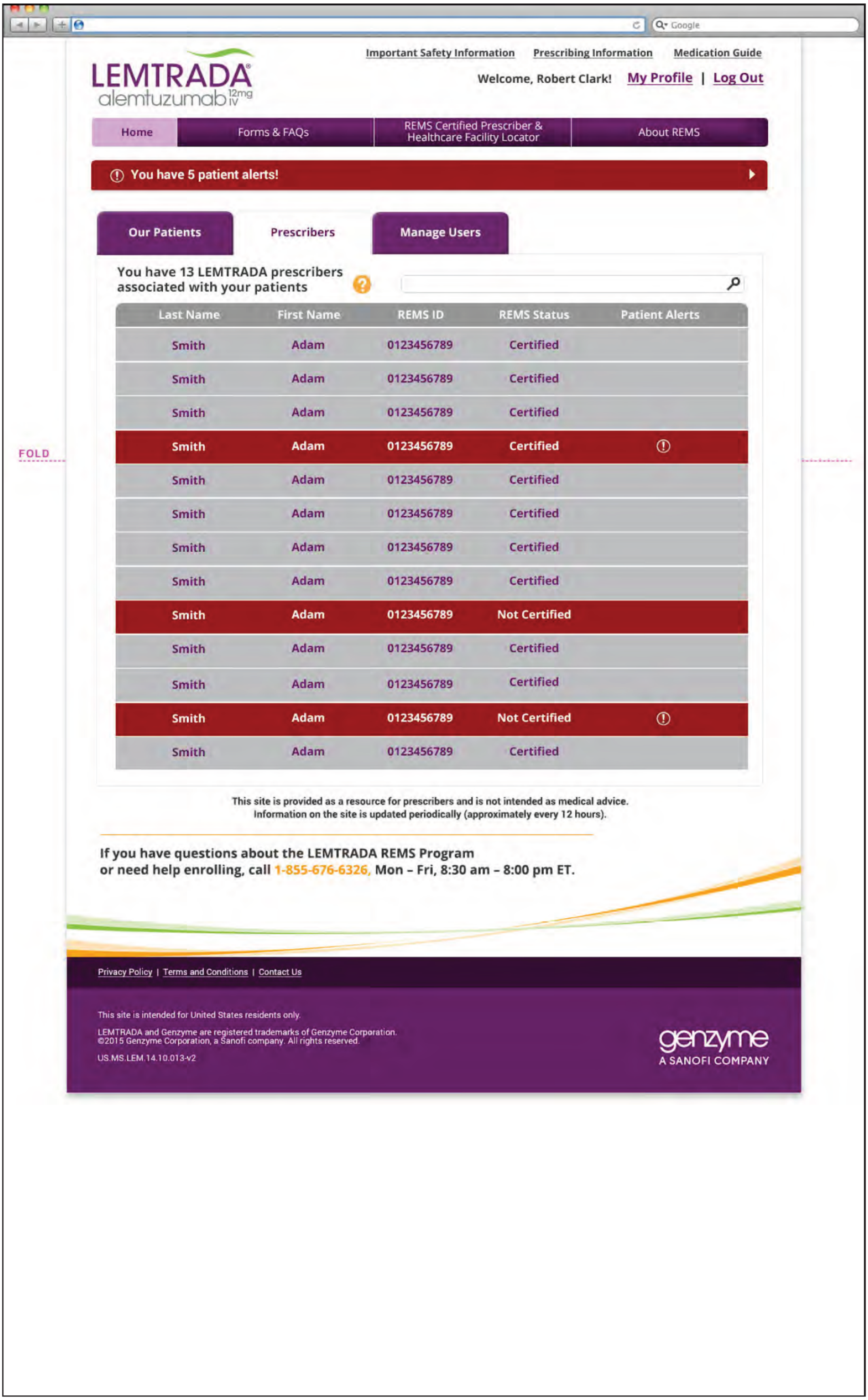
FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Single Patient Detail, 2nd Infusion Checklist Completed

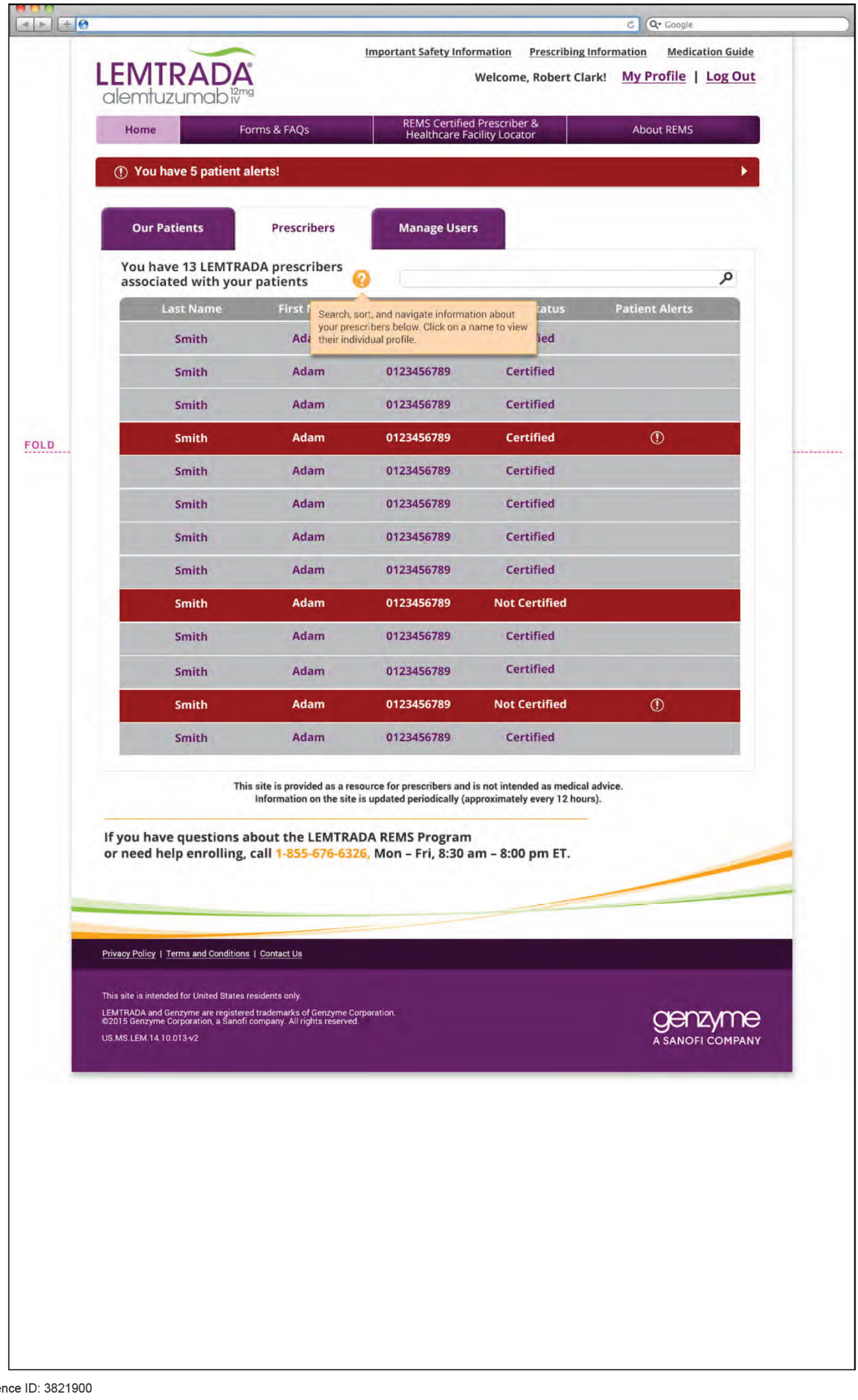


FOLD

LEMTRADA REMS Desktop - HCF Dashboard - Prescribers



LEMTRADA REMS Desktop - HCF Dashboard - Prescribers, Tool Tip Expanded



LEMTRADA REMS Desktop - HCF Dashboard - Prescribers, Single Prescriber Detail, REMS Certified

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Mobile Phone: xxx-xxx-xxxx
Fax: xxx-xxx-xxxx



View Map

Patients Seeing This Prescriber

You have 4 patient alerts!

FOLD

You have 10 LEMTRADA patients associated with this prescriber

	Last Name	First Name	Year of Birth	REMS ID	REMS Status	Next Infusion Date
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	___
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	___
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015

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Patients Seeing This Prescriber

You have 4 patient alerts!

FOLD

You have 10 LEMTRADA patients associated with this prescriber

Search, sort, and navigate information about your patients below. Click on a name to view their individual profile.

	Last Name	First N			MS Status	Next Infusion Date
	Doe	Joh			uthorized	8/4/2015
	Doe	John	1980	129684352	Authorized	—
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	—
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015

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View Map

Patients Seeing This Prescriber

You have 4 patient alerts!

You have **4 patients** who have authorization requirements.

- **3 patients** are overdue for the LEMTRADA REMS Patient Authorization and Baseline Lab Form.
- **1 patient** is due for the LEMTRADA REMS Patient Status Form in 1 month.

Manage my patient alert email preferences

FOLD

You have 10 LEMTRADA patients associated with this prescriber

	Last Name	First Name	Year of Birth	REMS ID	REMS Status	Next Infusion Date
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	—
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	—
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015

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Patients Seeing This Prescriber

You have 4 patient alerts!

FOLD

You have 10 LEMTRADA patients associated with this prescriber

	Last Name	First Name	Year of Birth	REMS ID	REMS Status	Next Infusion Date
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	___
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
!	Doe	John	1980	129684352	Not Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	___
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015
	Doe	John	1980	129684352	Authorized	8/4/2015

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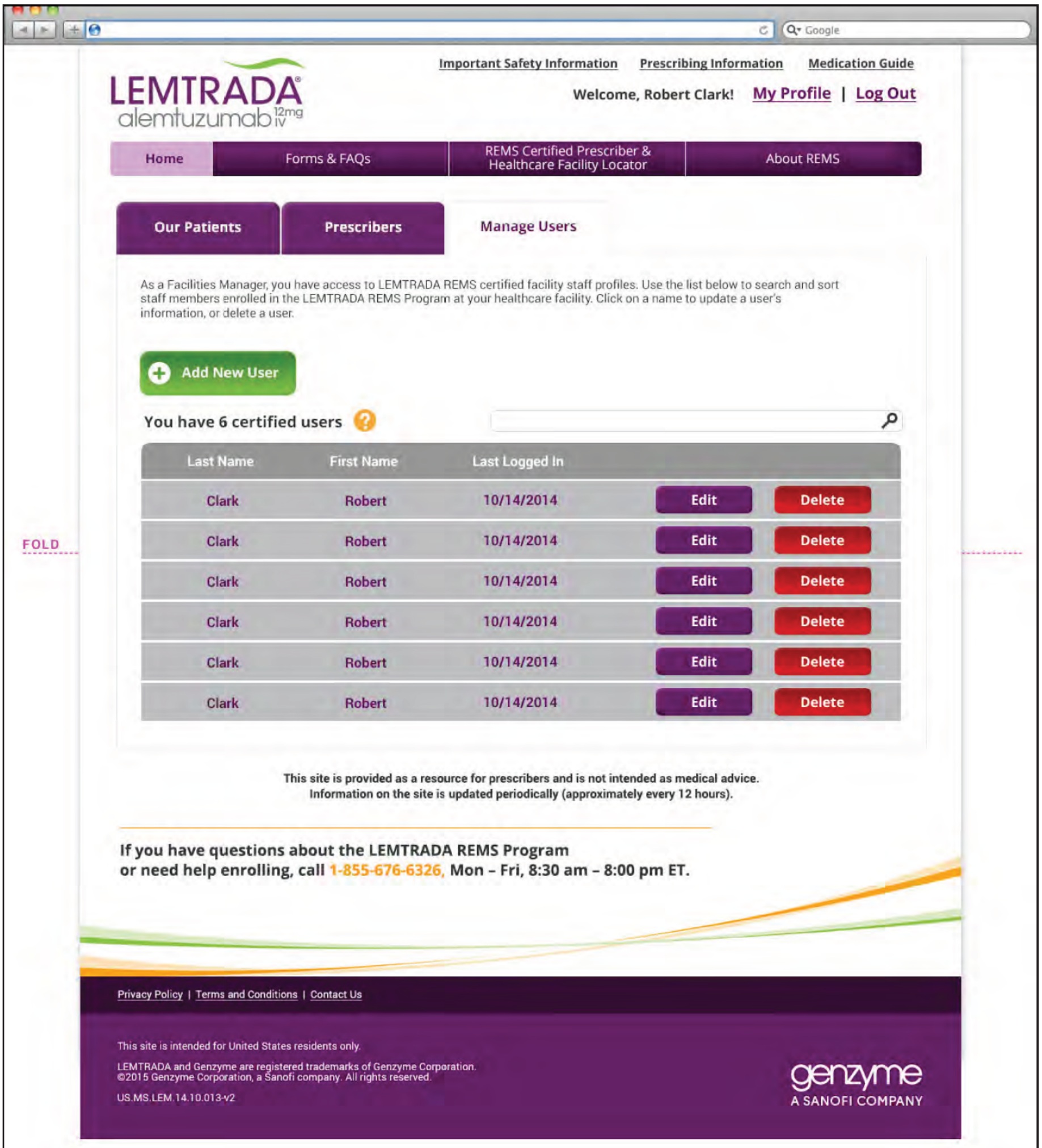
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users



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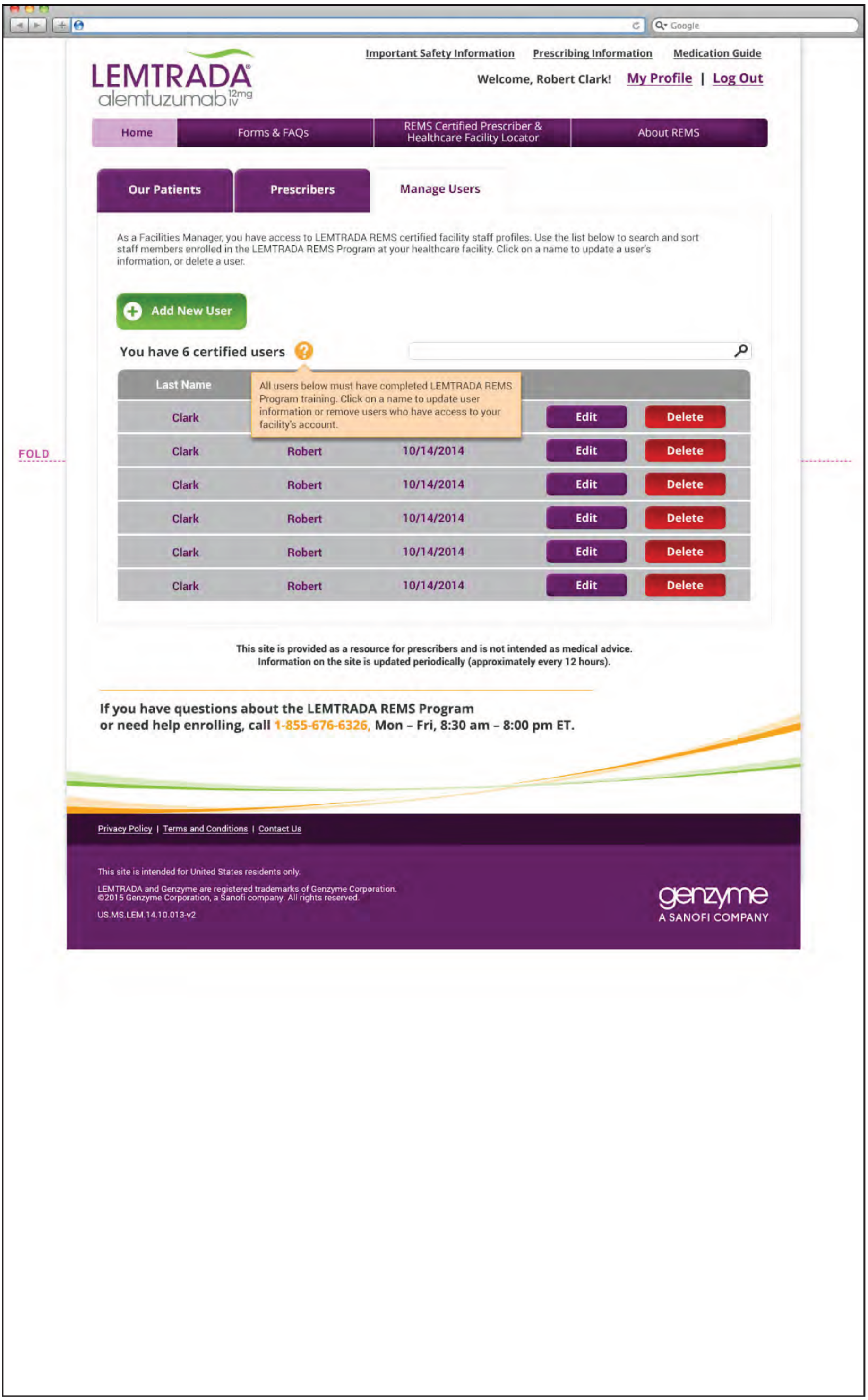
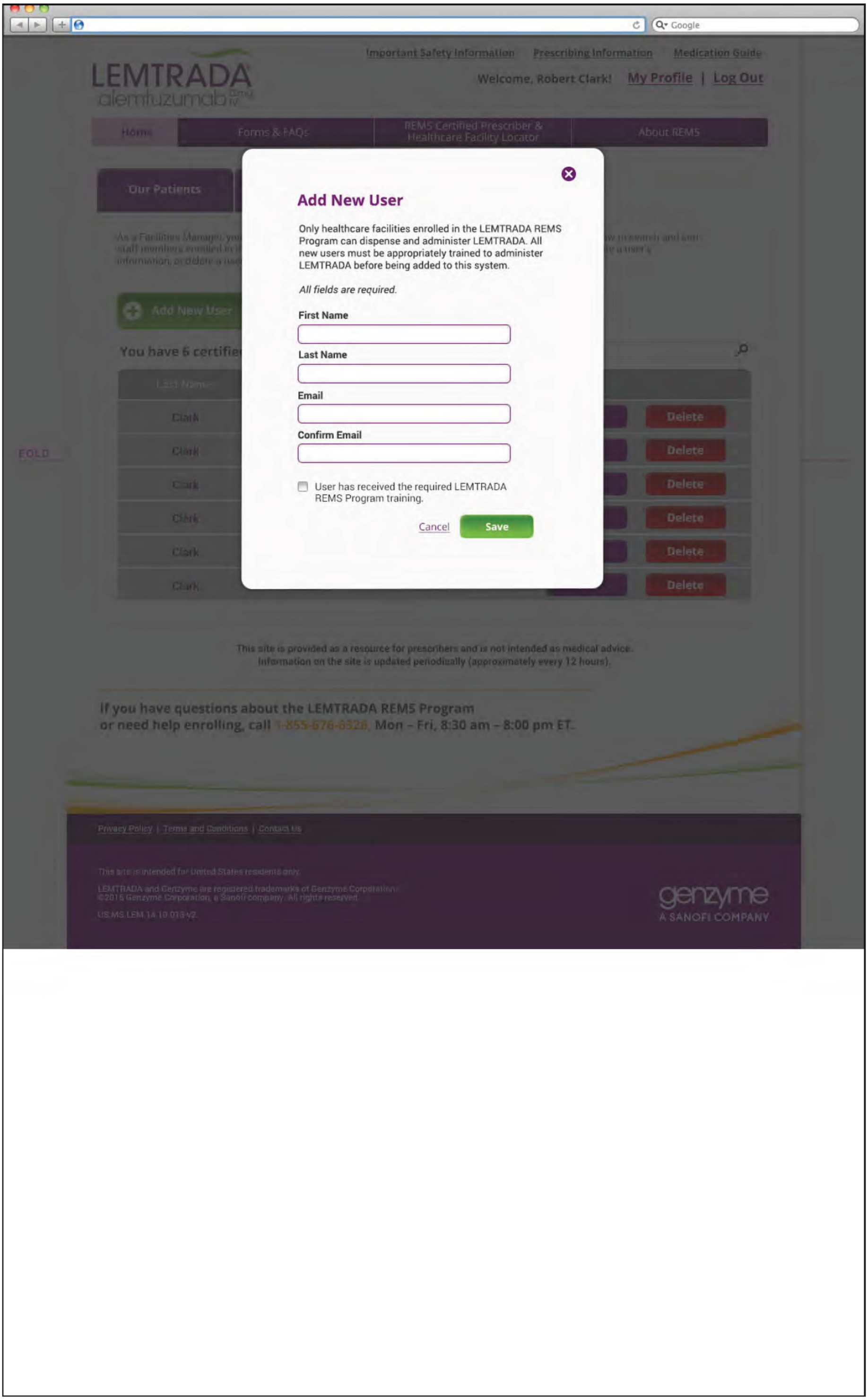
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users, Tool Tip Expanded

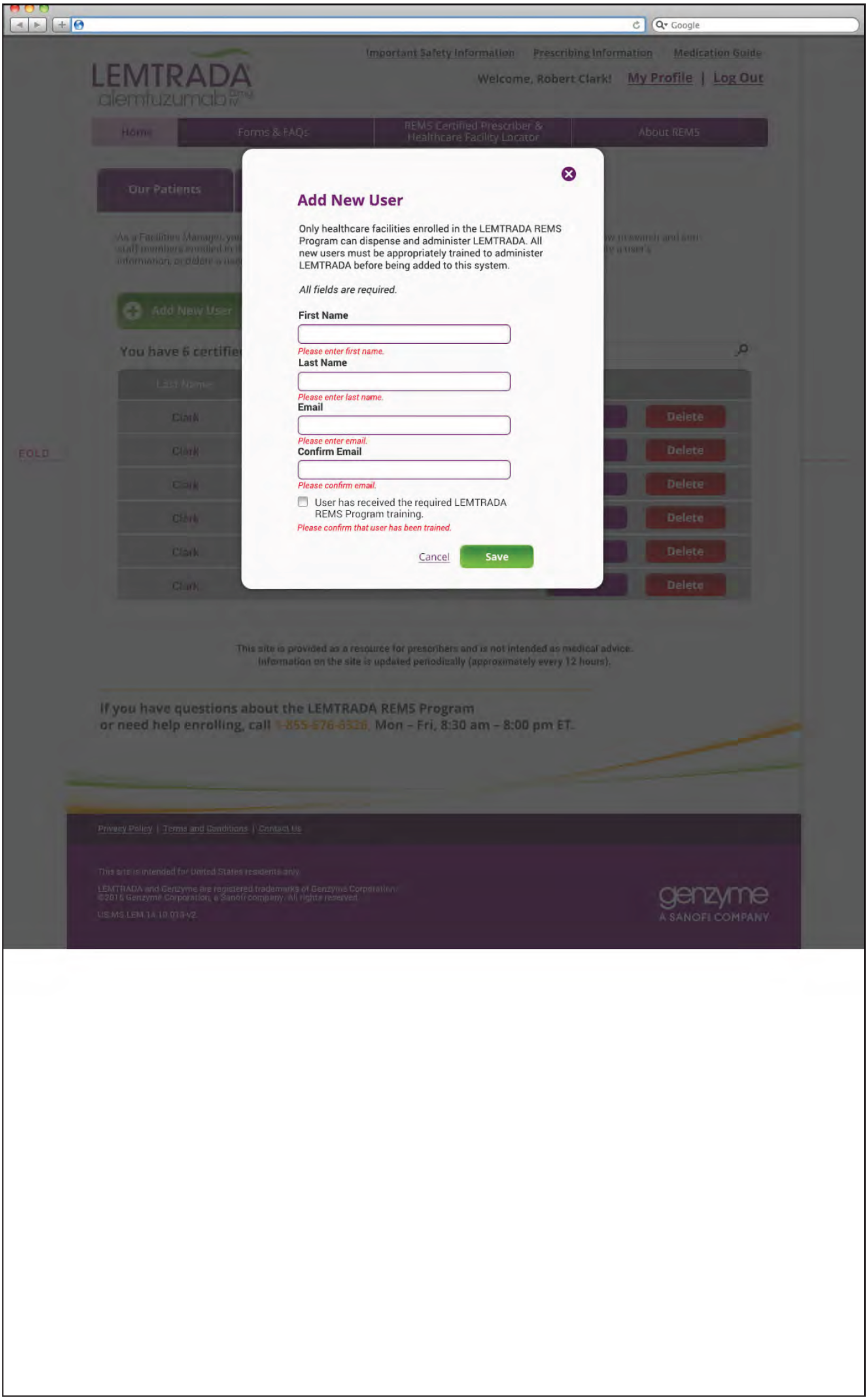


FOLD

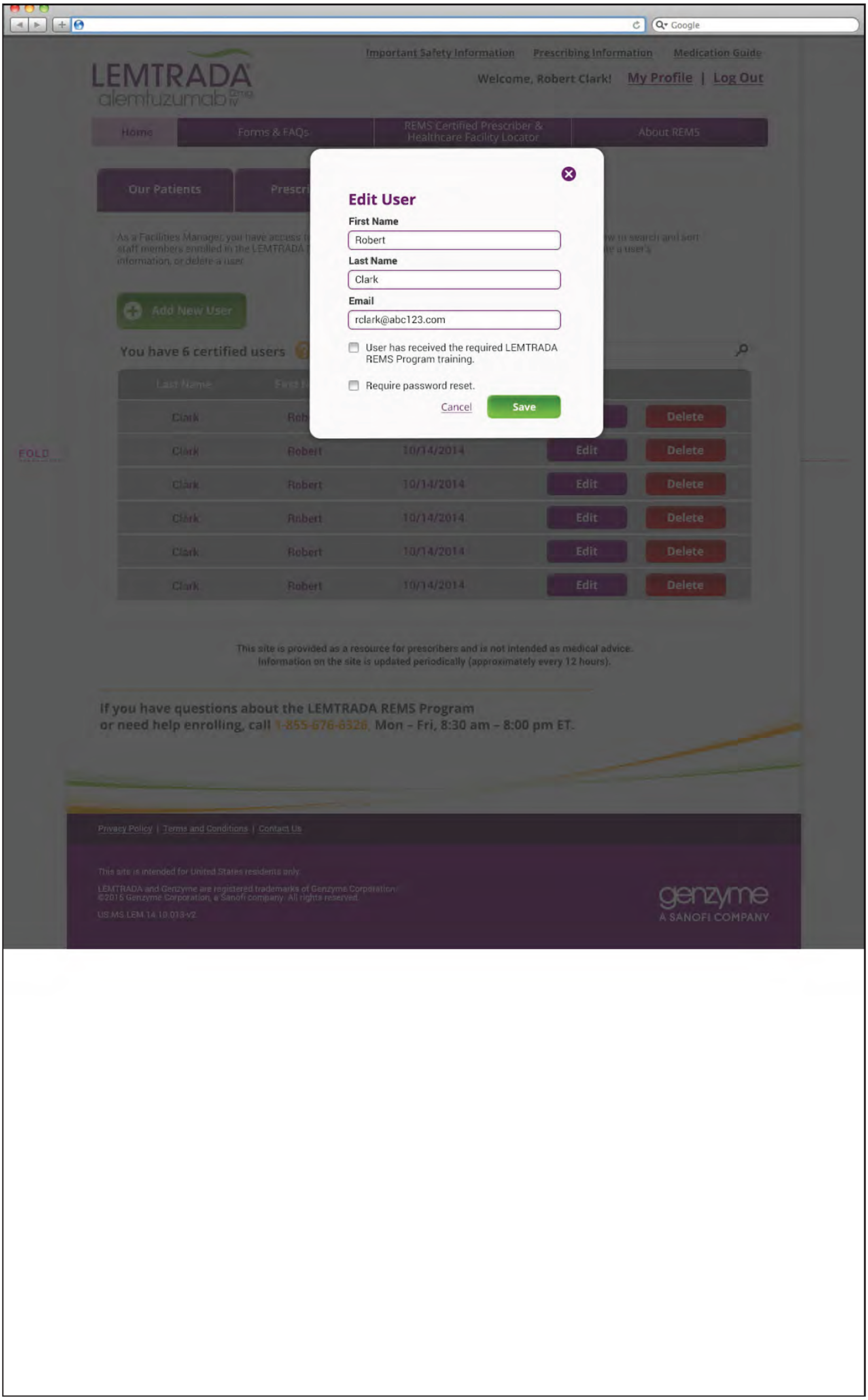
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users, Add New User



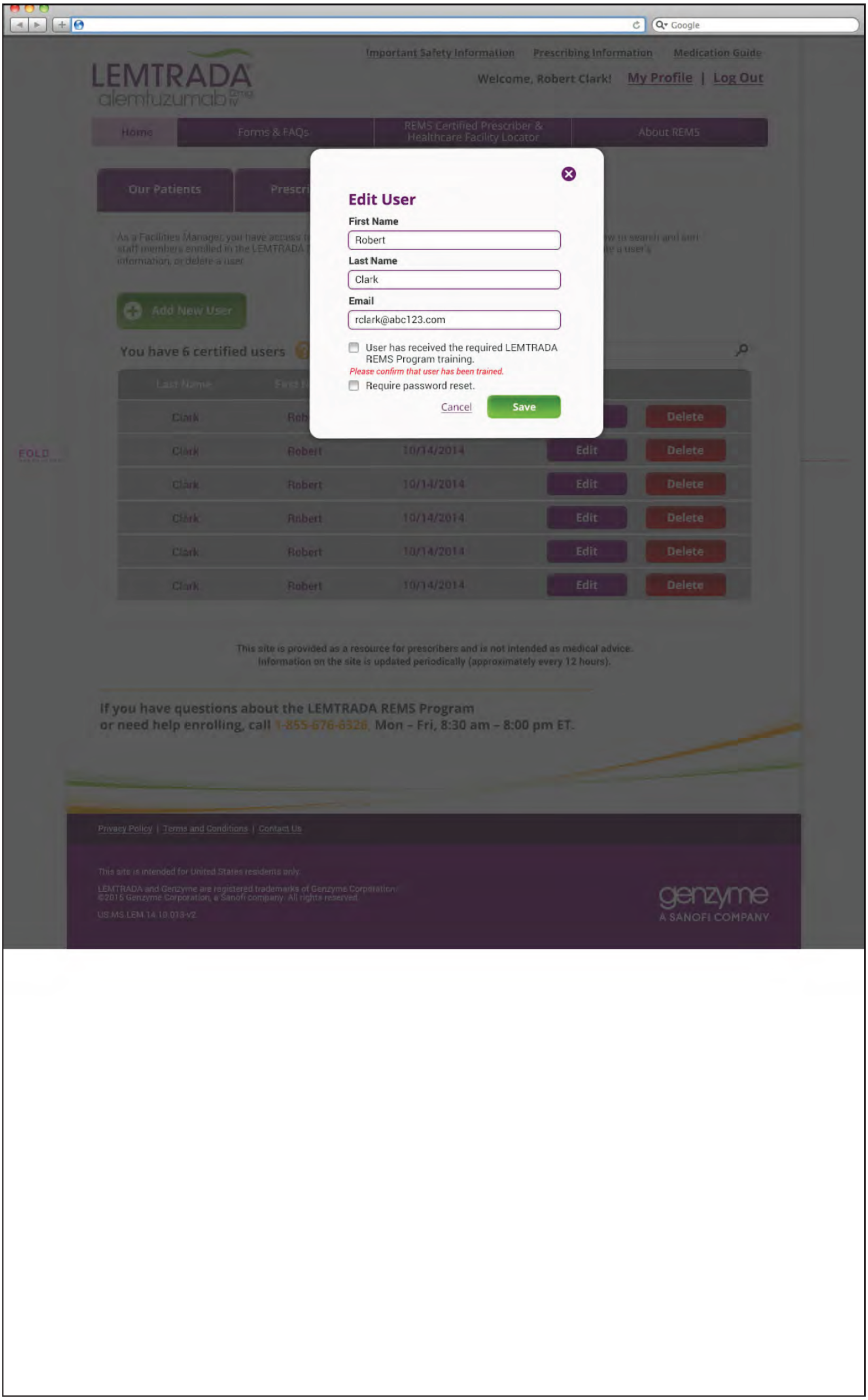
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users, Add New User, Error



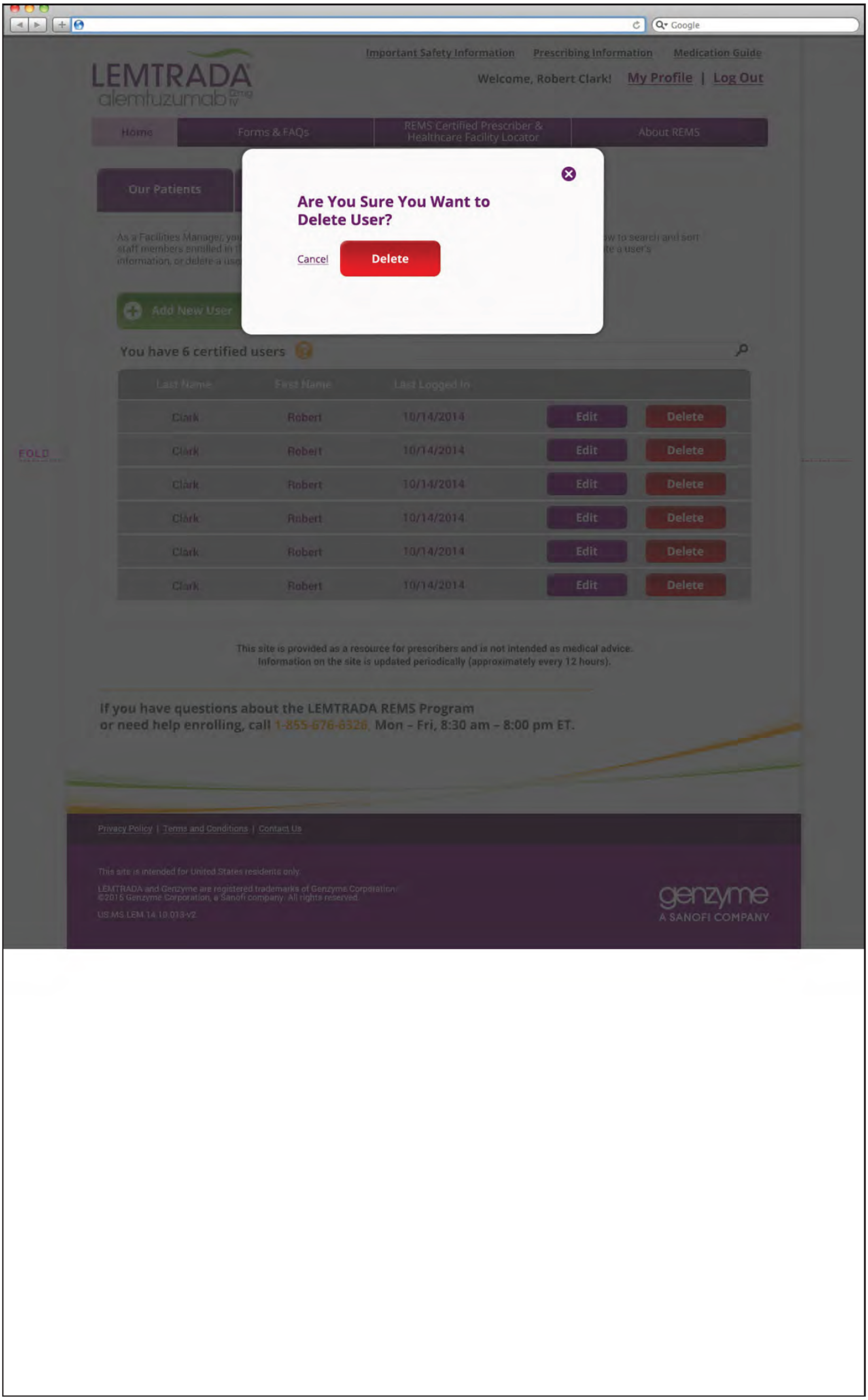
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users, Edit User



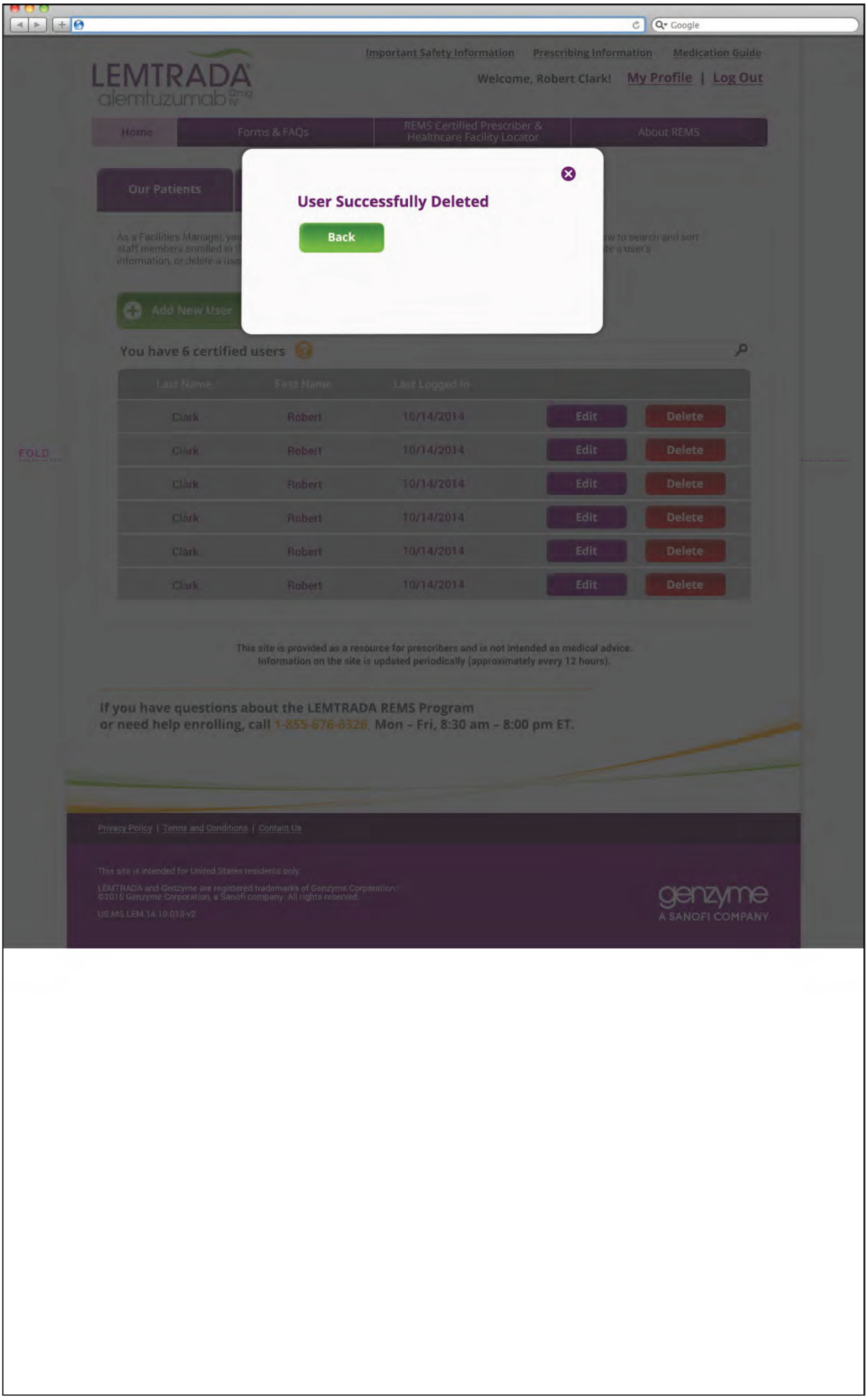
LEMTRADA REMS Desktop - HCF Dashboard - Manage Users, Edit User Error



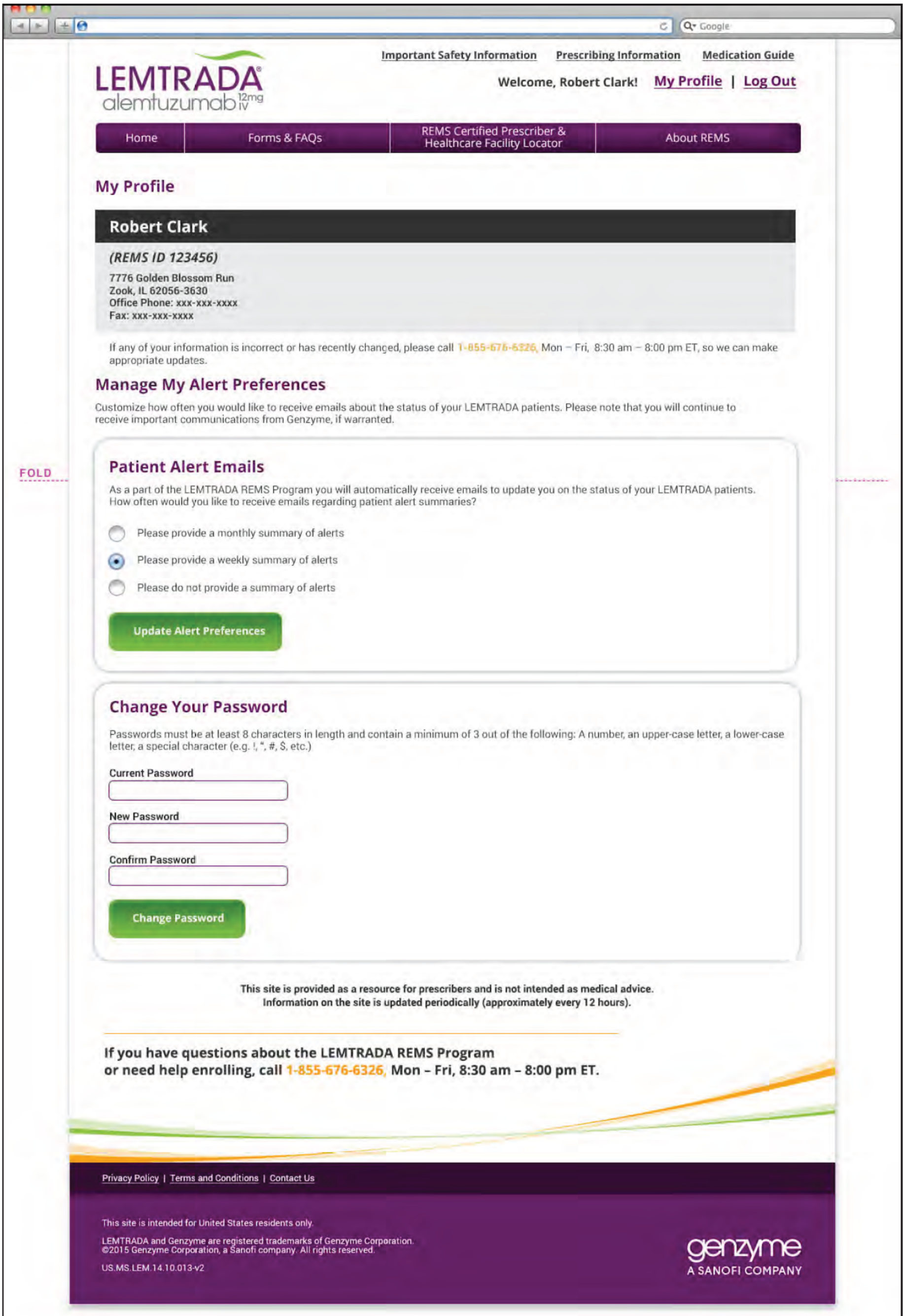
LEMTRADA REMS Desktop - HCF Dashboard - Delete User, Interstitial Page



LEMTRADA REMS Desktop - HCF Dashboard - Delete User, Confirmation



LEMTRADA REMS Desktop - HCF Dashboard - My Profile



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Robert Clark

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Manage My Alert Preferences

Customize how often you would like to receive emails about the status of your LEMTRADA patients. Please note that you will continue to receive important communications from Genzyme, if warranted.

FOLD

Patient Alert Emails

As a part of the LEMTRADA REMS Program you will automatically receive emails to update you on the status of your LEMTRADA patients. How often would you like to receive emails regarding patient alert summaries?

- ○ Please provide a monthly summary of alerts
- ◉ Please provide a weekly summary of alerts
- ○ Please do not provide a summary of alerts

Update Alert Preferences

Change Your Password

Passwords must be at least 8 characters in length and contain a minimum of 3 out of the following: A number, an upper-case letter, a lower-case letter, a special character (e.g. !, ", #, $, etc.)

Current Password

Please enter password.

New Password

Please enter a valid password.

Confirm Password

Please confirm new password.

Change Password

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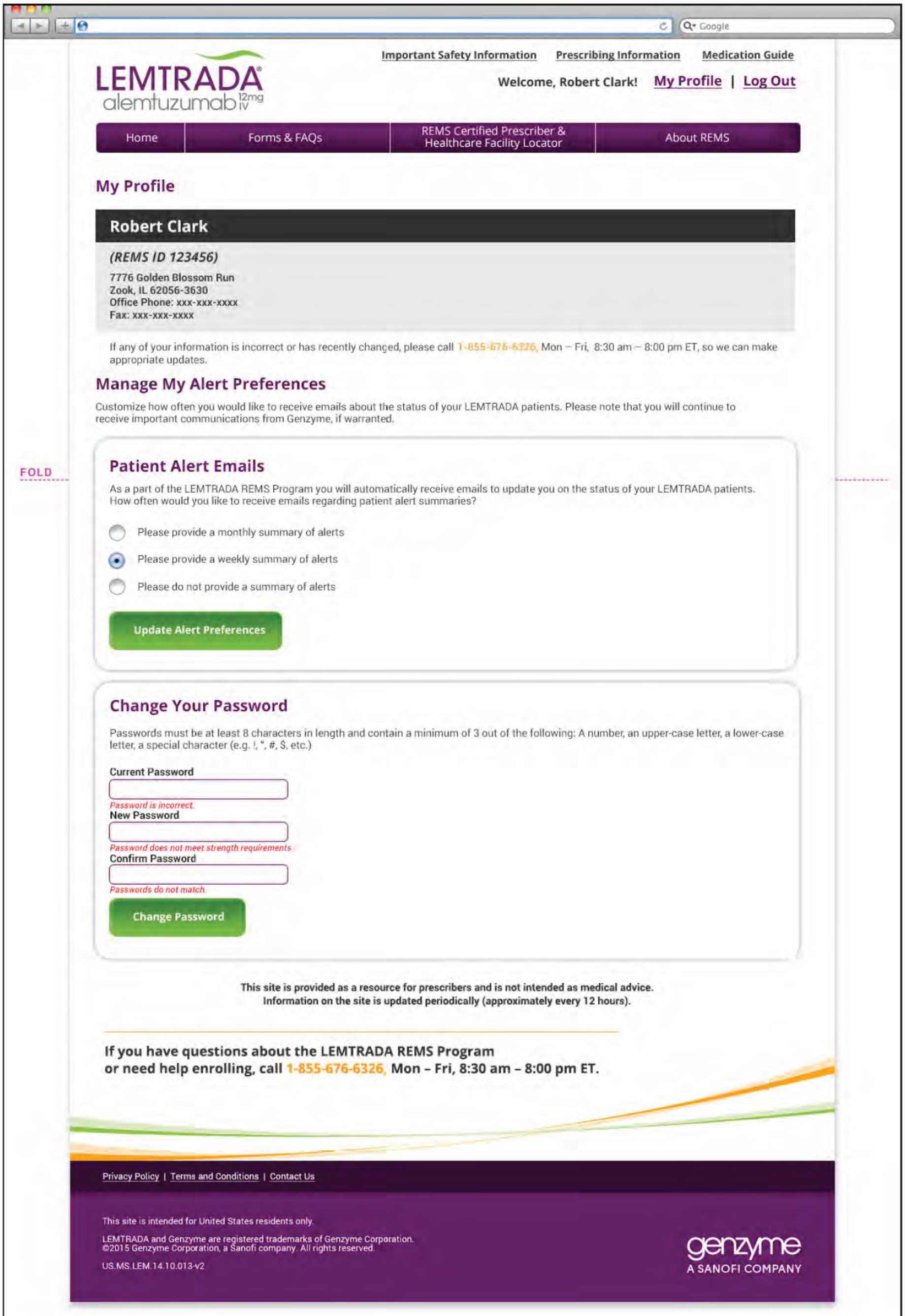
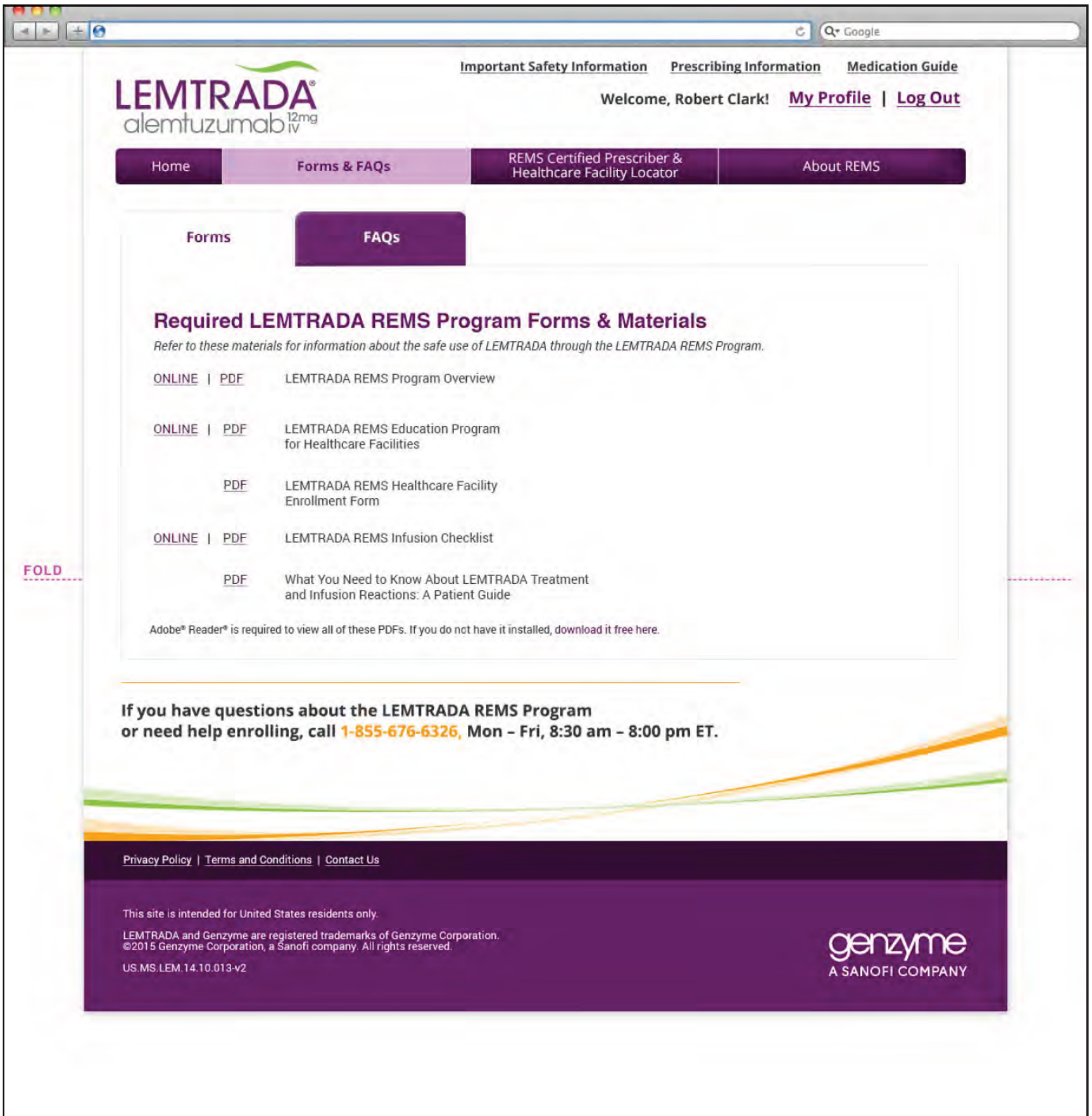


LEMTRADA REMS Desktop - HCF Dashboard - Support, Forms



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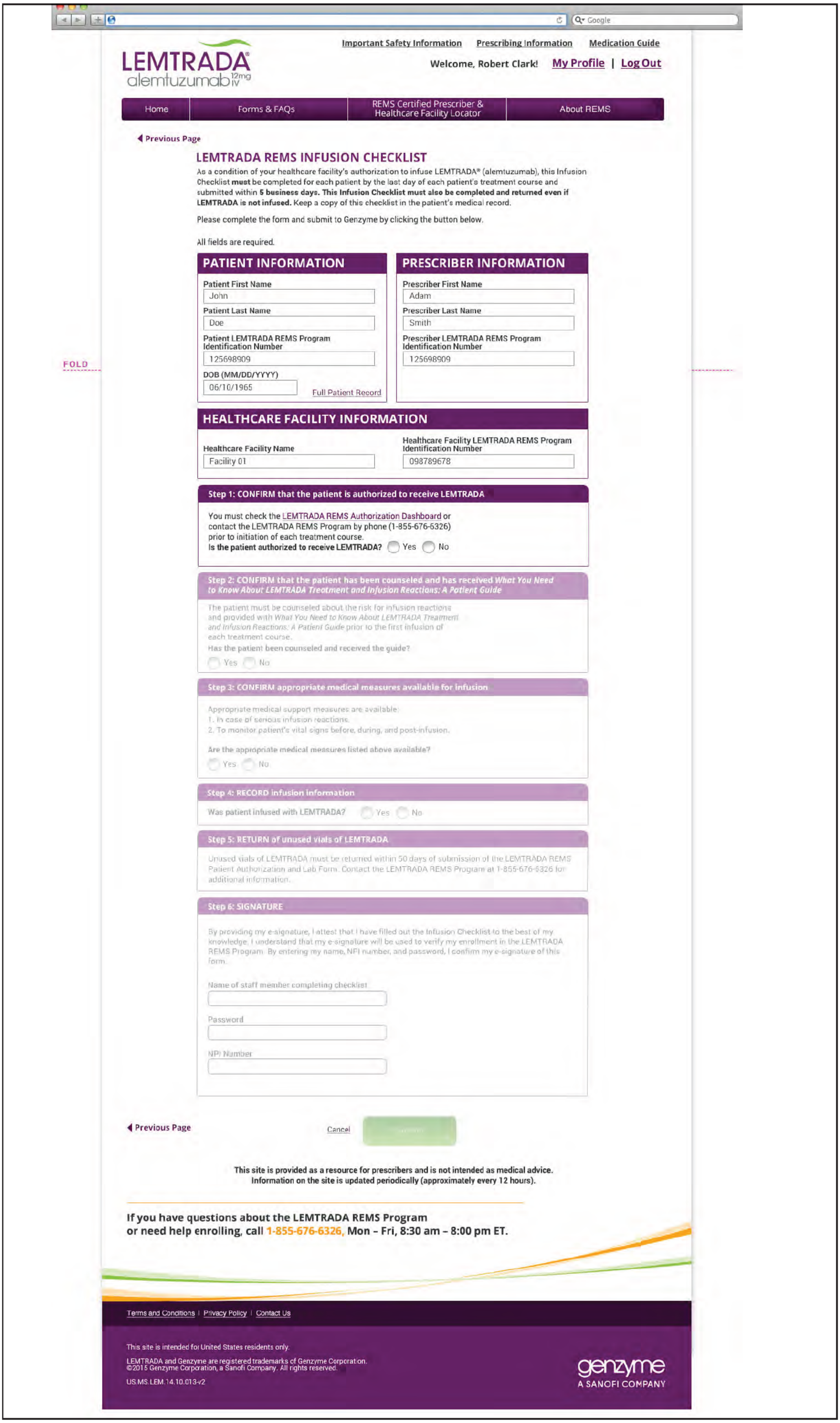
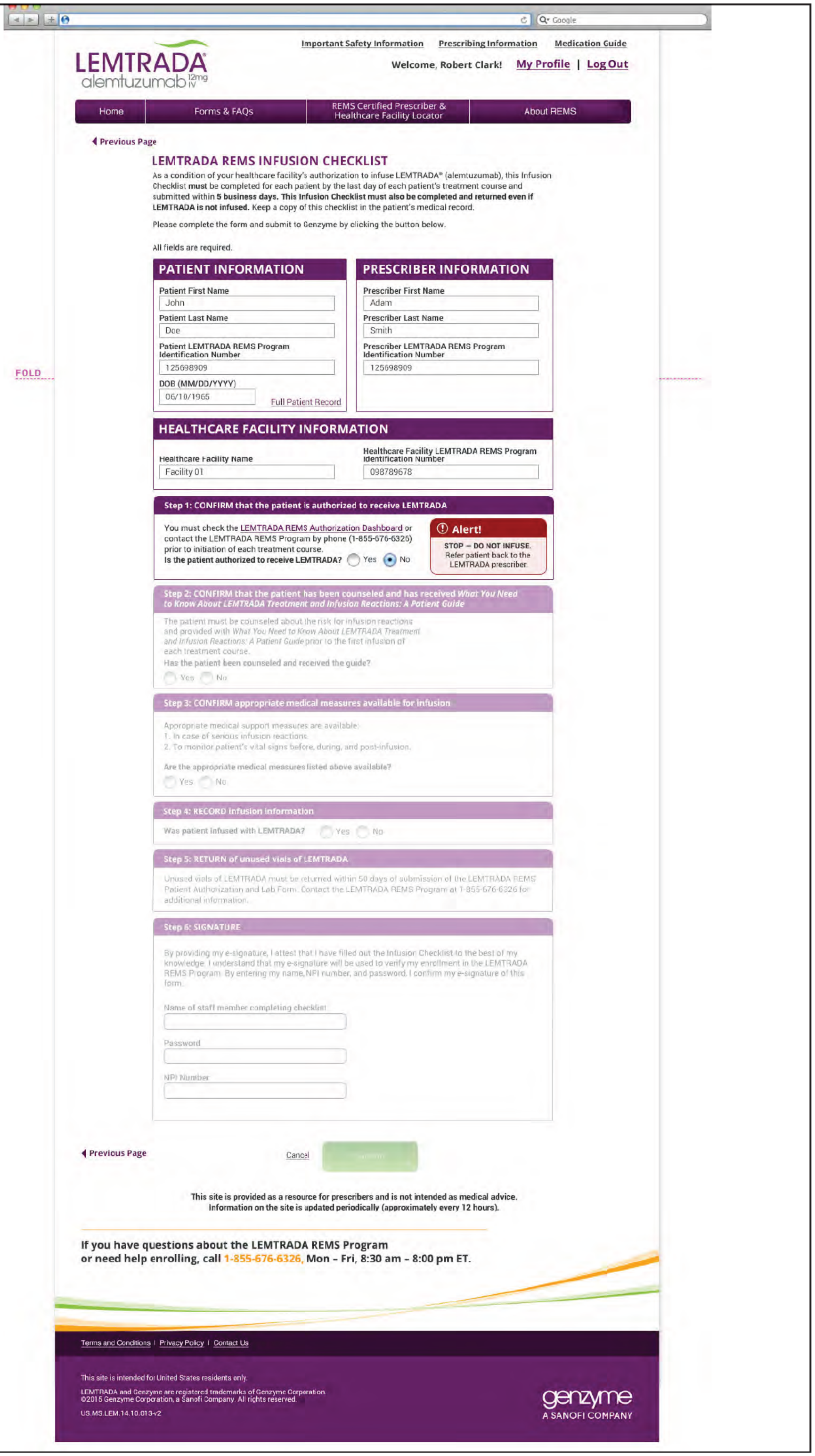
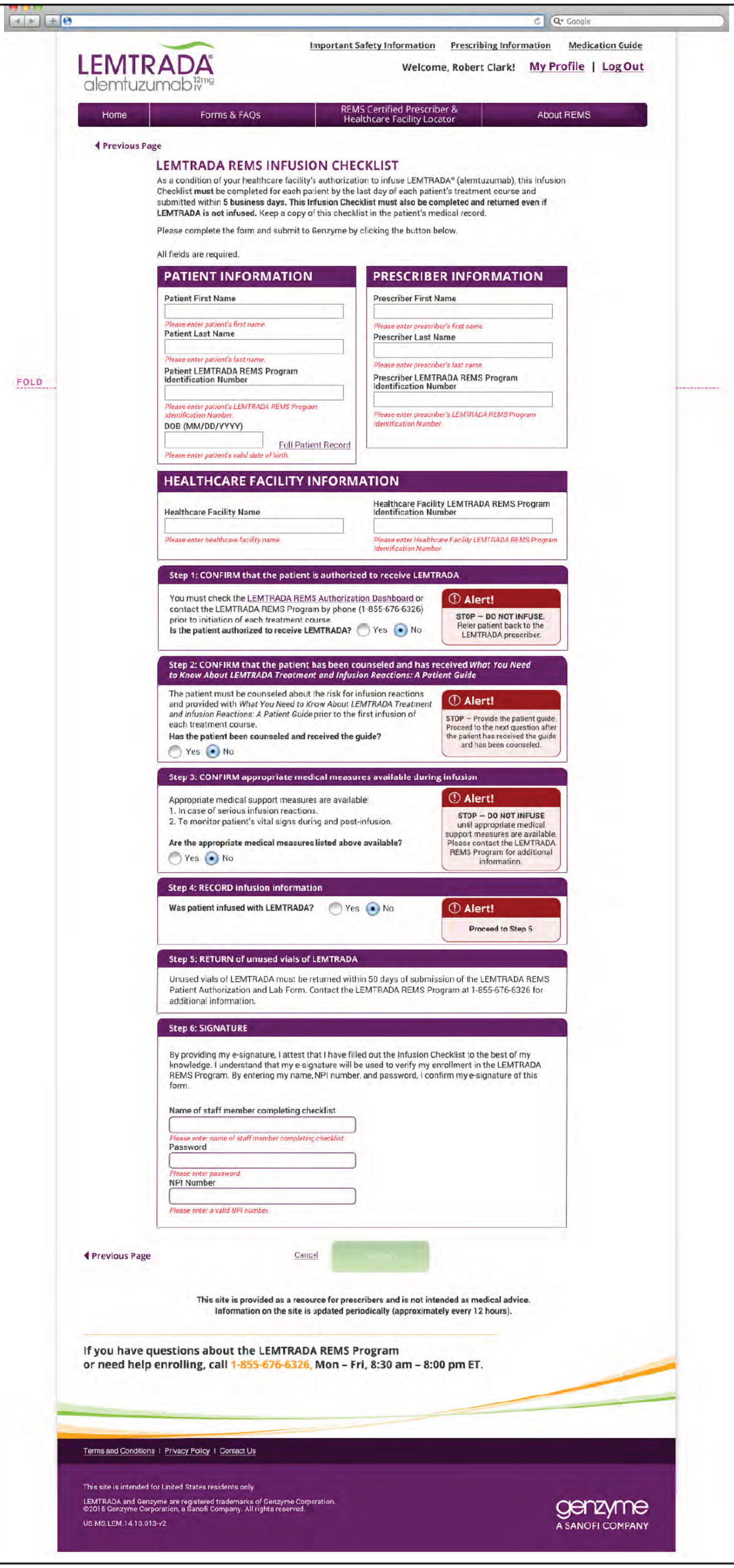
LEMTRADA REMS Desktop - Infusion Checklist Form - Default



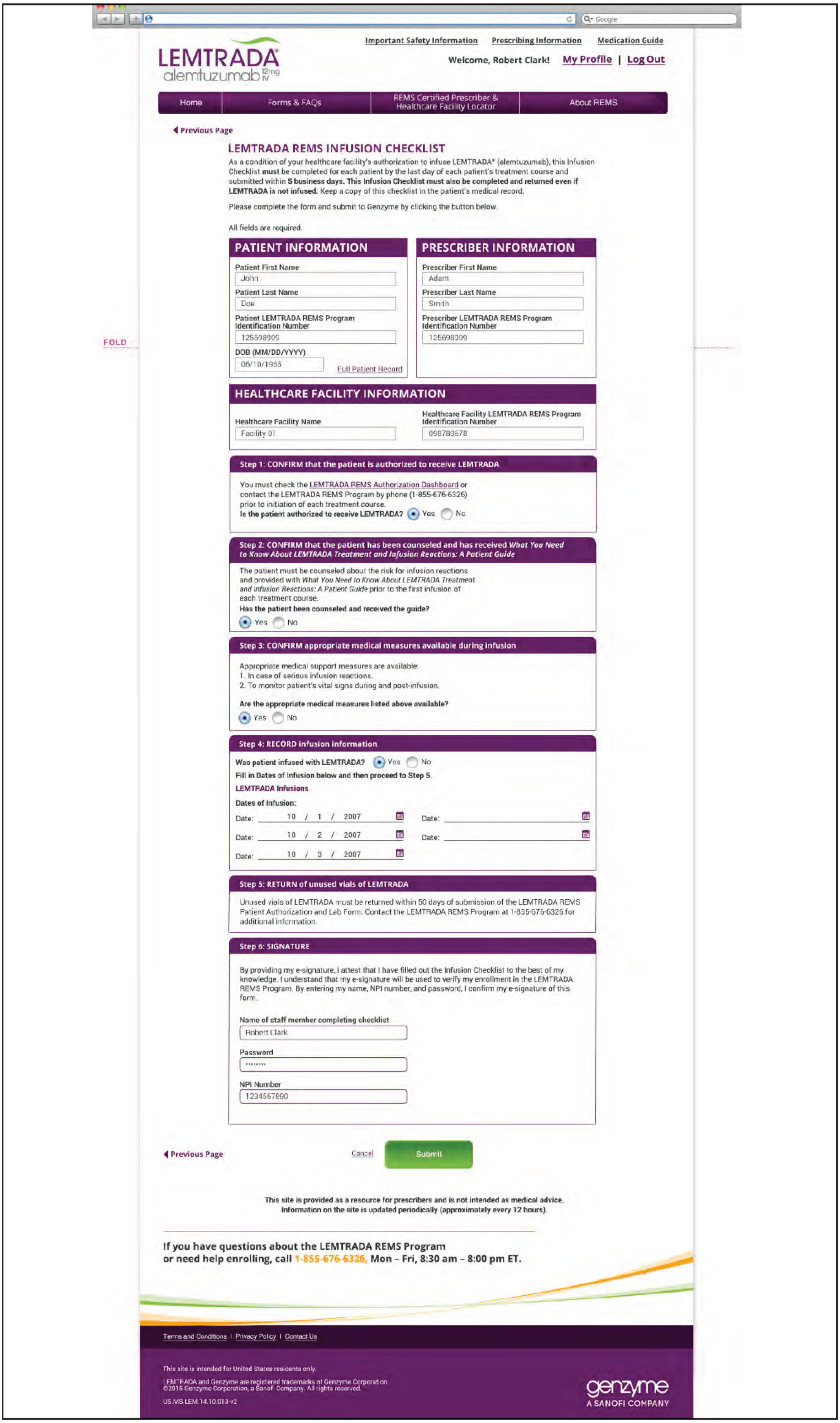
LEMTRADA REMS Desktop - Infusion Checklist Form - "No" Selected



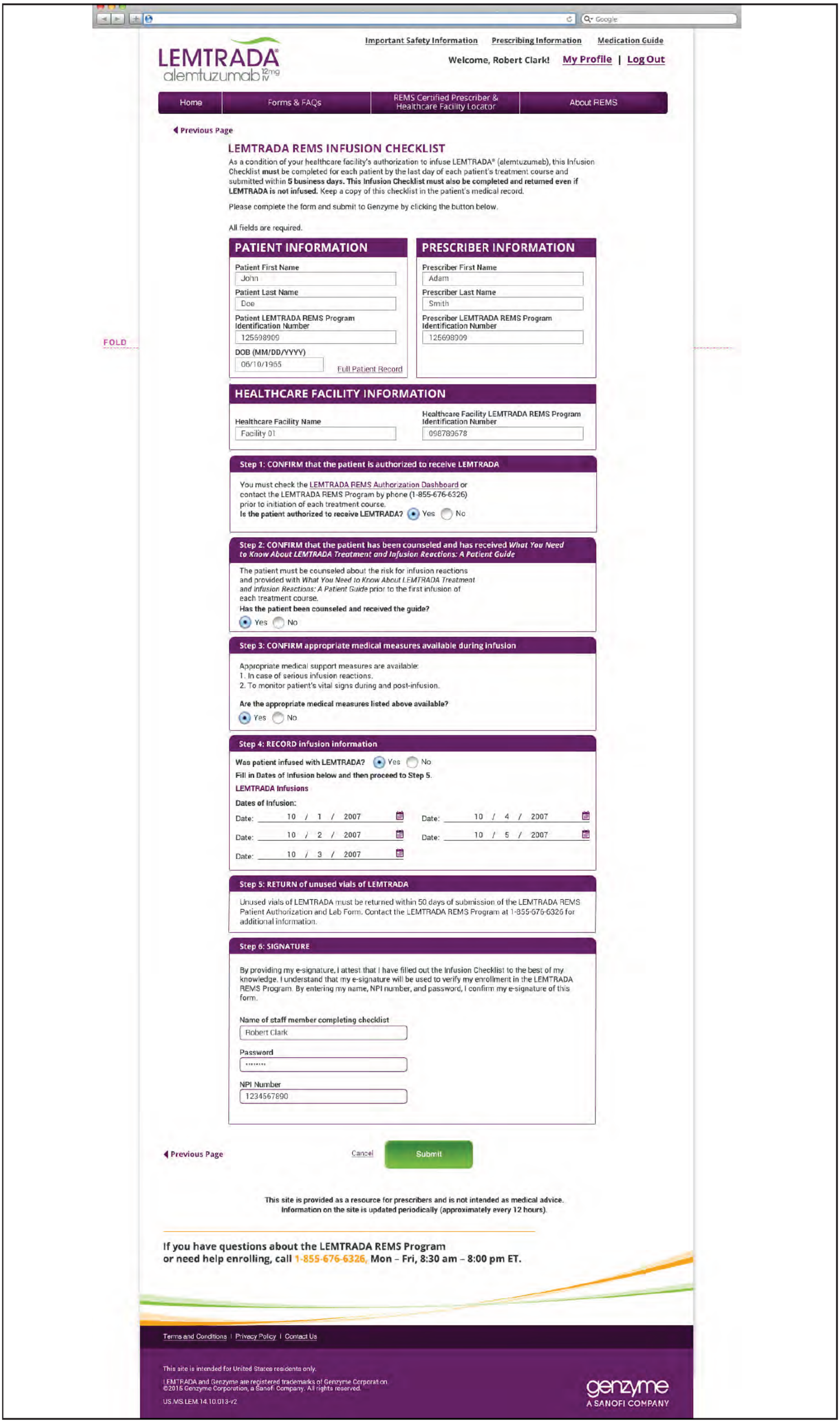
LEMTRADA REMS Desktop - Infusion Checklist Form - Error



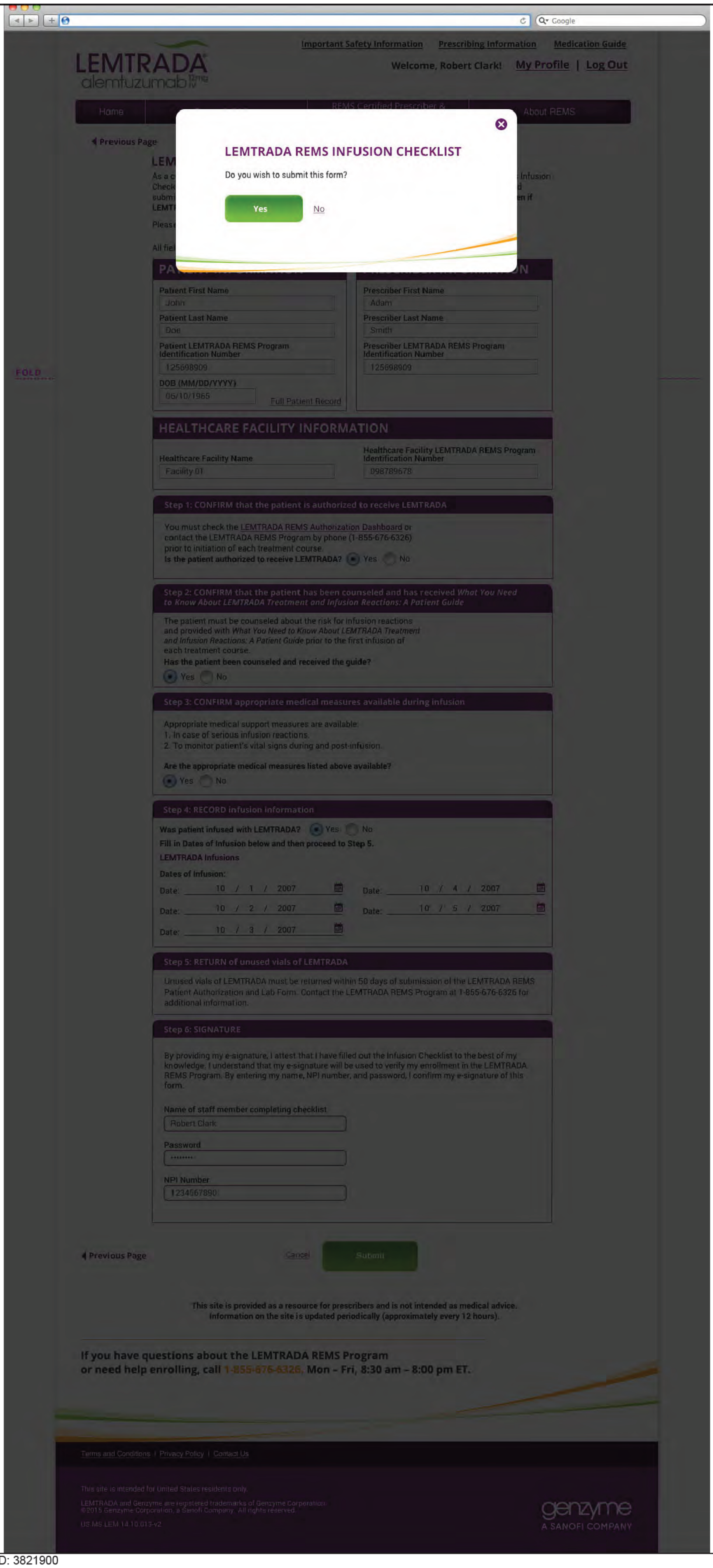
LEMTRADA REMS Desktop - Infusion Checklist Form - "Yes" Selected



LEMTRADA REMS Desktop - Infusion Checklist Form - "Yes" Selected, Infusion Dates Added



LEMTRADA REMS Desktop - Infusion Checklist Form - Submit Confirmation



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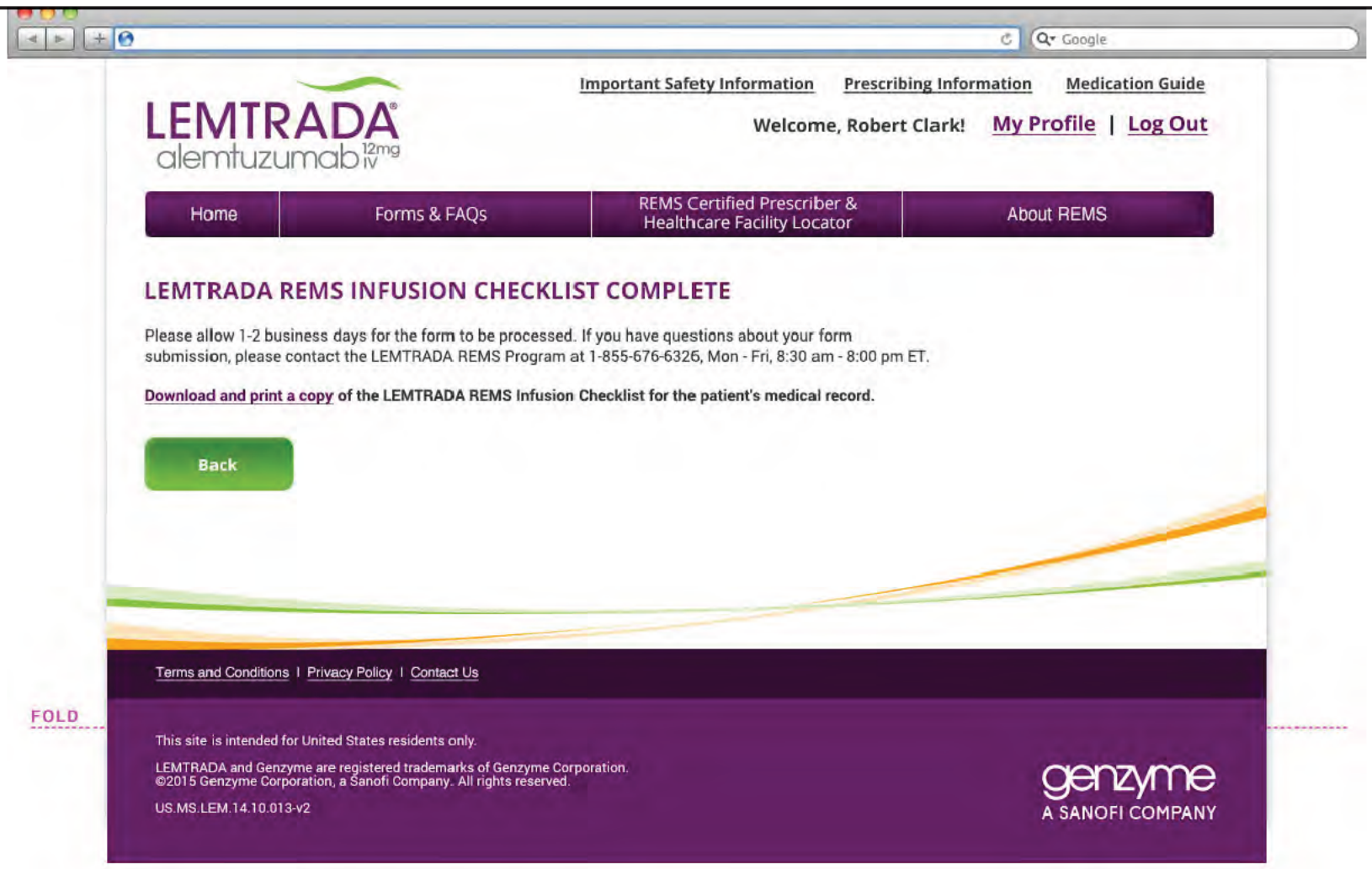

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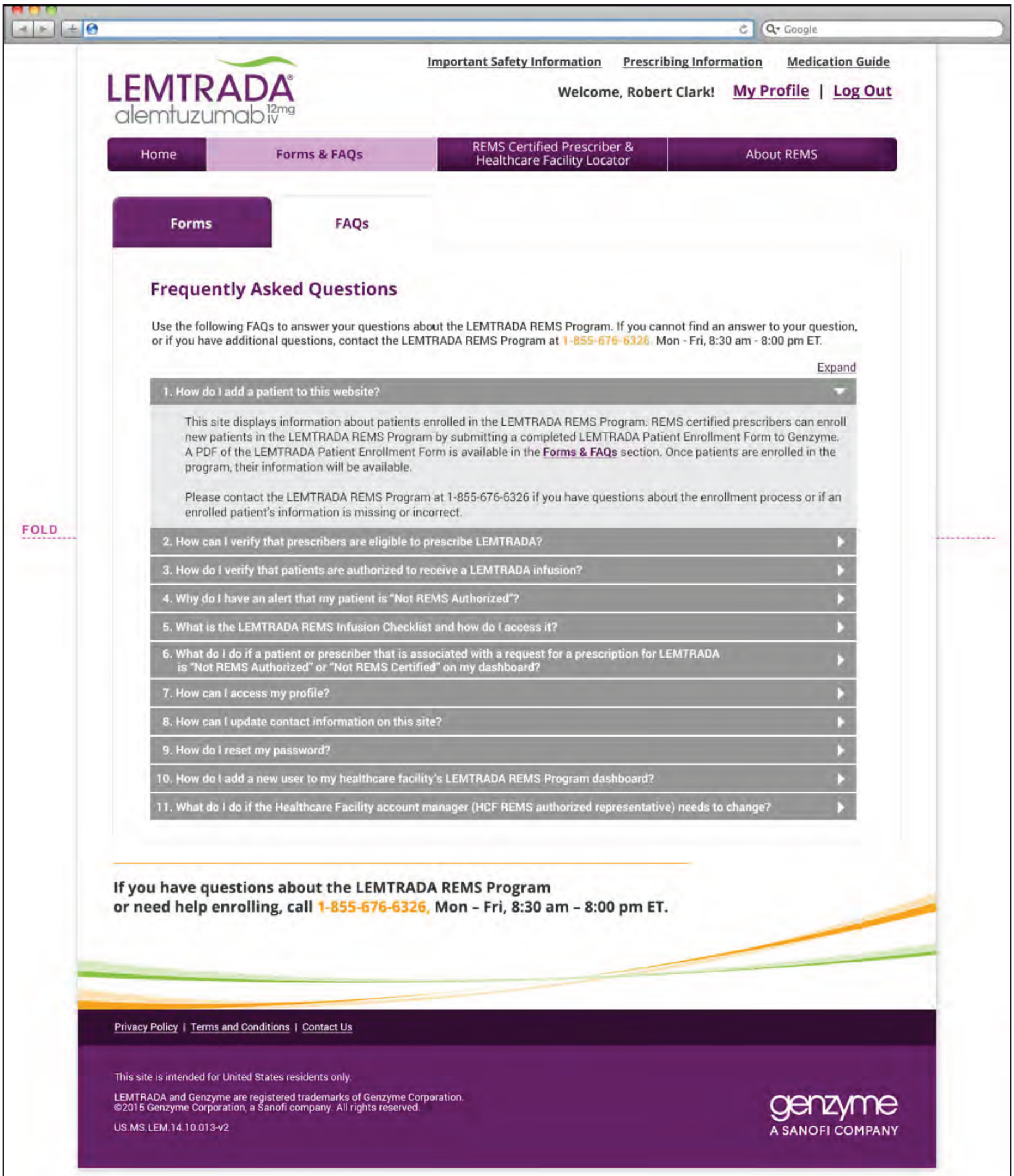

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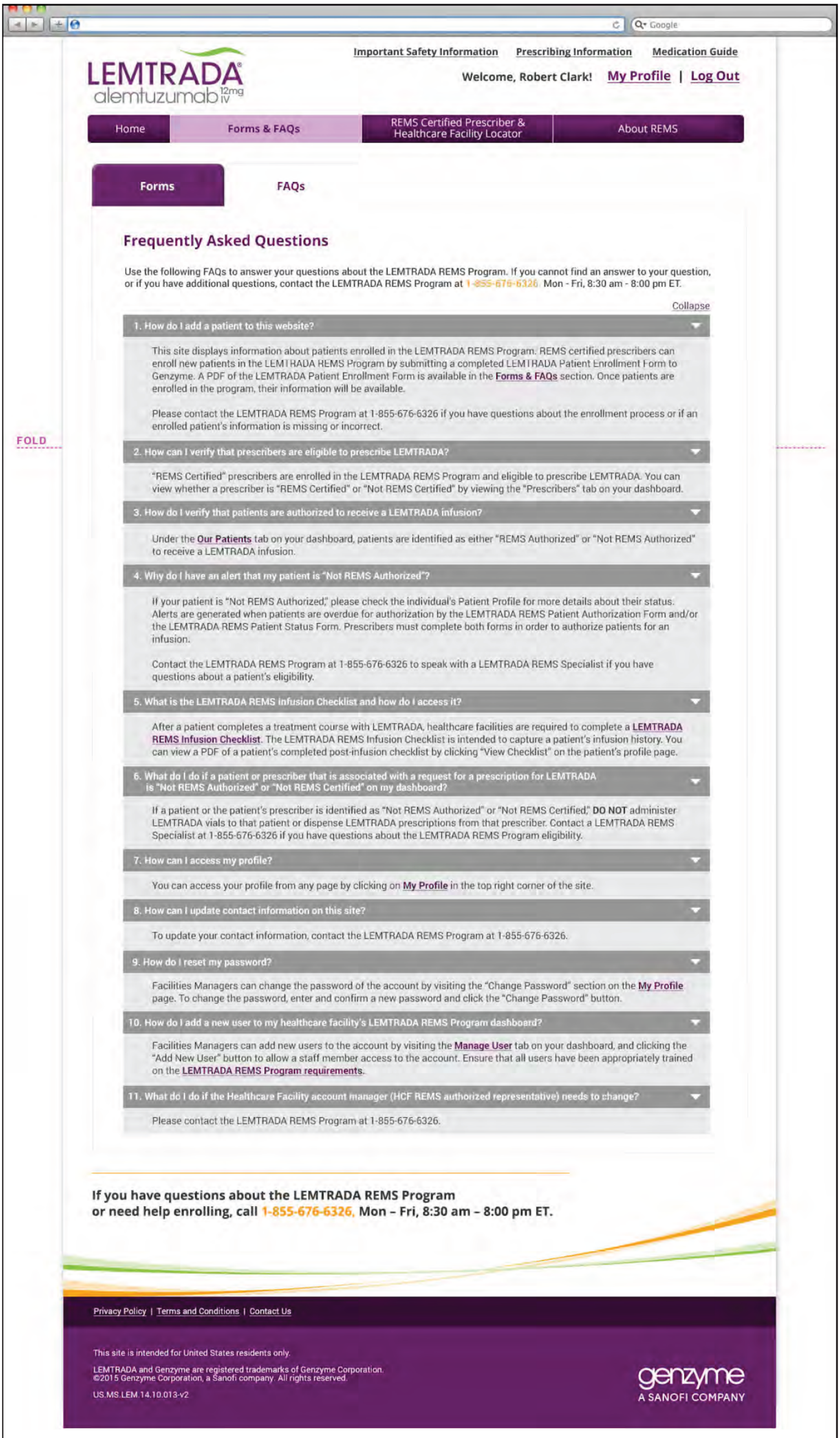
LEMTRADA REMS Desktop - HCF Dashboard - Support, FAQs Expanded



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Reference ID: 3821900

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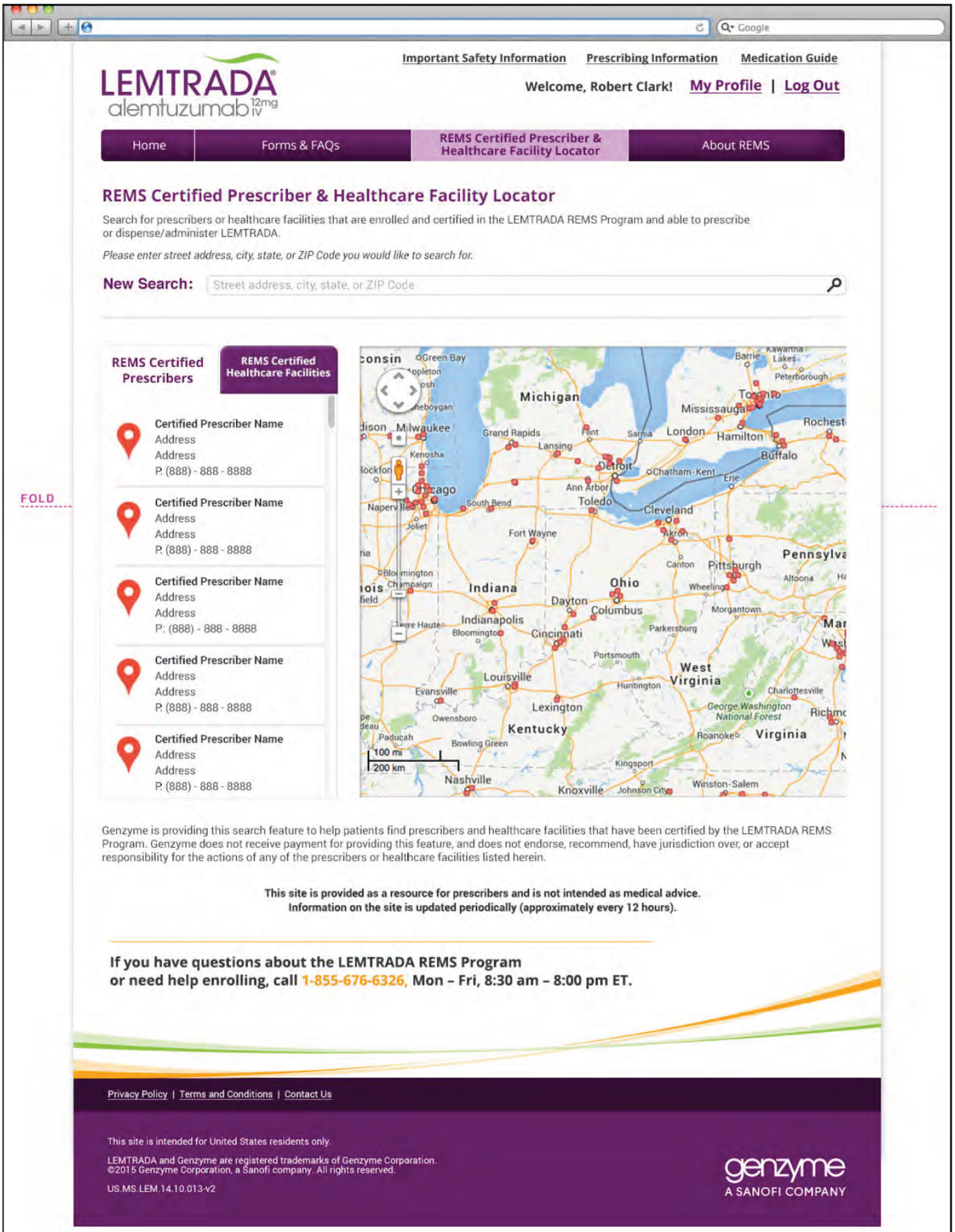

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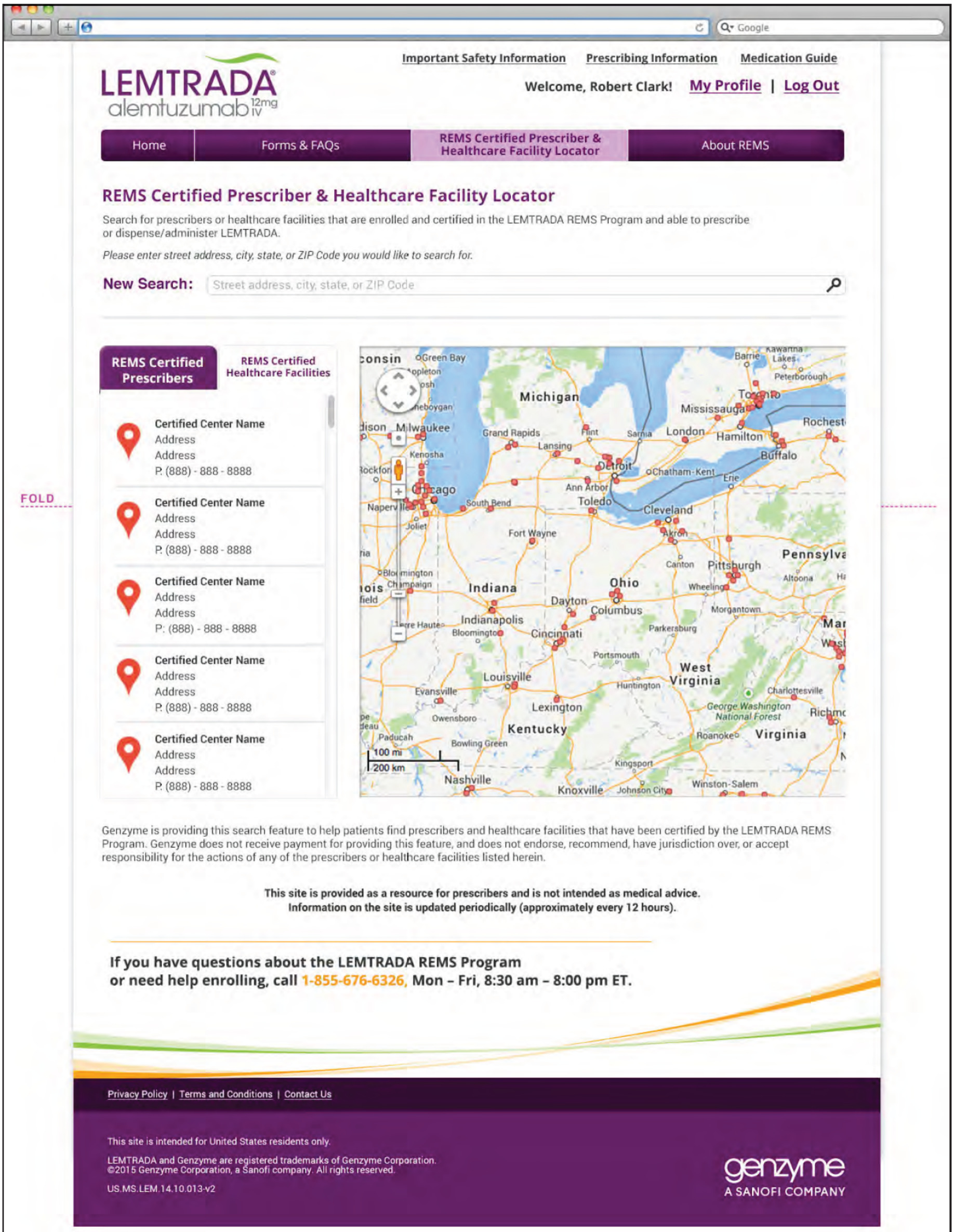
LEMTRADA REMS Desktop - HCF Dashboard - REMS Certified Prescriber & Healthcare Facility Locator



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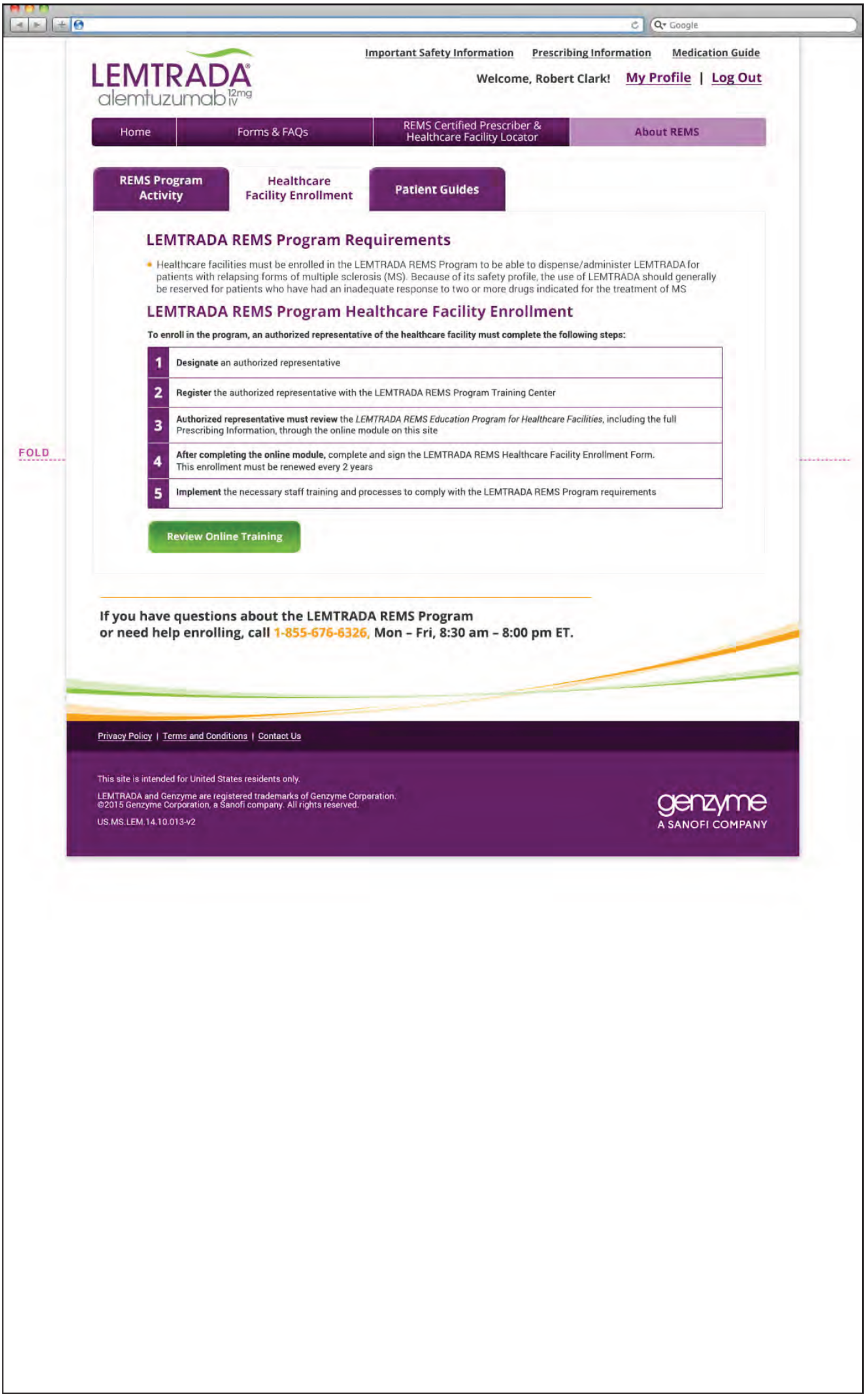
LEMTRADA REMS Desktop - HCF Dashboard - About REMS, REMS Program Activity



LEMTRADA REMS Desktop - HCF Dashboard - About REMS, HCF Enrollment



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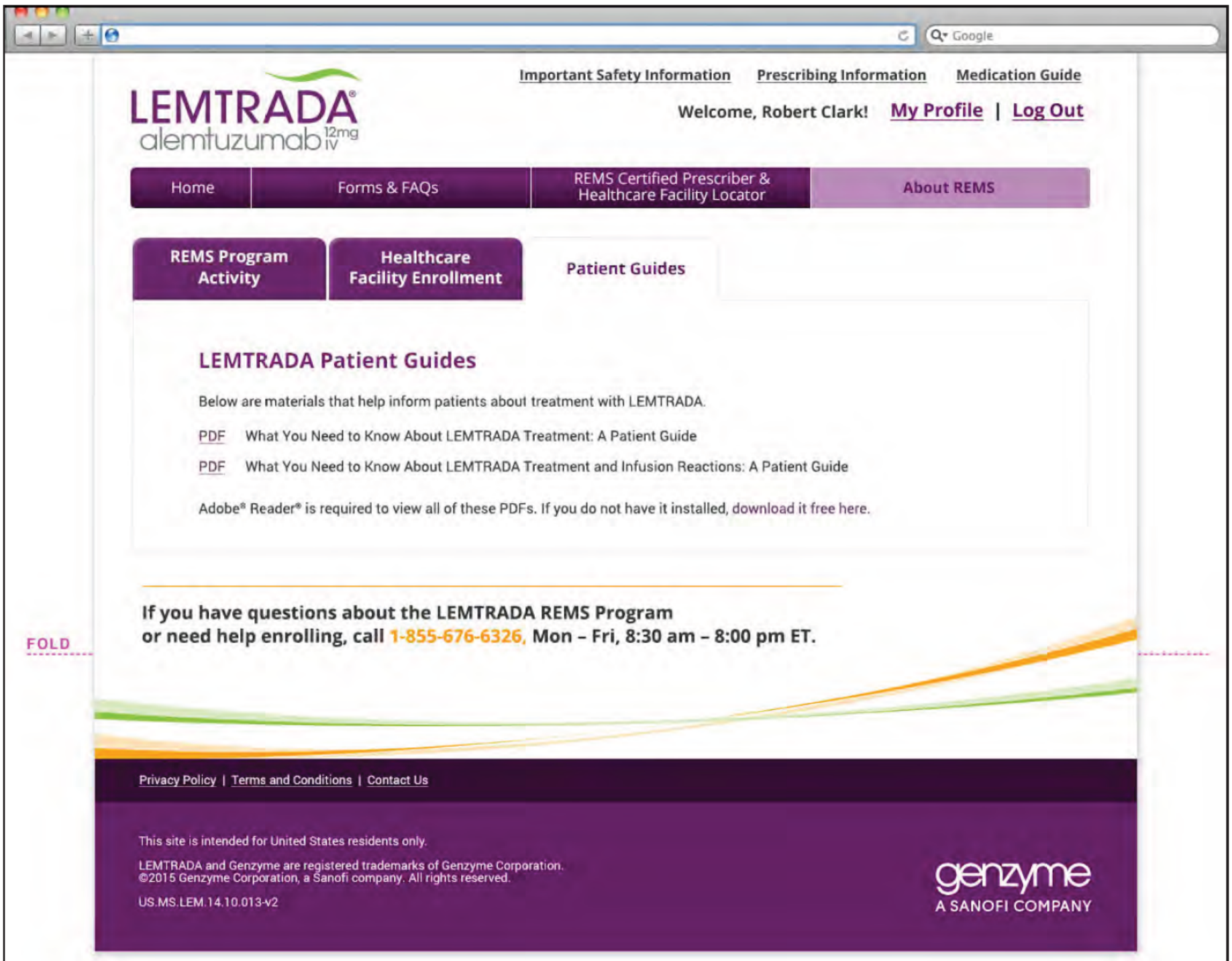
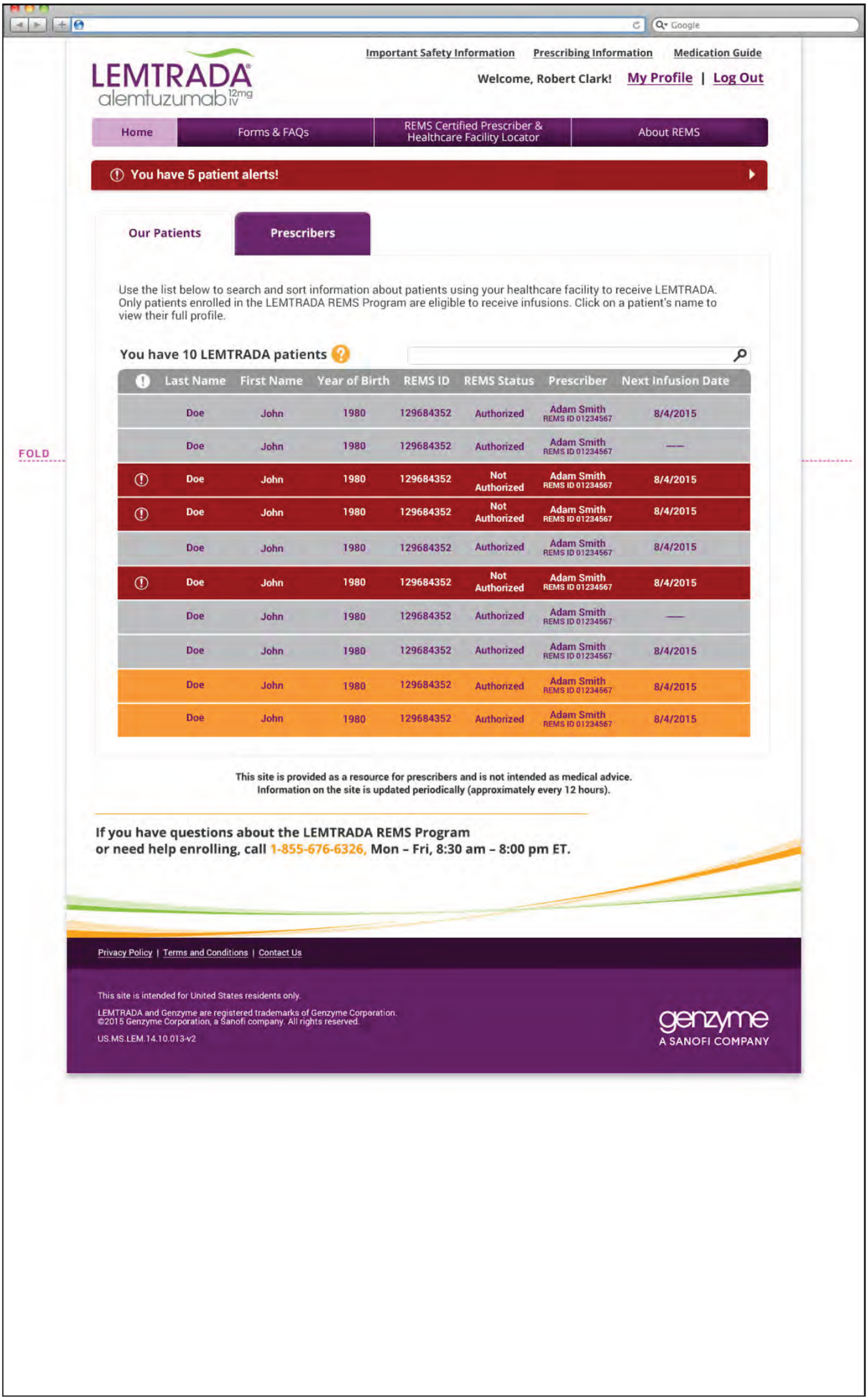
LEMTRADA REMS Desktop - HCF Dashboard - About REMS, Patient Guide

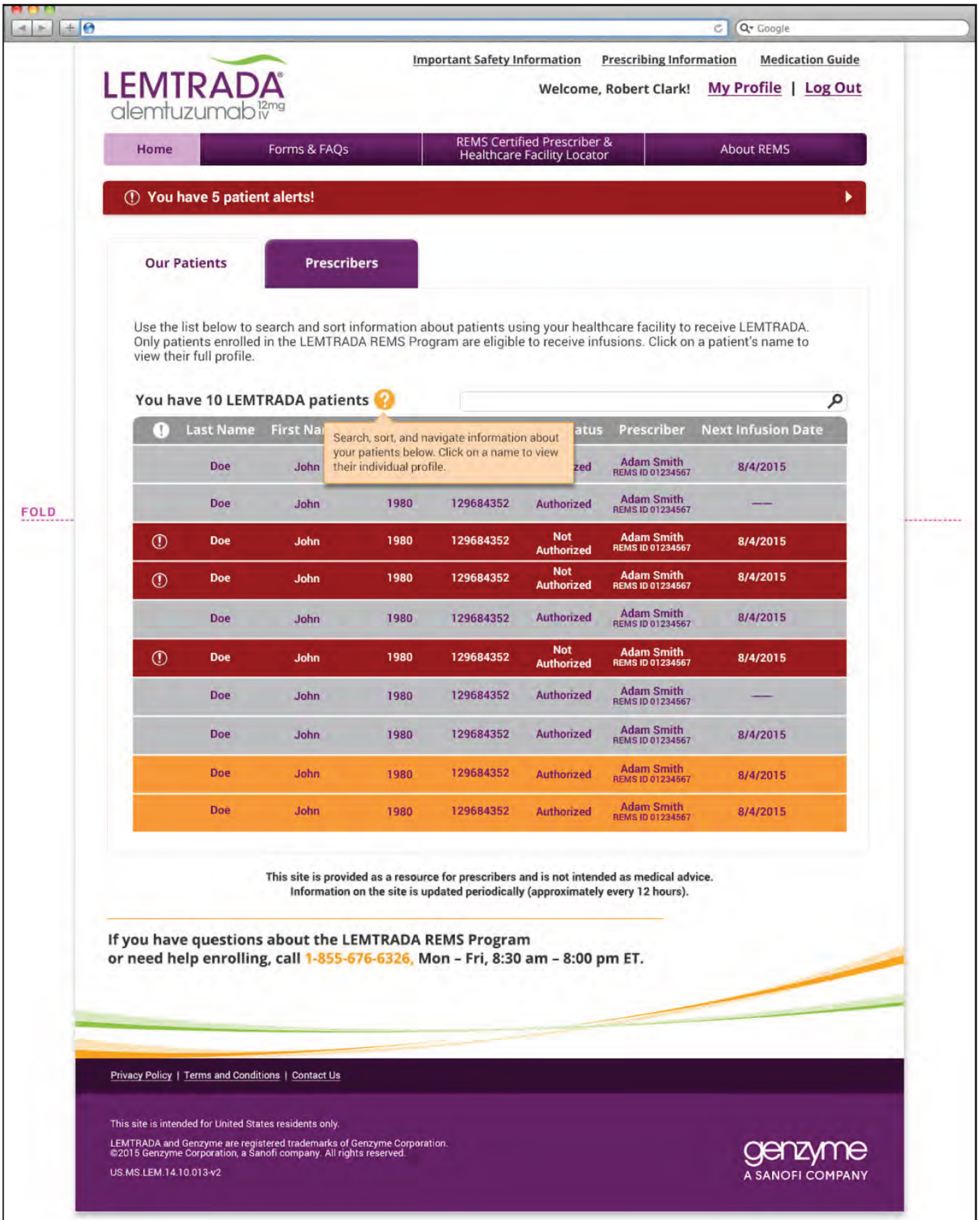


DASHBOARD PAGES FOR HCF USERS WHO ARE NON-MANAGERS

LEMTRADA REMS Desktop - HCF NON-MANAGER Dashboard - Patient List, Alert On



LEMTRADA REMS Desktop - HCF NON-MANAGER Dashboard - Patient List, Tool Tip Expanded



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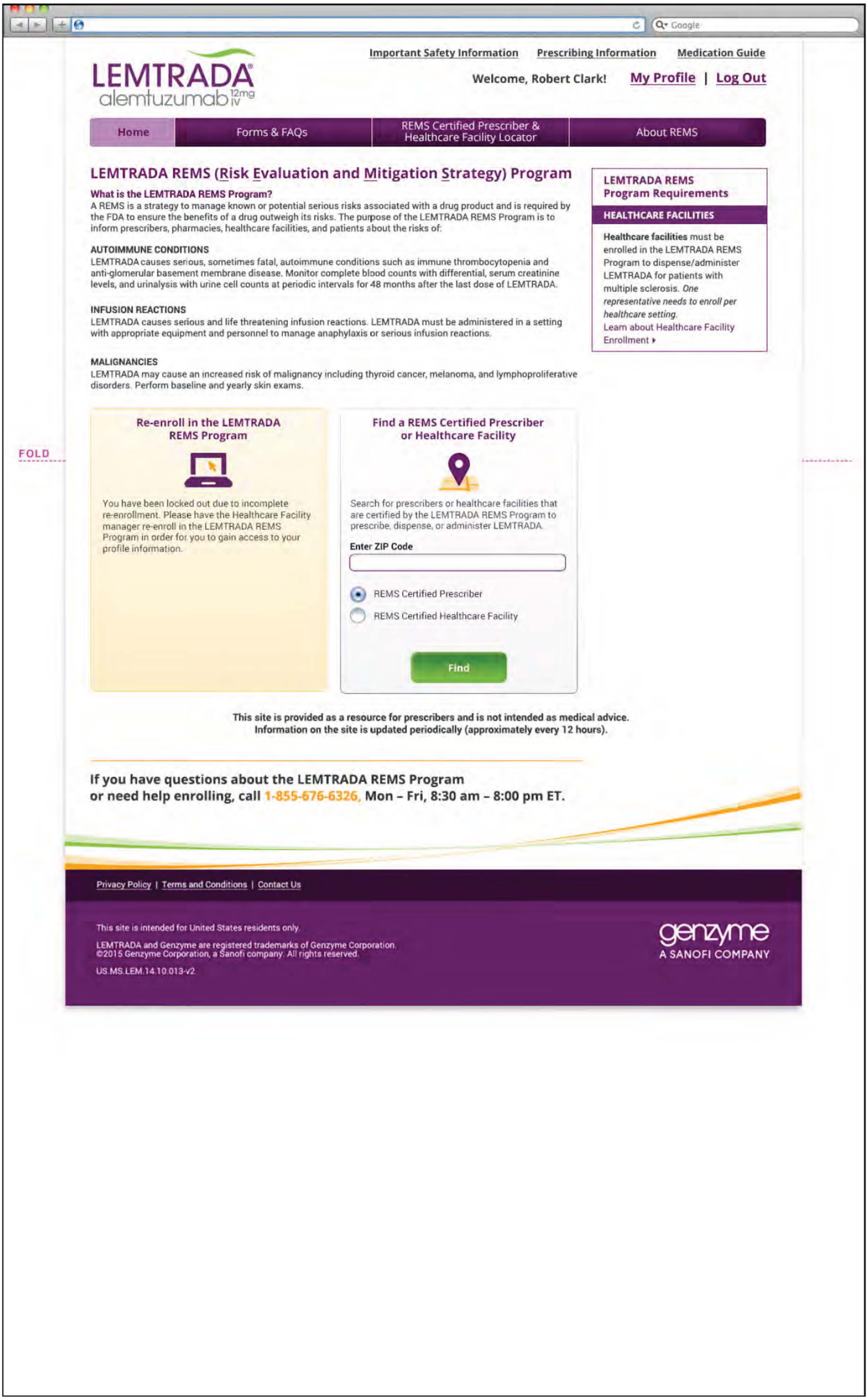
Reference ID: 3821900

LEMTRADA REMS Desktop - HCF User Dashboard - Re-enrollment Lockout



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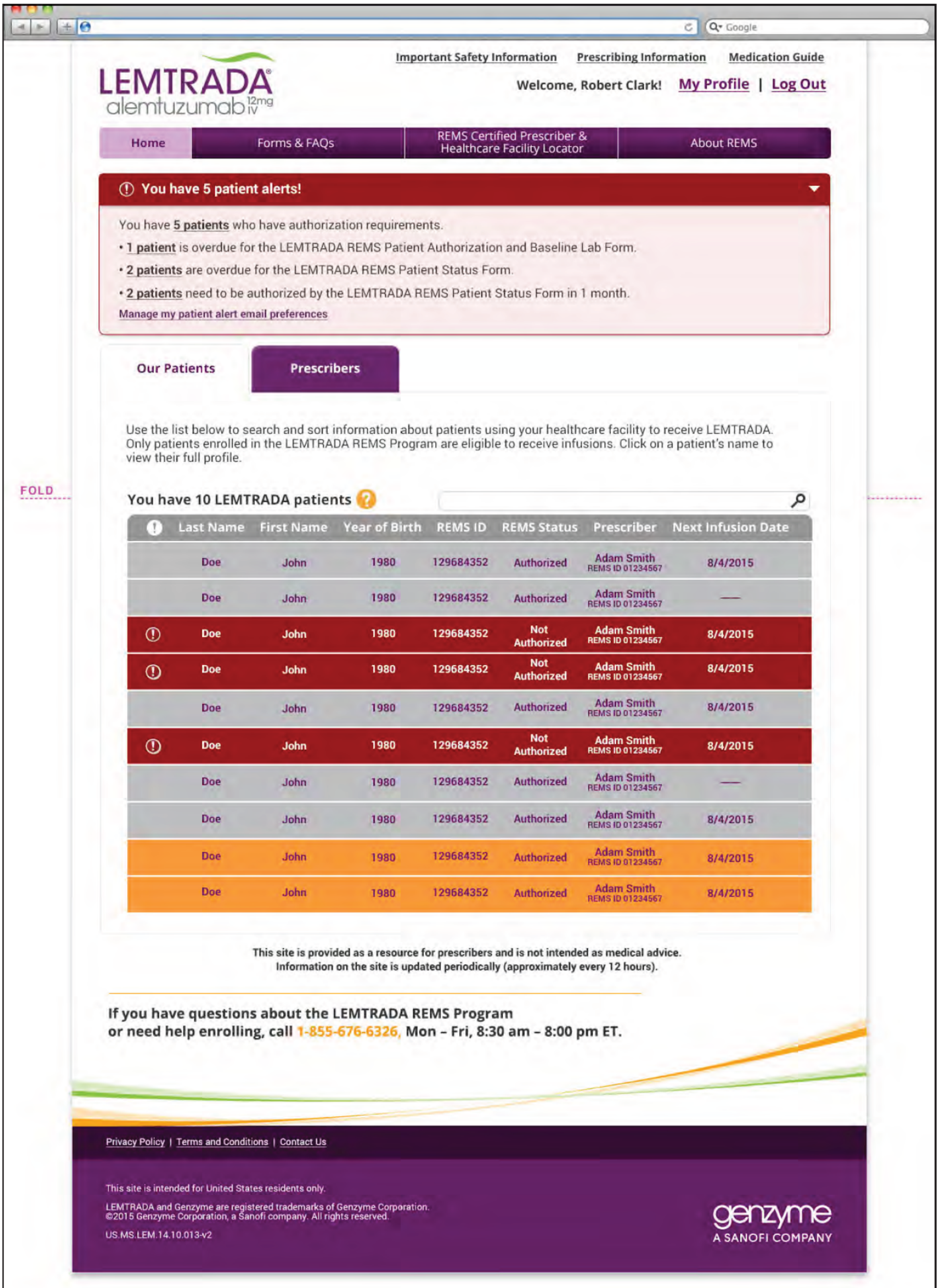
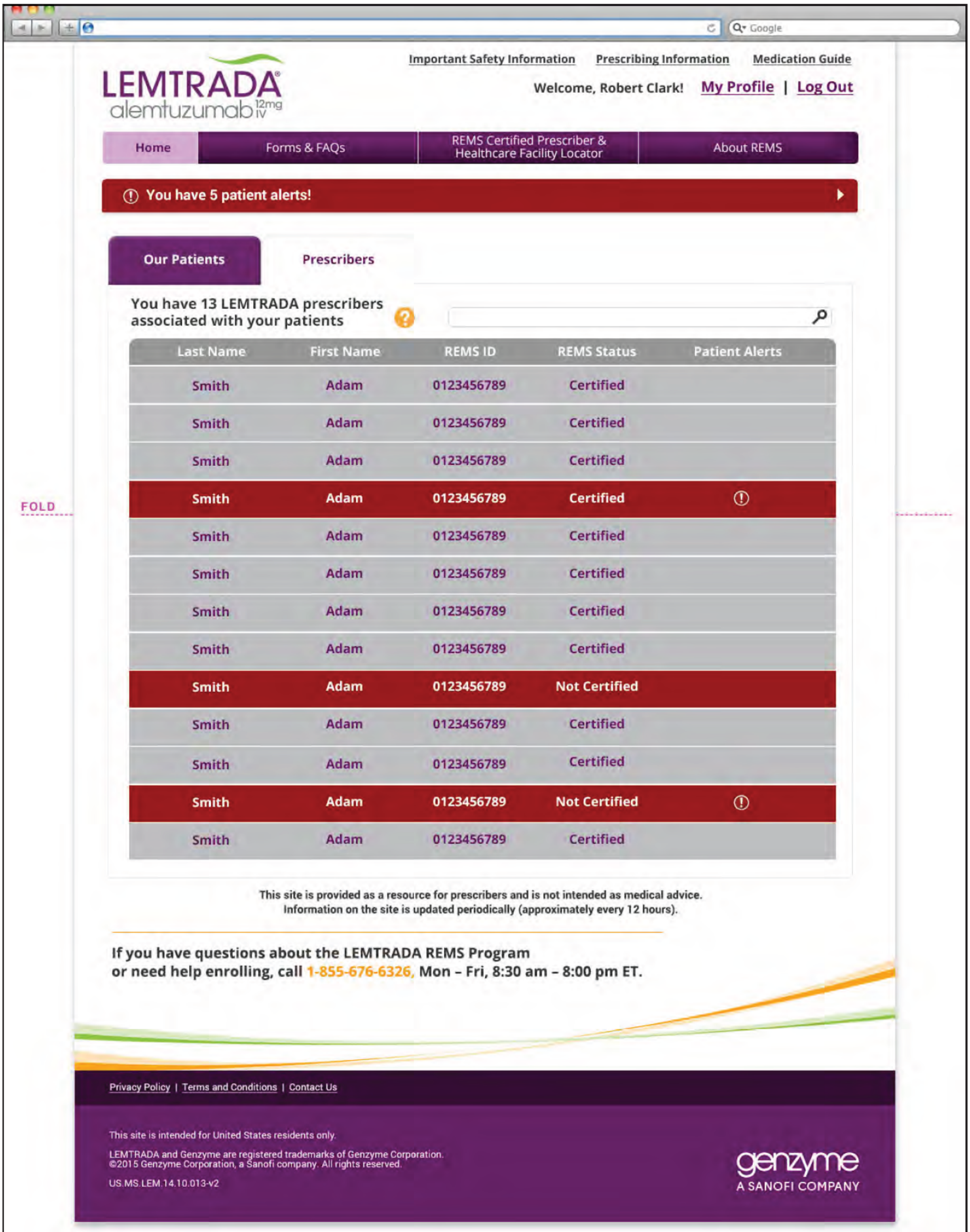
LEMTRADA REMS Desktop - HCF NON-MANAGER Dashboard - Patient List, Alert Expanded



LEMTRADA REMS Desktop - HCF NON-MANAGER Dashboard - Prescribers



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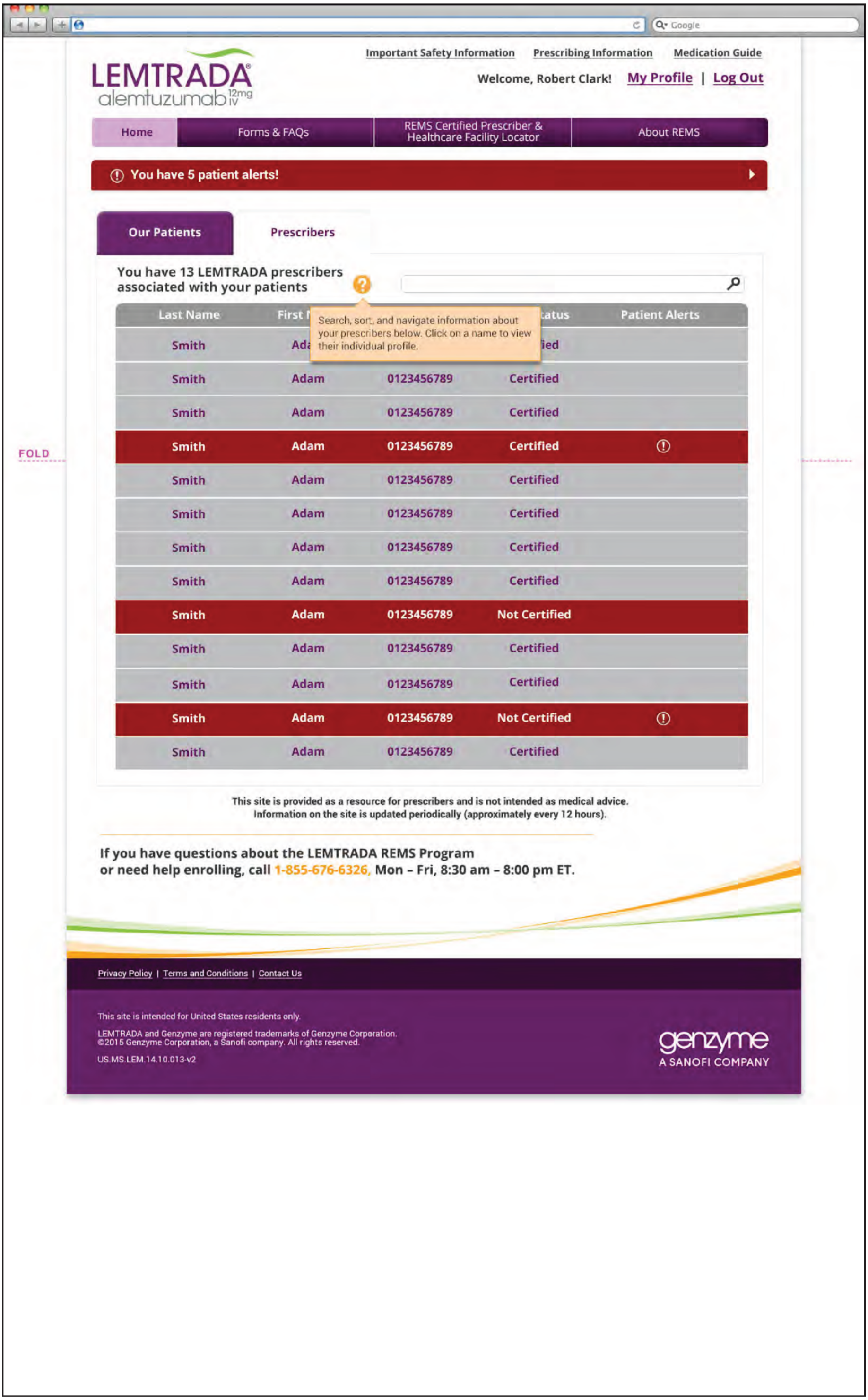
LEMTRADA REMS Desktop - HCF NON-MANAGER Dashboard - Prescribers, Tool Tip Expanded

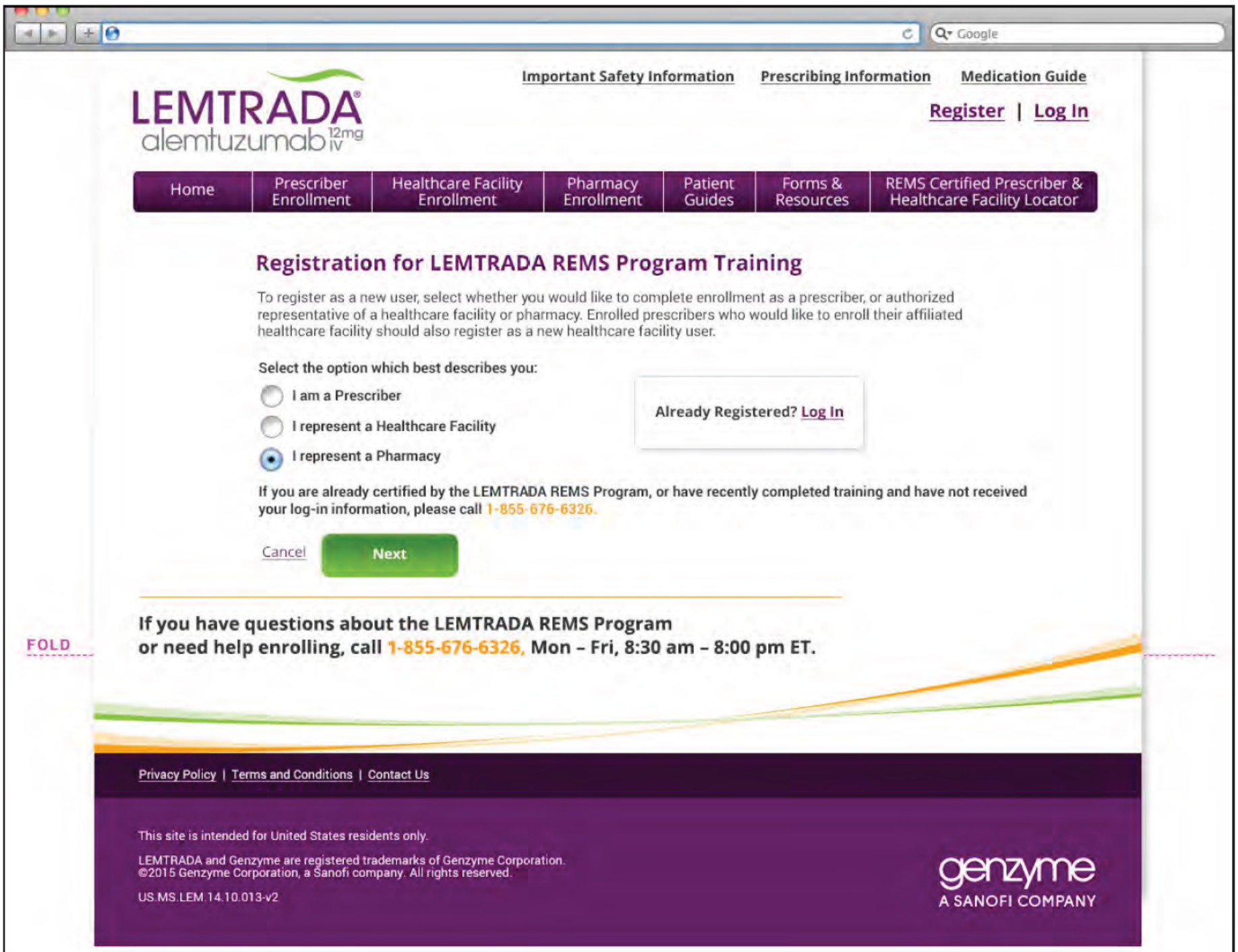


LEMTRADA REMS DESKTOP

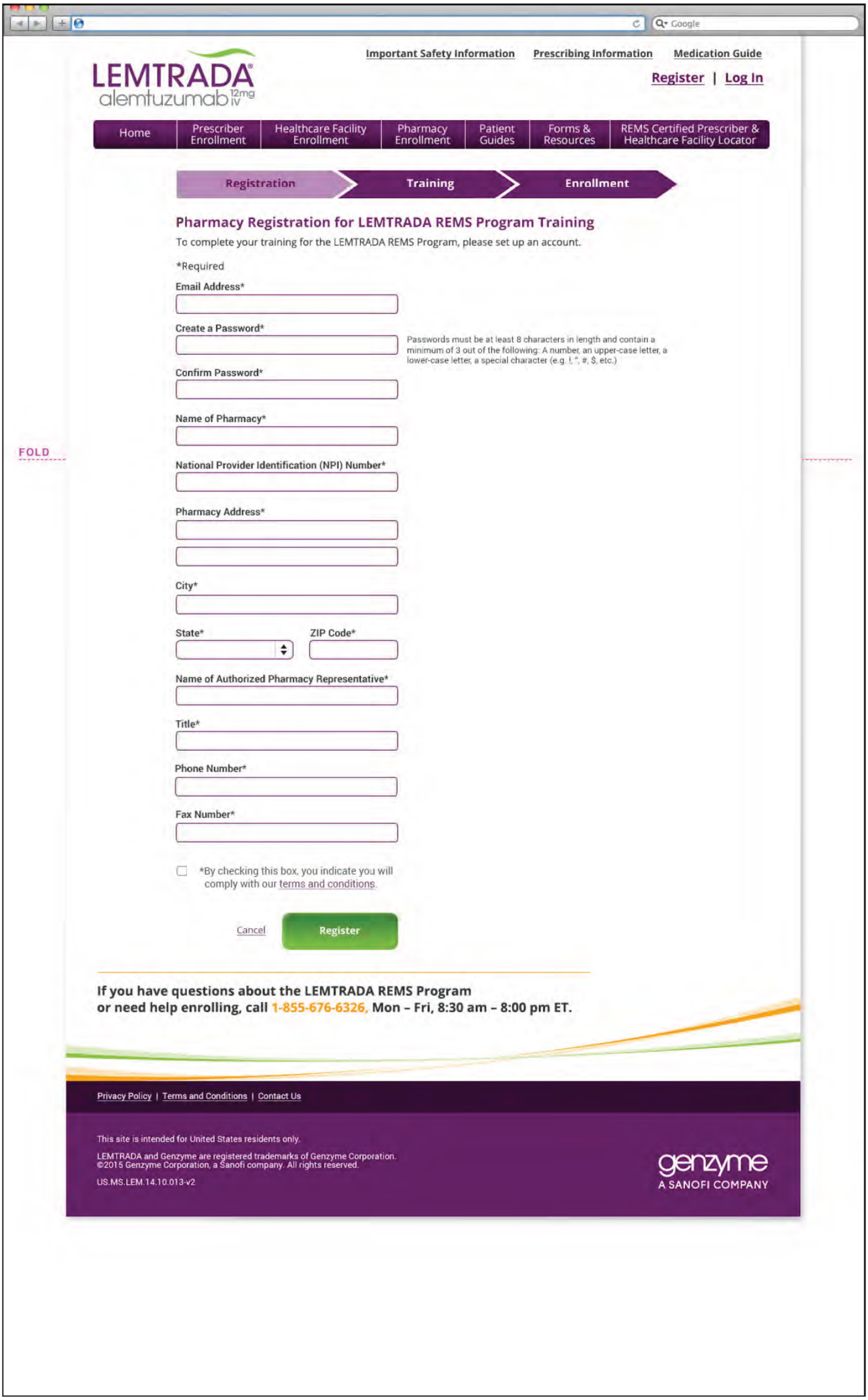
Pharmacy Desktop Pages Only

PHARMACY TRAINING PAGES

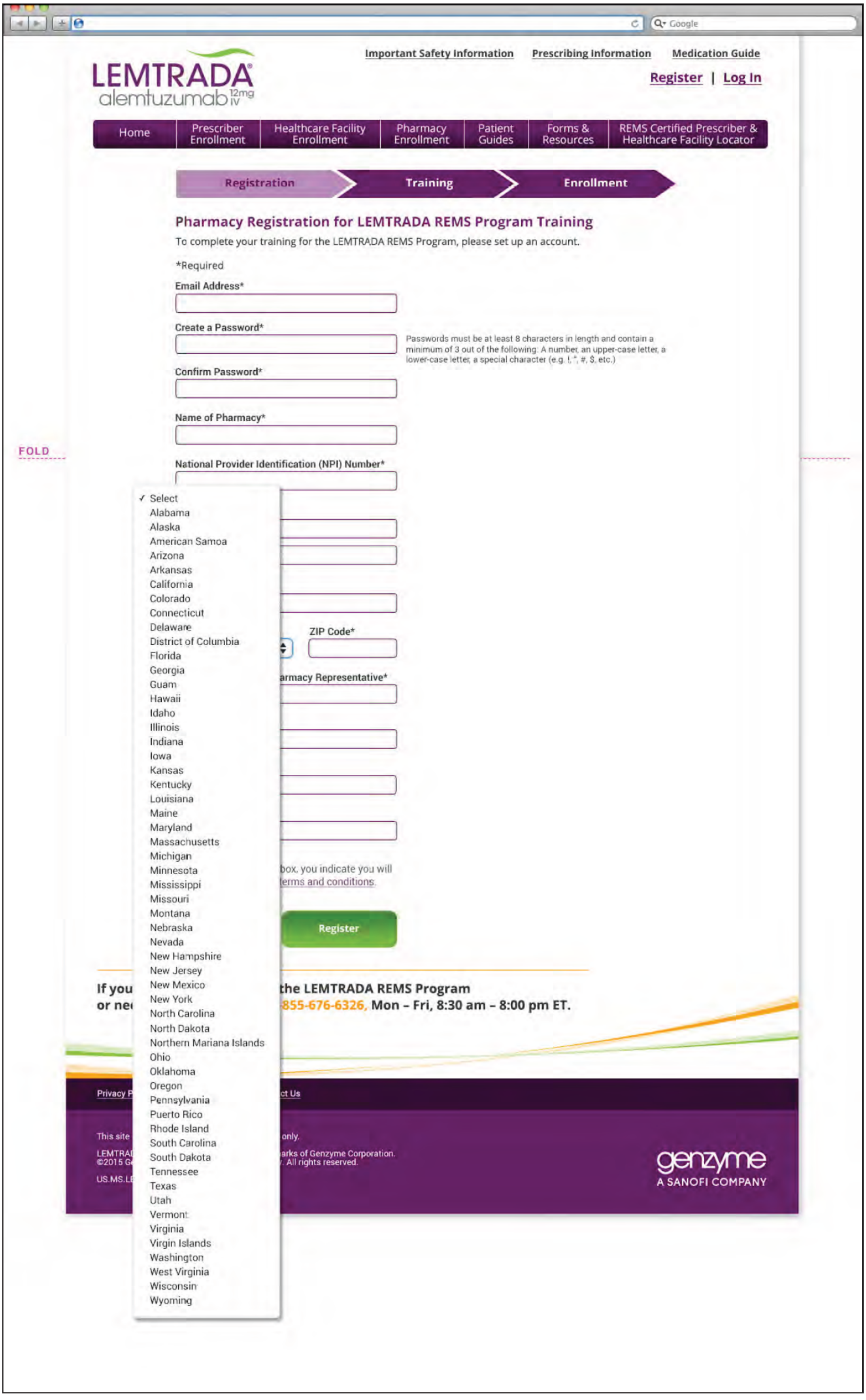
LEMTRADA REMS Desktop - Pharmacy Training - Registration Home Selection



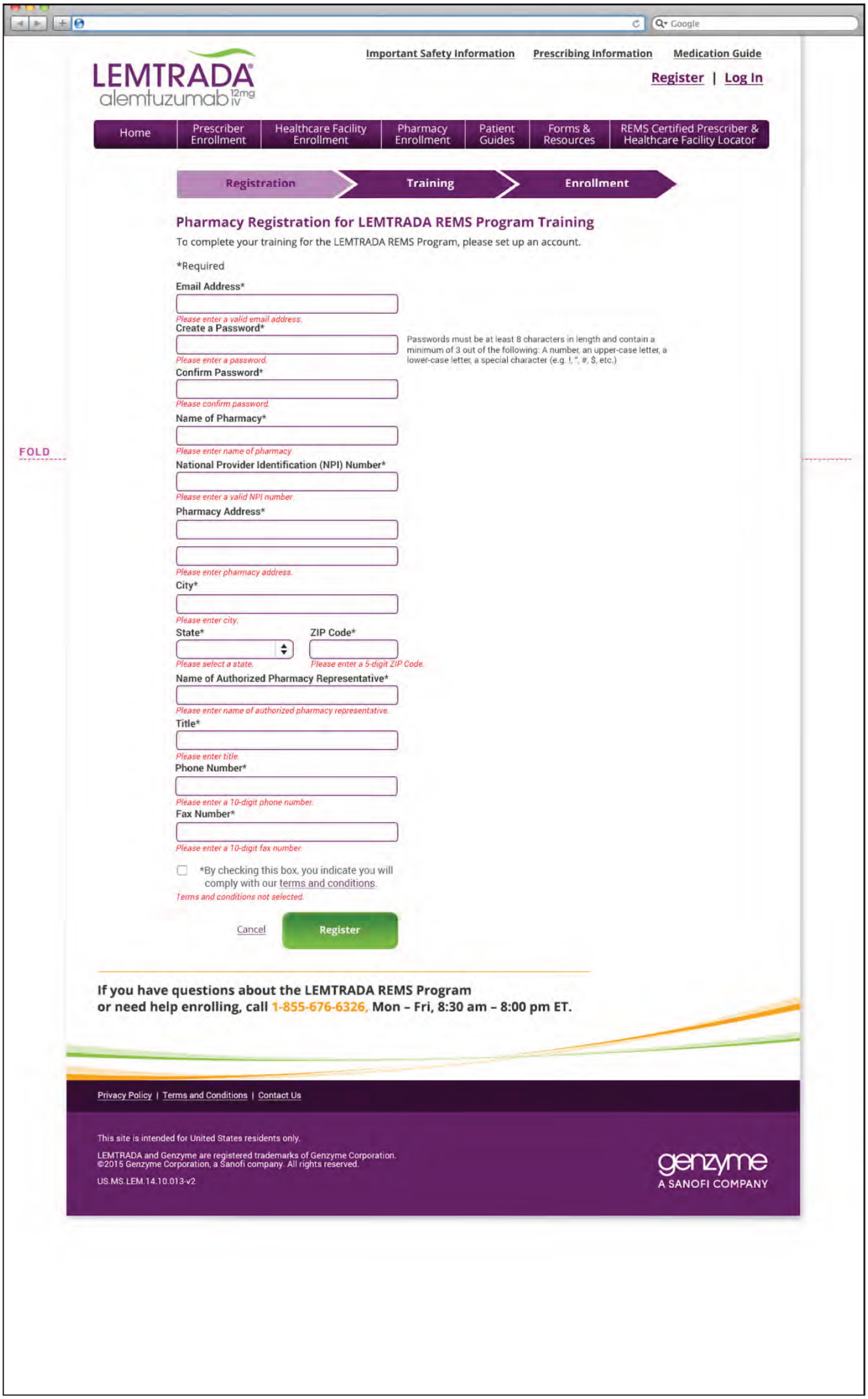
LEMTRADA REMS Desktop - Pharmacy Training - Facility Info Registration



LEMTRADA REMS Desktop - Pharmacy Training - Facility Info Registration, State Dropdown



LEMTRADA REMS Desktop - Pharmacy Training - Facility Info Registration, Error



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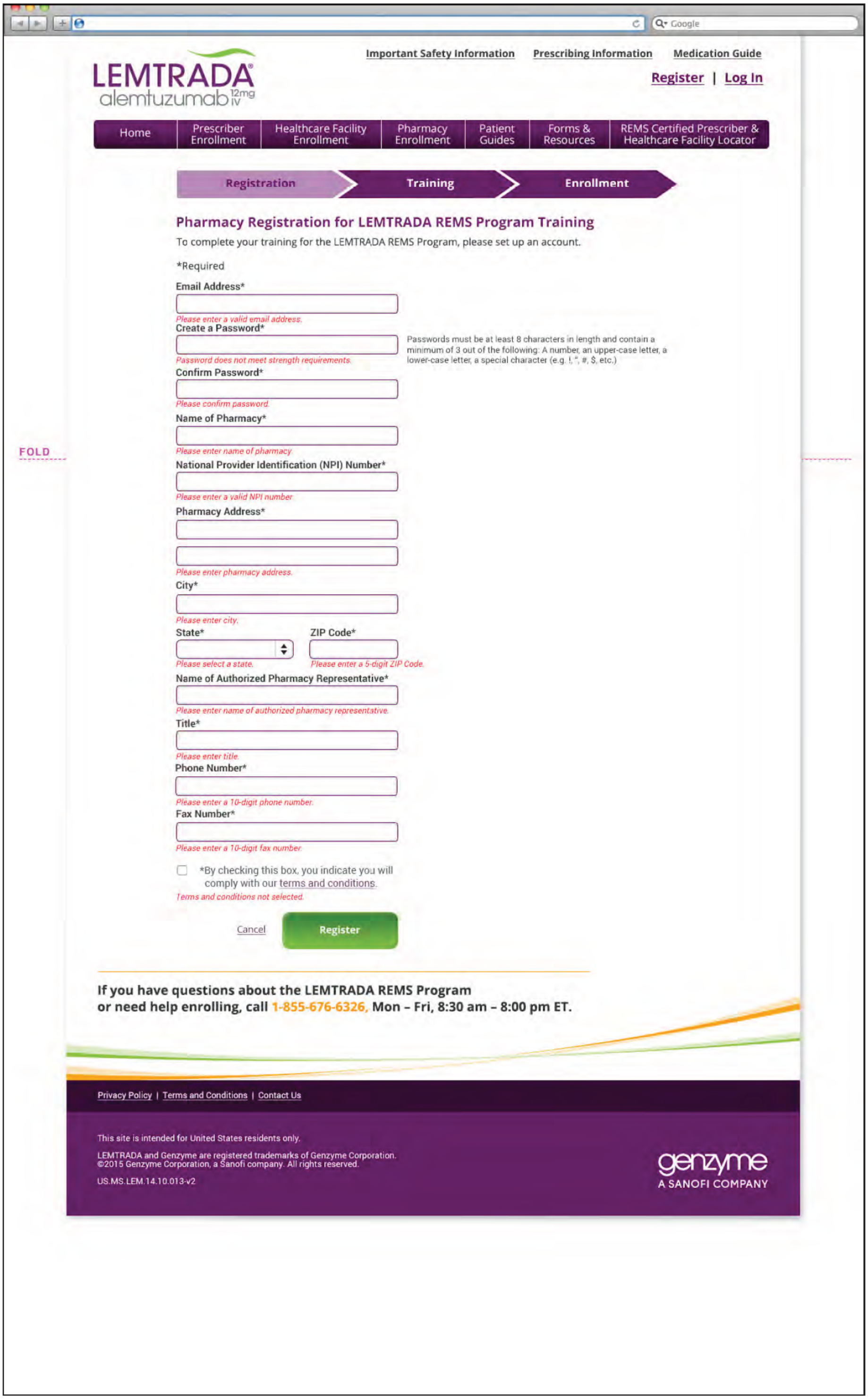
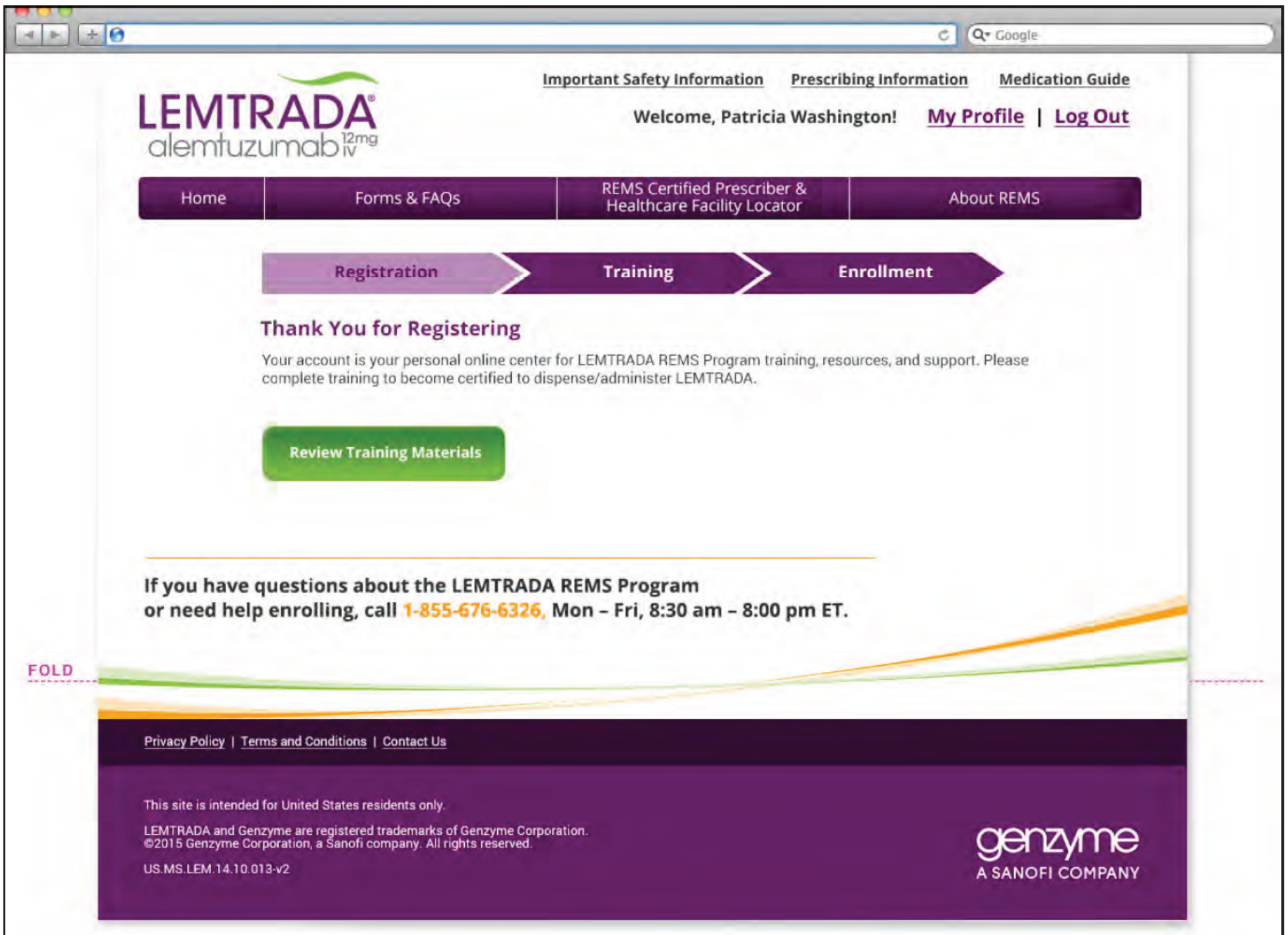
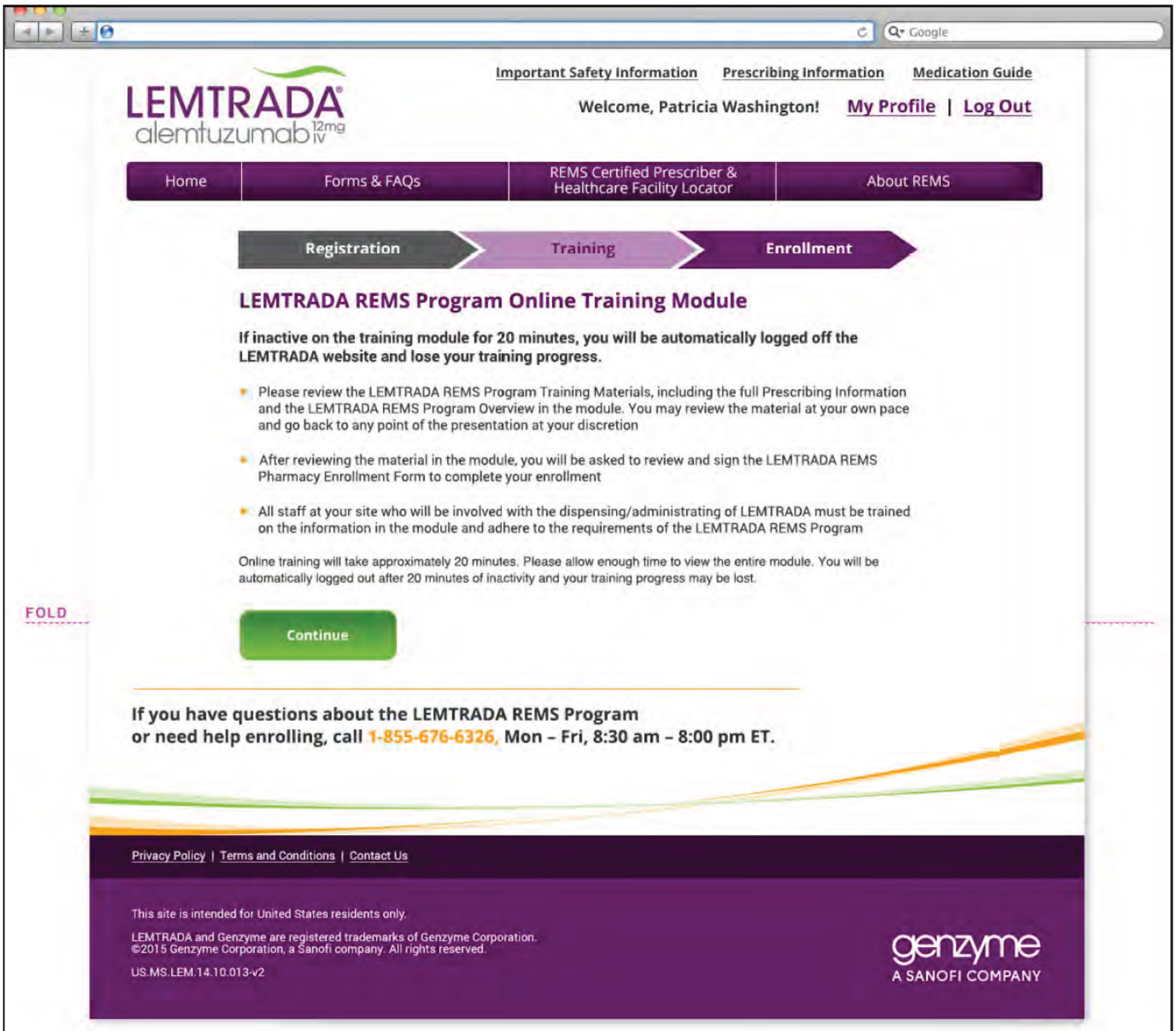
LEMTRADA REMS Desktop - Pharmacy Training - Facility Info Registration, Password Strength Error



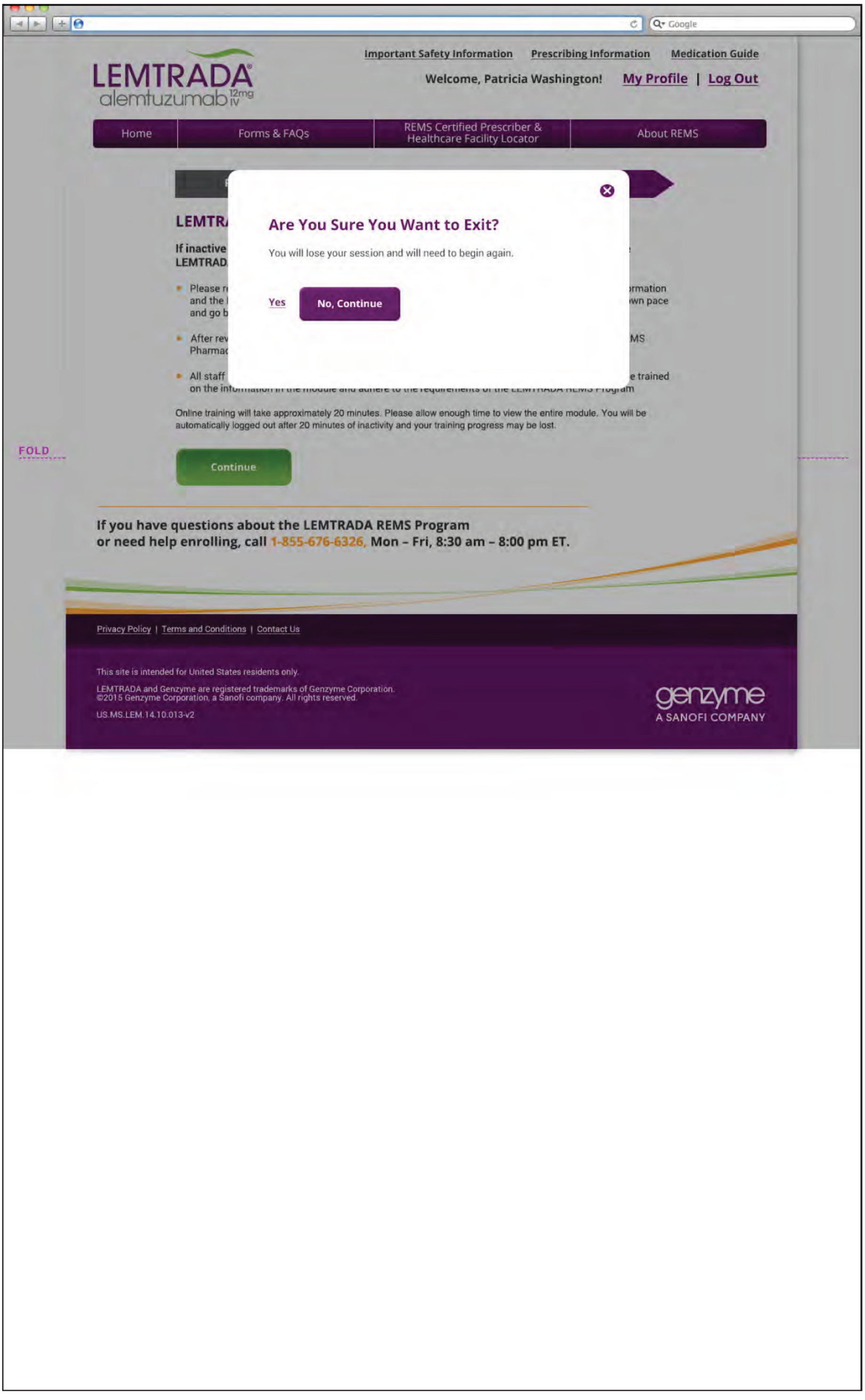
LEMTRADA REMS Desktop - Pharmacy Training - Registration Confirmation



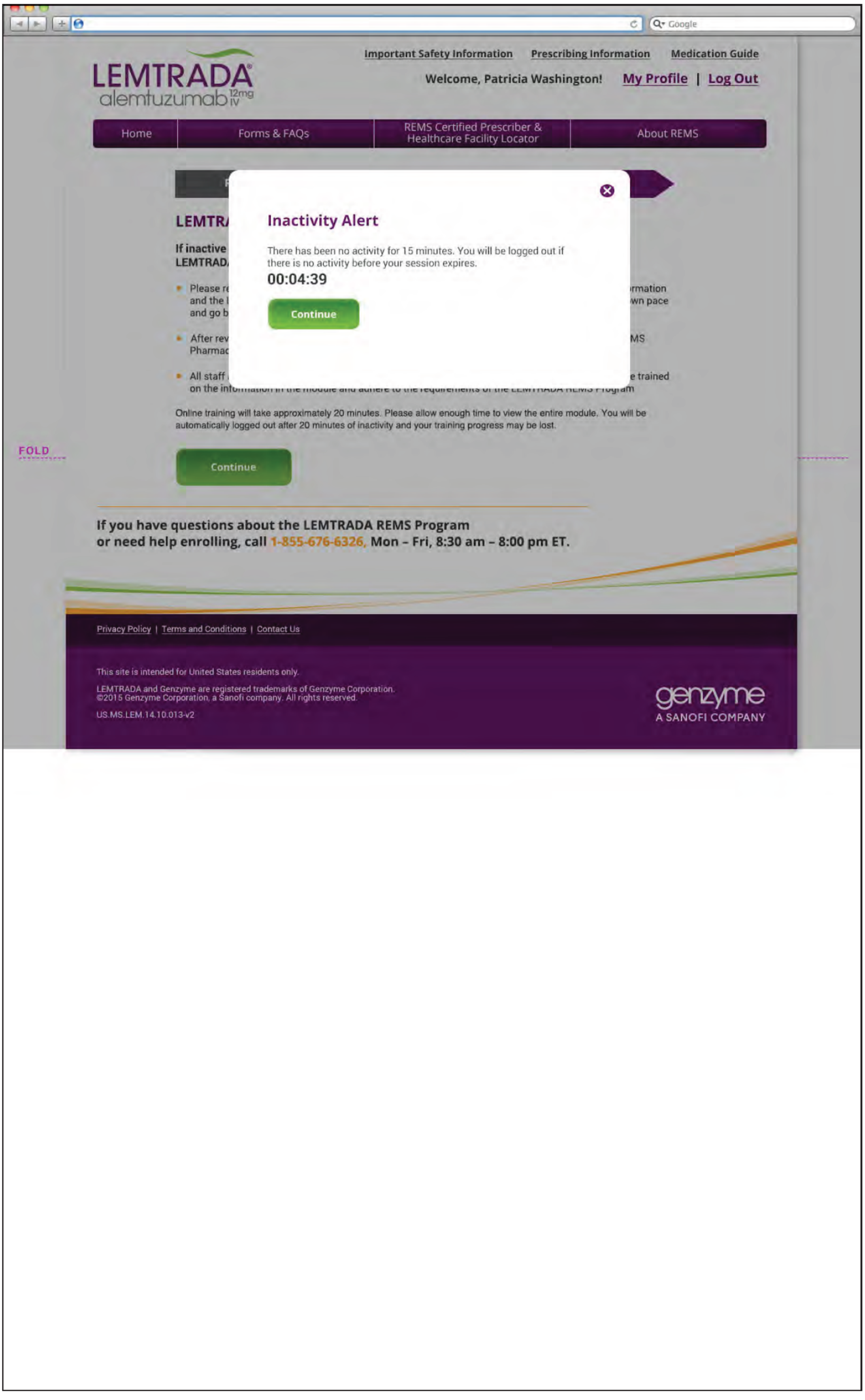
LEMTRADA REMS Desktop - Pharmacy Training - Registration, Training Introduction



LEMTRADA REMS Desktop - Pharmacy Training - Training Module, Exit



LEMTRADA REMS Desktop - Pharmacy Training - Training Module, Timer



LEMTRADA REMS Desktop - Pharmacy Training - Training Module, Timed Out



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Registration → Training → Enrollment

LEMTRADA REMS Program Training

Full Prescribing Information (1 of 8) Total Training Screens: 1 of 10

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- LEMTRADA is available only through a restricted distribution program. (5.4)

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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- 2.2 Vaccinations
- 2.3 Recommended Premedication and Concomitant Medication
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17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

Next (1 of 10)

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

Full Prescribing Information (2 of 8)

Total Training Screens: 2 of 10

FULL PRESCRIBING INFORMATION

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA *[see Warnings and Precautions (5.1)]*.
- LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period *[see Warnings and Precautions (5.2)]*.
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams *[see Warnings and Precautions (5.3)]*.
- Because of the risk of autoimmunity, infusion reactions, and malignancies, LEMTRADA is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS program *[see Warnings and Precautions (5.4)]*.

1 INDICATIONS AND USAGE

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Information

The recommended dosage of LEMTRADA is 12 mg/day administered by intravenous infusion for 2 treatment courses.

- First Treatment Course: 12 mg/day on 5 consecutive days (60 mg total dose)
- Second Treatment Course: 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course.

2.2 Vaccinations

Patients should complete any necessary immunizations at least 6 weeks prior to treatment with LEMTRADA *[see Warnings and Precautions (5.8)]*.

Prior to LEMTRADA treatment determine whether patients have a history of varicella or have been vaccinated for varicella zoster virus (VZV). If not, test the patient for antibodies to VZV and consider vaccination for those who are antibody-negative. Postpone treatment with LEMTRADA until 6 weeks after VZV vaccination.

2.3 Recommended Premedication and Concomitant Medication

Corticosteroids

Premedicate patients with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course *[see Warnings and Precautions (5.2)]*.

Herpes Prophylaxis

Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later *[see Warnings and Precautions (5.8)]*.

2.4 Preparation Instructions

Follow the steps below to prepare the diluted solution of LEMTRADA for intravenous infusion:

- Inspect LEMTRADA visually for particulate matter and discoloration prior to administration. Do not use if particulate matter is present or the solution is discolored. Do not freeze or shake vials prior to use.
- Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique and inject into a 100 mL bag of sterile 0.9% Sodium Chloride, USP or 5% Dextrose in Water, USP.
- Gently invert the bag to mix the solution. Ensure the sterility of the prepared solution, because it contains no antimicrobial preservatives. Each vial is for single use only.

Prior to administration, protect diluted LEMTRADA solution from light and store for as long as 8 hours either at room temperature 15°C to 25°C (59°F to 77°F) or keep refrigerated at conditions 2°C to 8°C (36°F to 46°F).

2.5 Infusion Instructions

Infuse LEMTRADA over 4 hours starting within 8 hours after dilution. Extend the duration of the infusion if clinically indicated.

Administer LEMTRADA in a setting in which equipment and personnel to appropriately manage anaphylaxis or serious infusion reactions are available *[see Warnings and Precautions (5.4)]*.

Do not add or simultaneously infuse other drug substances through the same intravenous line. Do not administer as an intravenous push or bolus.

Monitor vital signs before the infusion and periodically during the infusion. Provide appropriate symptomatic treatment for infusion reactions as needed. Consider immediate discontinuation of the intravenous infusion if severe infusion reactions occur.

Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Inform patients that they should report symptoms that occur during and after each infusion because they may indicate a need for prompt medical intervention *[see Warnings and Precautions (5.2)]*.

2.6 Laboratory Testing and Monitoring to Assess Safety

Conduct the following laboratory tests at baseline and at periodic intervals for 48 months following the last treatment course of LEMTRADA in order to monitor for early signs of potentially serious adverse effects.

- Complete blood count (CBC) with differential (prior to treatment initiation and at monthly intervals thereafter)
- Serum creatinine levels (prior to treatment initiation and at monthly intervals thereafter)
- Urinalysis with urine cell counts (prior to treatment initiation and at monthly intervals thereafter)
- A test of thyroid function, such as thyroid stimulating hormone (TSH) level (prior to treatment initiation and every 3 months thereafter)

Conduct baseline and yearly skin exams to monitor for melanoma *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. LEMTRADA is a clear and colorless to slightly yellow solution that requires dilution prior to intravenous infusion.

4 CONTRAINDICATIONS

LEMTRADA is contraindicated in patients who are infected with Human Immunodeficiency Virus (HIV) because LEMTRADA causes prolonged reductions of CD4+ lymphocyte counts.

5 WARNINGS AND PRECAUTIONS

5.1 Autoimmunity

Treatment with LEMTRADA can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions. In clinical studies LEMTRADA-treated patients experienced thyroid disorders (34%), immune thrombocytopenia (2%), and glomerular nephropathies (0.3%) *[see Warnings and Precautions (5.6, 5.6, 5.7)]*. Autoimmune hemolytic anemia and autoimmune pancytopenia *[see Warnings and Precautions (5.6)]*, undifferentiated connective tissue disorders, and acquired hemophilia A (anti-Factor VIII antibodies) each occurred in 0.2% of patients. Rheumatoid arthritis, type I diabetes, vitiligo, and retinal pigment epitheliopathy occurred in 0.1% of patients. During postmarketing use, additional autoimmune events including Guillain-Barré syndrome and chronic inflammatory demyelinating polyradiculoneuropathy have been reported in the treatment of patients with B-cell chronic lymphocytic leukemia (B-CLL), as well as other disorders, generally at higher and more frequent doses than recommended in MS. An oncology patient treated with alemtuzumab had fatal transfusion-associated graft-versus-host disease.

Autoantibodies may be transferred from the mother to the fetus during pregnancy. A case of transplacental transfer of anti-thyrotropin receptor antibodies resulting in neonatal Graves' disease occurred after alemtuzumab treatment in the mother *[see Use in Specific Populations (8.1)]*.

LEMTRADA may increase the risk of other autoimmune conditions because of the broad range of autoantibody formation with LEMTRADA.

Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts before starting treatment and then at monthly intervals for 48 months after the last dose of LEMTRADA to allow for early detection and treatment of autoimmune adverse reactions *[see Dosage and Administration (2.6)]*. After 48 months, testing should be performed based on clinical findings suggestive of autoimmunity.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.2 Infusion Reactions

LEMTRADA causes cytokine release syndrome resulting in infusion reactions, some of which may be serious and life threatening. In clinical studies, 92% of LEMTRADA-treated patients experienced infusion reactions. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients and included anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

During postmarketing use, other serious and sometimes fatal infusion reactions included hypotension, syncope, acute respiratory distress syndrome, respiratory arrest, myocardial infarction, acute cardiac insufficiency, and cardiac arrest have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Premedicate patients with corticosteroids immediately prior to LEMTRADA infusion for the first 3 days of each treatment course. In clinical trials, patients received 1,000 mg of methylprednisolone for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment.

Consider additional monitoring in patients with medical conditions which predispose them to cardiovascular or pulmonary compromise.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.3 Malignancies

Thyroid cancer

LEMTRADA may increase the risk of thyroid cancer. In controlled clinical studies, 3 of 919 (0.3%) LEMTRADA-treated patients developed thyroid cancer, compared to none in the interferon beta-1a-treated group. However, screening for thyroid cancer was performed more frequently in the LEMTRADA-treated group, because of the higher incidence of autoimmune thyroid disorders in those patients. Two additional cases of thyroid cancer in LEMTRADA-treated patients occurred in uncontrolled studies.

Patients and healthcare providers should monitor for symptoms of thyroid cancer including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

Melanoma

LEMTRADA may increase the risk of melanoma. In uncontrolled studies, 4 of 1486 (0.3%) LEMTRADA-treated patients developed melanoma or melanoma in situ. One of those patients had evidence of locally advanced disease.

Perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.

Lymphoproliferative disorders and lymphoma

Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS, including a MALT lymphoma, Castleman's Disease, and a fatality following treatment of non-Epstein Barr Virus-associated Burkitt's lymphoma. There are postmarketing reports of Epstein Barr Virus-associated lymphoproliferative disorders in non-MS patients.

Because LEMTRADA is an immunomodulatory therapy, caution should also be exercised in initiating LEMTRADA in patients with pre-existing or ongoing malignancies.

LEMTRADA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.4)]*.

5.4 LEMTRADA REMS Program

LEMTRADA is available only through a restricted program under a REMS called the LEMTRADA REMS Program, because of the risks of autoimmunity, infusion reactions, and malignancies *[see Warnings and Precautions (5.1, 5.2, 5.3)]*.

FOLD

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Program Training

Full Prescribing Information (3 of 8)

Total Training Screens: 3 of 10

Notable requirements of the LEMTRADA REMS Program include the following:
- Prescribers must be certified with the program by enrolling and completing training.
- Patients must enroll in the program and comply with ongoing monitoring requirements [see Dosage and Administration (2.6)].
- Pharmacies must be certified with the program and must only dispense to certified healthcare facilities that are authorized to receive LEMTRADA.
- Healthcare facilities must enroll in the program and verify that patients are authorized before infusing LEMTRADA. Healthcare facilities must have on-site access to equipment and personnel trained to manage infusion reactions.

Further information, including a list of qualified healthcare facilities, is available at 1-855-676-6326.

5.5 Immune Thrombocytopenia

Immune thrombocytopenia (ITP) occurred in 2% of LEMTRADA-treated patients in clinical studies in MS.

In a controlled clinical trial in patients with MS, one LEMTRADA-treated patient developed ITP that went unrecognized prior to the implementation of monthly blood monitoring requirements, and died from intracerebral hemorrhage. Nadir platelet counts ≤20,000 cells per microliter as a result of ITP occurred in 2% of all LEMTRADA-treated patients in clinical studies in MS. Anti-platelet antibodies did not precede ITP onset. ITP has been diagnosed more than 3 years after the last LEMTRADA dose.

Symptoms of ITP include easy bruising, petechiae, spontaneous mucocutaneous bleeding (e.g., epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. Hemoptysis may also be indicative of anti-glomerular basement membrane (GBM) disease [see Warnings and Precautions (5.6)], and an appropriate differential diagnosis has to be undertaken. Remind the patient to remain vigilant for symptoms they may experience and to seek immediate medical help if they have any concerns.

Obtain complete blood counts (CBCs) with differential prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion [see Dosage and Administration (2.6)]. After this period of time, testing should be performed based on clinical findings suggestive of ITP. If ITP is suspected, a complete blood count should be obtained immediately. If ITP onset is confirmed, promptly initiate appropriate medical intervention.

5.6 Glomerular Nephropathies

Glomerular nephropathies occurred in 0.3% of LEMTRADA-treated patients in MS clinical trials. There were 3 cases of membranous glomerulonephritis and 2 cases of anti-glomerular basement membrane (anti-GBM) disease. There are published and post-marketing cases of MS patients treated with alemtuzumab who developed anti-GBM disease and subsequently developed end stage renal disease requiring renal transplantation. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA. Urgent evaluation and treatment is required because anti-GBM disease can lead to renal failure requiring dialysis or transplantation and can be life-threatening if left untreated. Clinical manifestations of nephropathy may include elevated serum creatinine levels, hematuria, or proteinuria. Alveolar hemorrhage manifested as hemoptysis is a common component of anti-GBM disease but did not occur in clinical trials.

Obtain serum creatinine levels and urinalysis with cell counts prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

If clinically significant changes from baseline in serum creatinine, unexplained hematuria, or proteinuria are observed, perform further evaluation for nephropathies. Early detection and treatment of nephropathies may decrease the risk of poor outcomes.

5.7 Thyroid Disorders

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Autoimmune thyroid disorders included Graves' disease, hyperthyroidism and hypothyroidism. Graves' ophthalmopathy with decreased vision, eye pain, and exophthalmos occurred in 1% of LEMTRADA-treated patients. Two patients required surgical orbital decompression. Serious thyroid events occurred in about 2% of LEMTRADA-treated patients in clinical studies and included cardiac and psychiatric events associated with thyroid disease. Of all LEMTRADA-treated patients, 3% underwent thyroidectomy.

Thyroid disease poses special risks in women who are pregnant [see Use in Specific Populations (8.1)].

Obtain thyroid function tests, such as TSH levels, prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

In patients with ongoing thyroid disorder, LEMTRADA should be administered only if the potential benefit justifies the potential risks.

5.8 Other Autoimmune Cytopenias

Autoimmune cytopenias such as neutropenia (0.1%), hemolytic anemia (0.2%), and pancytopenia (0.2%) occurred in LEMTRADA-treated patients in clinical studies in MS. In cases of autoimmune hemolytic anemia, patients tested positive for direct antiglobulin antibodies, and nadir hemoglobin levels ranged from 2.9-8.6 g/dL. Symptoms of autoimmune hemolytic anemia include weakness, chest pain, jaundice, dark urine, and tachycardia. One LEMTRADA-treated patient with autoimmune pancytopenia died from sepsis.

During postmarketing use, additional autoimmune cytopenias including fatal autoimmune hemolytic anemia and aplastic anemia have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Use CBC results to monitor for cytopenias. Prompt medical intervention is indicated if a cytopenia is confirmed.

5.9 Infections

Infections occurred in 71% of LEMTRADA-treated patients compared to 53% of patients treated with interferon beta-1a in controlled clinical trials in MS up to 2 years in duration. Infections that occurred more often in LEMTRADA-treated patients than interferon beta-1a patients included nasopharyngitis, urinary tract infection, upper respiratory tract infection, sinusitis, herpetic infections, influenza, and bronchitis. Serious infections occurred in 3% of patients treated with LEMTRADA as compared to 1% of patients treated with interferon beta-1a. Serious infections in the LEMTRADA group included appendicitis, gastroenteritis, pneumonia, herpes zoster, and tooth infection.

Do not administer live viral vaccines following a course of LEMTRADA. Patients treated with LEMTRADA have altered immunity and may be at increased risk of infection following administration of live viral vaccines.

Consider delaying LEMTRADA administration in patients with active infection until the infection is fully controlled.

Concomitant use of LEMTRADA with antineoplastic or immunosuppressive therapies could increase the risk of immunosuppression.

Herpes Viral Infections

In controlled clinical trials, 16% of LEMTRADA-treated patients developed a herpes viral infection compared to 3% of interferon beta-1a patients. These events included oral herpes (8.8%), herpes zoster (4.2%), herpes simplex (1.8%), and genital herpes (1.3%). Serious herpetic infections in LEMTRADA-treated patients included primary varicella (0.1%), herpes zoster (0.2%), and herpes meningitis (0.1%). Administer antiviral agents for herpetic prophylaxis at appropriate suppressive dosing regimens. Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥ 200 cells per microliter, whichever occurs later [see Dosage and Administration (2.3)].

Human Papilloma Virus

Cervical human papilloma virus (HPV) infection, including cervical dysplasia, occurred in 2% of LEMTRADA-treated patients. Annual HPV screening is recommended for female patients.

Tuberculosis

Tuberculosis occurred in patients treated with LEMTRADA and interferon beta-1a in controlled clinical trials. Active and latent tuberculosis cases occurred in 0.3% of LEMTRADA-treated patients, most often in endemic regions. Perform tuberculosis screening according to local guidelines prior to initiation of LEMTRADA. For patients testing positive in tuberculosis screening, treat by standard medical practice prior to therapy with LEMTRADA.

Fungal Infections

Fungal infections, especially oral and vaginal candidiasis, occurred more commonly in LEMTRADA-treated patients (12%) than in patients treated with interferon beta-1a (3%) in controlled clinical trials in MS.

Listeria Infections

Listeria meningitis has been reported in LEMTRADA-treated patients. Cases of listeria meningitis occurred within 1 month of alemtuzumab dosing. The duration of increased risk for listeria meningitis is unclear. Patients should avoid or adequately heat foods that are potential sources of *Listeria monocytogenes*.

Infections in non-MS patients

During postmarketing use, serious and sometimes fatal viral, bacterial, protozoan, and fungal infections, including some due to reactivation of latent infections, have been reported in the treatment of patients with B-CLL, as well as other disorders, generally at higher and more frequent doses than recommended in MS.

Hepatitis

No cases are available on the association of LEMTRADA with Hepatitis B virus (HBV) or Hepatitis C virus (HCV) reactivation because patients with evidence of active or chronic infections were excluded from the clinical trials. Consider screening patients at high risk of HBV and/or HCV infection before initiation of LEMTRADA and exercise caution in prescribing LEMTRADA to patients identified as carriers of HBV and/or HCV as these patients may be at risk of irreversible liver damage relative to a potential virus reactivation as a consequence of their pre-existing status.

5.10 Pneumonitis

In clinical studies, 6 of 1217 (0.5%) LEMTRADA-treated patients had pneumonitis of varying severity. Cases of hypersensitivity pneumonitis and pneumonitis with fibrosis occurred in clinical studies. Patients should be advised to report symptoms of pneumonitis, which include shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

5.11 Drug Products with Same Active Ingredient

LEMTRADA contains the same active ingredient (alemtuzumab) found in CAMPATH®. If LEMTRADA is considered for use in a patient who has previously received CAMPATH, exercise increased vigilance for additive and long-lasting effects on the immune system.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling:
- Autoimmunity [see Boxed Warning and Warnings and Precautions (5.1)]
- Infusion reactions [see Boxed Warning and Warnings and Precautions (5.2)]
- Malignancies [see Warnings and Precautions (5.3)]
- Immune Thrombocytopenia [see Warnings and Precautions (5.5)]
- Glomerular Nephropathies [see Warnings and Precautions (5.6)]
- Thyroid Disorder [see Warnings and Precautions (5.7)]
- Other Autoimmune Cytopenias [see Warnings and Precautions (5.8)]
- Infections [see Warnings and Precautions (5.9)]
- Pneumonitis [see Warnings and Precautions (5.10)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In controlled clinical trials (Study 1 and Study 2), a total of 811 patients with relapsing forms of MS received LEMTRADA. A total of 811 patients received 1 course of therapy, and 799 patients received a second course of therapy at 12 months. The overall follow-up in the controlled trials was equivalent to 1622 patient years, with an additional 3411 person-years of follow-up in an open label extension study. The population was 18-55 years of age, 65% were female, and 92% were Caucasian.

Most Common Adverse Reactions

In clinical trials, the most common adverse reactions with LEMTRADA (in at least 10% of patients and more frequently than in interferon beta-1a) were rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting.

Table 1 lists adverse reactions occurring in ≥5% of LEMTRADA-treated patients in Study 1 and 2 and at the same or at a higher rate than interferon beta-1a.

Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=389) %
Rash	53	6
Headache	52	23
Pyrexia	26	9

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Table 1: Adverse Reactions in the Pooled 2-Year Active-Controlled Studies in Patients with Relapsing-Remitting Multiple Sclerosis (continued)

	LEMTRADA (N=811) %	Interferon beta-1a 44 mcg (N=669) %
Nasopharyngitis	25	19
Nausea	21	9
Urinary tract infection	19	8
Fatigue	18	13
Insomnia	16	15
Upper respiratory tract infection	16	13
Herpes viral infection	16	3
Urticaria	16	2
Pruritus	14	2
Thyroid gland disorders	13	3
Fungal infection	13	4
Arthralgia	12	9
Pain in extremity	12	9
Back pain	12	8
Diarrhea	12	6
Sinusitis	11	8
Oropharyngeal pain	11	5
Paresthesia	10	8
Dizziness	10	5
Abdominal pain	10	5
Flushing	10	4
Vomiting	10	3
Cough	9	4
Chills	9	3
Dysgeusia	8	7
Influenza	8	6
Dermatitis	8	5
Dyspepsia	8	4
Blood in urine	8	3
Dyspnea	8	1
Tachycardia	8	1
Anxiety	7	6
Muscular weakness	7	6
Bronchitis	7	4
Chest discomfort	7	2
Muscle spasms	6	5
Myalgia	6	5
Decrease in CD4 lymphocytes	6	2
Decrease in CD8 lymphocytes	6	2
Asthenia	5	4
Decrease in T-lymphocyte count	5	3
Erythema	5	2
Peripheral edema	5	2
Epistaxis	5	2
Neck Pain	5	2
Abnormal uterine bleeding	5	1

6.2 Lymphopenia

Nearly all (99.9%) patients treated with LEMTRADA in MS clinical trials experienced lymphopenia. The lowest lymphocyte counts occurred approximately by 1 month after each course of treatment. The mean lymphocyte count at 1 month after LEMTRADA treatment was 0.25 x 10⁹/L (range 0.00-3.30 x 10⁹/L) and 0.32 (0.00-1.81 x 10⁹/L) for treatment courses 1 and 2, respectively. Total lymphocyte counts increased to reach the lower limit of normal in approximately 42% of patients by 6 months after each LEMTRADA treatment course and approximately 80% of patients by 12 months after each course [see *Clinical Pharmacology (12.2)*].

6.3 Suicidal Behavior or Ideation

In clinical studies, 0.6% of patients in both the LEMTRADA and interferon beta-1a groups had events of attempted suicide or suicidal ideation. There were no completed suicides in either clinical study treatment group. Suicidal behavior or ideation occurred in patients with or without a history of a psychiatric or thyroid disorder. Advise patients to report immediately any symptoms of depression or suicidal ideation to the prescribing physician.

6.4 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Using an enzyme-linked immunosorbent assay (ELISA) and a competitive binding assay, anti-alemtuzumab binding antibodies were detected in 62%, 67%, and 29% of LEMTRADA-treated patients, at months 1, 3, 12 (Course 1) as well as 83%, 83%, and 75% of LEMTRADA-treated patients at months 13, 15, and 24 (Course 2). Samples that tested positive for binding antibodies were further evaluated for evidence of *in vitro* inhibition using a flow cytometry assay. Neutralizing antibodies were detected in 87%, 46%, and 5% of positive binding antibody patients at months 1, 3, 12 (Course 1) as well as 94%, 88%, and 42% of positive binding antibody patients at months 13, 15, and 24 (Course 2). Anti-alemtuzumab antibodies were associated with decreased alemtuzumab concentration during Course 2 but not Course 1. There was no evidence from clinical trials that the presence of binding or inhibitory anti-alemtuzumab antibodies had a significant effect on clinical outcomes, total lymphocyte count, or adverse events.

The incidence of antibodies is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including inhibitory antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to LEMTRADA with the incidence of antibodies to other products may be misleading.

6.5 Postmarketing Experience

The following adverse reactions, not described elsewhere, were identified during post-approval use of alemtuzumab (CAMPATH) for the treatment of B-cell chronic lymphocytic leukemia (B-CLL), as well as for the treatment of other disorders, generally at higher and more frequent doses (e.g., 30 mg) than that recommended in the treatment of MS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac Disorders

Congestive heart failure, cardiomyopathy, and decreased ejection fraction in non-MS patients previously treated with potentially cardiotoxic agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. LEMTRADA was embryolethal in pregnant huCD52 transgenic mice when administered during organogenesis. Auto-antibodies may develop after administration of LEMTRADA. Placental transfer of anti-thyroid antibodies resulting in neonatal Graves' disease has been reported. LEMTRADA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

When LEMTRADA was administered to pregnant huCD52 transgenic mice during organogenesis (gestation days [GD] 6-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, no teratogenic effects were observed. However, there was an increase in embryolethality (increased post-implantation loss and the number of dams with all fetuses dead or resorbed) in pregnant animals dosed during GD 11-15.

In a separate study in pregnant huCD52 transgenic mice, administration of LEMTRADA during organogenesis (GD 6-10 or GD 11-15) at doses of 3 or 10 mg/kg IV, decreases in B lymphocytes and T-lymphocyte populations were observed in the offspring at both doses tested. The effects of LEMTRADA, administered during organogenesis, on postnatal development have not been adequately assessed.

Clinical Considerations

To avoid in utero exposure to LEMTRADA, women of child bearing potential should use effective contraceptive measures when receiving a course of treatment with LEMTRADA and for 4 months following that course of treatment.

LEMTRADA induces persistent thyroid disorders [see *Warnings and Precautions (5.7)*]. Untreated hypothyroidism in pregnant women increases the risk for miscarriage and may have effects on the fetus including mental retardation and dwarfism. In mothers with Graves' disease, maternal thyroid stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause neonatal Graves' disease. In a patient who developed Graves' disease after treatment with alemtuzumab, placental transfer of anti-thyrotropin receptor antibodies resulted in neonatal Graves' Disease with thyroid storm in her infant who was born 1 year after alemtuzumab dosing [see *Warnings and Precautions (5.1)*].

8.3 Nursing Mothers

Alemtuzumab was detected in the milk of lactating mice administered 10 mg/kg LEMTRADA on Days 9 through 12 postpartum. Serum levels of alemtuzumab were similar in lactating mice and offspring on Day 13 postpartum, and were associated with evidence of pharmacological activity (decrease in lymphocyte counts) in the offspring.

It is not known whether alemtuzumab is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from LEMTRADA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients less than 17 years of age have not been established. Use of LEMTRADA is not recommended in pediatric patients due to the risks of autoimmunity, infusion reactions, and because it may increase the risk of malignancies (thyroid, melanoma, lymphoproliferative disorders, and lymphoma) [see *Warnings and Precautions (5.1, 5.2, 5.3)*].

8.5 Geriatric Use

Clinical studies of LEMTRADA did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

10 OVERDOSAGE

Two MS patients experienced serious reactions (headache, rash, and either hypotension or sinus tachycardia) after a single accidental infusion up to 60 mg of LEMTRADA. Doses of LEMTRADA greater than those recommended may increase the intensity and/or duration of infusion reactions or its immune effects. There is no known antidote for alemtuzumab overdosage.

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11 DESCRIPTION

LEMTRADA (alemtuzumab) is a recombinant humanized IgG1 kappa monoclonal antibody directed against the cell surface glycoprotein, CD52. Alemtuzumab has an approximate molecular weight of 150kD. LEMTRADA is produced in mammalian cell (Chinese hamster ovary) suspension culture in a nutrient medium containing neomycin. Neomycin is not detectable in the final product. LEMTRADA is a sterile, clear and colorless to slightly yellow, solution (pH 7.2±0.2) for infusion.

Each 1 mL of solution contains alemtuzumab 12 mg, dibasic sodium phosphate (1.15 mg), disodium edetate dihydrate (0.0187 mg), polysorbate 80 (0.1 mg), potassium chloride (0.2 mg), potassium dihydrogen phosphate (0.2 mg), sodium chloride (8 mg), and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which alemtuzumab exerts its therapeutic effects in multiple sclerosis is unknown, but is presumed to involve binding to CD52, a cell surface antigen present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

12.2 Pharmacodynamics

Effects of LEMTRADA on the Lymphocyte Population

LEMTRADA depletes circulating T and B lymphocytes after each treatment course. In clinical trials, the lowest cell counts occurred 1 month after a course of treatment at the time of the first post-treatment blood count. Lymphocyte counts then increased over time: B cell counts usually recovered within 6 months; T cell counts increased more slowly and usually remained below baseline 12 months after treatment. Approximately 60% of patients had total lymphocyte counts below the lower limit of normal 6 months after each treatment course and 20% had counts below the lower limit of normal after 12 months.

Reconstitution of the lymphocyte population varies for the different lymphocyte subtypes. At Month 1 in clinical trials, the mean CD4+ lymphocyte count was 40 cells per microliter, and, at Month 12, 270 cells per microliter. At 30 months, approximately half of patients had CD4+ lymphocyte counts that remained below the lower limit of normal.

Cardiac Electrophysiology

In a study of 63 MS patients, alemtuzumab 12 mg per day for 5 days caused no changes in the QTc interval greater than 20ms. An average 22 to 26 beats-per-minute increase in heart rate was observed for at least 2 hours after the first but not subsequent infusions.

12.3 Pharmacokinetics

The pharmacokinetics of LEMTRADA were evaluated in a total of 148 patients with relapsing forms of MS who received 12 mg/day on 5 consecutive days, followed by 12 mg/day on 3 consecutive days 12 months following the first treatment course.

Absorption

Serum concentrations increased with each consecutive dose within a treatment course, with the highest observed concentrations occurring following the last infusion of a treatment course. The mean maximum concentration was 3014 ng/mL on Day 5 of the first treatment course, and 2276 ng/mL on Day 3 of the second treatment course.

Distribution

LEMTRADA is largely confined to the blood and interstitial space with a central volume of distribution of 14.1 L.

Elimination

The elimination half-life was approximately 2 weeks and was comparable between courses. The serum concentrations were generally undetectable (< 60 ng/mL) within approximately 30 days following each treatment course.

Specific Populations

Age, race, or gender had no effect on the pharmacokinetics of LEMTRADA.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to assess the carcinogenic or genotoxic potential of LEMTRADA have not been conducted.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic male mice on 5 consecutive days prior to cohabitation with untreated wild-type females, no effect on fertility or reproductive performance was observed. However, adverse effects on sperm parameters (including abnormal morphology (detached /no head) and reduced total count and motility) were observed at both doses tested.

When LEMTRADA (3 or 10 mg/kg IV) was administered to huCD52 transgenic female mice for 5 consecutive days prior to cohabitation with untreated wild-type males, there was a decrease in the average number of corpora lutea and implantation sites and an increase in post-implantation loss, resulting in fewer viable embryos at the higher dose tested.

14 CLINICAL STUDIES

The efficacy of LEMTRADA was demonstrated in two studies (Study 1 and 2) that evaluated LEMTRADA 12 mg in patients with relapsing-remitting multiple sclerosis (RRMS). LEMTRADA was administered by intravenous infusion once daily over a 5-day course, followed one year later by intravenous infusion once daily over a 3-day course. Both studies included patients who had experienced at least 2 relapses during the 2 years prior to trial entry and at least 1 relapse during the year prior to trial entry. Neurological examinations were performed every 12 weeks and at the time of suspected relapse. Magnetic resonance imaging (MRI) evaluations were performed annually.

Study 1

Study 1 was a 2 year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 1 had Expanded Disability Status Scale (EDSS) scores of 5 or less and had to have experienced at least one relapse while on interferon beta or glatiramer acetate therapy.

Patients were randomized to receive LEMTRADA (n=426) or interferon beta-1a (n=202). At baseline, the mean age was 35 years, the mean disease duration was 4.5 years, and the mean EDSS score was 2.7.

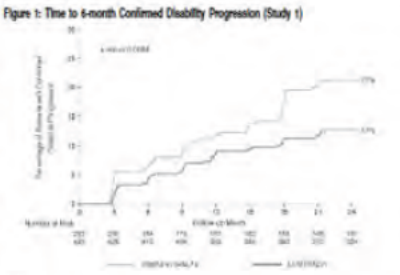
The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression. Confirmed disability progression was defined as at least a 1 point increase above baseline EDSS (1.5 point increase for patients with baseline EDSS of 0) sustained for 6 months. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. Time to onset of 6-month confirmed disability progression was significantly delayed with LEMTRADA treatment compared to interferon beta-1a. There was no significant difference between the treatment groups for the change in T2 lesion volume. The results of Study 1 are shown in Table 2 and Figure 1.

Table 2: Clinical and MRI Results of Study 1

	LEMTRADA (N=426)	Interferon beta-1a 44 mcg (N=202)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.26 49%	0.52	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	13% 42%	21%	0.0084
Percent of patients remaining relapse-free at Year 2	65%	47%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-1.3	-1.2	0.14

Figure 1: Time to 6-month Confirmed Disability Progression (Study 1)



Study 2

Study 2 was a 2-year randomized, open-label, rater-blinded, active comparator (interferon beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients entering Study 2 had EDSS scores of 3 or less and no prior treatment for multiple sclerosis. Patients were randomized to receive LEMTRADA (n=376) or interferon beta-1a (n=187). At baseline, the mean age was 33 years, the mean disease duration was 2 years, and the mean EDSS score was 2.

The clinical outcome measures were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression, as defined in Study 1. The MRI outcome measure was the change in T2 lesion volume.

The annualized relapse rate was significantly lower in patients treated with LEMTRADA than in patients who received interferon beta-1a. There was no significant difference between the treatment groups for the time to confirmed disability progression and for the primary MRI endpoint (change in T2 lesion volume). The results for Study 2 are shown in Table 3.

Table 3: Clinical and MRI Results of Study 2

	LEMTRADA (N=376)	Interferon beta-1a 44 mcg (N=187)	p-value
Clinical Outcomes			
Annualized relapse rate Relative reduction	0.18 55%	0.39	<0.0001
Proportion of patients with disability progression at Year 2 Relative risk reduction	8% 30%	11%	0.22
Percent of patients remaining relapse-free at Year 2	78%	59%	<0.0001
MRI Outcomes			
Percent change in T2 lesion volume from baseline	-9.3	-6.5	0.31

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each LEMTRADA carton (NDC 58468-0200-1) contains 1 single-use vial that delivers 12 mg/1.2 mL (10 mg/mL). The vial stopper is not made with natural rubber latex.

LEMTRADA is a sterile, clear and colorless to slightly yellow solution for infusion, containing no antimicrobial preservatives.

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LEMTRADA REMS Program Training

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16.2 Storage and Handling
Store LEMTRADA vials at 2°C to 8°C (36°F to 46°F). Do not freeze or shake. Store in original carton to protect from light.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Autoimmunity
- Advise patients to contact their healthcare provider promptly if they experience any symptoms of potential autoimmune diseases. Give examples of important symptoms such as bleeding, easy bruising, petechiae, purpura, hematuria, edema, jaundice, or hemoptysis *[see Warnings and Precautions (5.1)]*.
- Advise patients of the importance of monthly blood and urine tests for 48 months following the last course of LEMTRADA to monitor for signs of autoimmunity because early detection and prompt treatment can help prevent serious and potentially fatal outcomes associated with these events. Advise patients that monitoring may need to continue past 48 months if they have signs or symptoms of autoimmunity.
- Advise patients that LEMTRADA may cause hyperthyroid or hypothyroid disorders.
- Advise patients to contact their healthcare provider if they experience symptoms reflective of a potential thyroid disorder such as unexplained weight loss or gain, fast heartbeat or palpitations, eye swelling, constipation, or feeling cold.
- Advise women of childbearing potential of the risks of pregnancy with concomitant thyroid disease. Advise women of childbearing potential to discuss pregnancy planning with their doctor.

Infusion Reactions
- Advise patients that infusion reactions can occur after they leave the infusion center *[see Warnings and Precautions (5.2)]*.
- Instruct the patient to remain at the infusion center for 2 hours after each LEMTRADA infusion, or longer at the discretion of the physician. Advise patients that symptoms of infusion reactions may occur after they leave the infusion center and to report these symptoms to their doctor.
- Advise patients to contact their healthcare provider promptly if they experience infusion reactions, which include swelling in the mouth or throat, difficulty breathing, weakness, abnormal heart rate (fast, slow, or irregular), chest pain, and rash.

Malignancies
- Advise patients that LEMTRADA may increase their risk of malignancies including thyroid cancer and melanoma *[see Warnings and Precautions (5.3)]*.
- Advise patients to report symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, hoarseness or other voice changes that do not go away, trouble swallowing or breathing, or a constant cough not due to a cold.
- Advise patients that they should have baseline and yearly skin examinations.

LEMTRADA REMS Program
- LEMTRADA is available only through a restricted program called the LEMTRADA REMS Program *[see Warnings and Precautions (5.4)]*. Inform the patient of the following notable requirements:
  - Patients and providers must be enrolled in the program.
  - Patients must comply with the ongoing monitoring requirements.
  - Patients must report any side effects or symptoms to their doctor.
- LEMTRADA is available only at certified infusion centers participating in the program. Therefore, provide patients with information on the LEMTRADA REMS Program in order to locate an infusion center.
- Advise patients to read the LEMTRADA REMS material for patients, *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*.
- Instruct patients to carry the LEMTRADA REMS Patient Safety Information Card with them in case of an emergency.

Infections
- Advise patients to contact their healthcare provider if they develop symptoms of serious infection such as fever or swollen glands *[see Warnings and Precautions (5.6)]*.
- Advise patients to complete any necessary immunizations at least 6 weeks prior to treatment with LEMTRADA *[see Dosage and Administration (2.3)]*. Advise patients that they should talk to their healthcare provider before taking any vaccine after recent treatment with LEMTRADA *[see Warnings and Precautions (5.9)]*.
- Advise patients to take their prescribed medication for herpes prophylaxis as directed by their healthcare provider *[see Warnings and Precautions (5.9)]*.
- Advise patients that yearly HPV screening is recommended *[see Warnings and Precautions (5.9)]*.
- Advise patients to avoid or adequately heat foods that are potential sources of *Listeria monocytogenes* if they have had a recent course of LEMTRADA. The duration of increased risk for listeria infection after LEMTRADA administration is not known *[see Warnings and Precautions (5.6)]*.

Pneumonitis
- Advise patients that pneumonitis has been reported in patients treated with LEMTRADA *[see Warnings and Precautions (5.10)]*. Advise patients to report symptoms of lung disease such as shortness of breath, cough, wheezing, chest pain or tightness, and hemoptysis.

Concomitant Use of Campath
- Advise patients that alemtuzumab is the same drug as Campath for use in B-CLL. Patients should inform their healthcare provider if they have taken Campath *[see Warnings and Precautions (5.11)]*.

Manufactured and distributed by:

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142

US License Number: 1596

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MEDICATION GUIDE
LEMTRADA™ (lem-TRA-da)
(alemtuzumab)
Injection for Intravenous Infusion
Read this Medication Guide before you start receiving LEMTRADA and before you begin each treatment course. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is the most important information I should know about LEMTRADA?
LEMTRADA can cause serious side effects, including:

1. **Serious autoimmune problems.** Some people receiving LEMTRADA develop a condition where the immune cells in your body attack other cells or organs in the body (autoimmunity) which can be serious and may cause death. Serious autoimmune problems may include:
   - **Immune thrombocytopenic purpura (ITP).** LEMTRADA may cause the number of platelets in your blood to be reduced (ITP). ITP can cause severe bleeding that, if not treated, may cause life-threatening problems. Call your healthcare provider right away if you have any of the following symptoms:
     - easy bruising
     - bleeding from a cut that is hard to stop
     - heavier menstrual periods than normal
     - bleeding from your gums or nose that is new or takes longer than usual to stop
     - small, scattered spots on your skin that are red, pink, or purple
   - **Kidney problems.** LEMTRADA may cause a serious kidney problem, called anti-glomerular basement membrane disease. If this happens and you do not get treated, anti-glomerular basement membrane disease can lead to severe kidney damage, kidney failure that needs dialysis, a kidney transplant, or death. Call your healthcare provider right away if you have any of the following symptoms:
     - blood in the urine (red or tea-colored urine)
     - swelling in your legs or feet
     - coughing up blood

   Side effects may happen while you receive LEMTRADA and for 4 years after you stop receiving LEMTRADA. Your healthcare provider will order blood and urine tests before you receive, while you are receiving, and every month for 4 years after you receive your last LEMTRADA infusion. You may need to continue these blood and urine tests after 4 years if you have any autoimmune signs or symptoms. The blood and urine tests will help your healthcare provider watch for signs and symptoms of serious autoimmune problems.
   It is important to have your blood and urine tested, even if you are feeling well and do not have any symptoms from LEMTRADA and your multiple sclerosis. This may help your healthcare provider find any problems early and will increase your chances of getting better.
2. **Serious infusion reactions.** LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.
   You will receive your infusion at a healthcare facility with equipment and staff trained to manage infusion reactions. You will be watched while you receive and for 2 hours after you receive LEMTRADA. **It is important** that you stay at the infusion center for 2 hours after your infusion is finished or longer if your healthcare provider decides you need to stay longer. If a serious infusion reaction happens while you are receiving LEMTRADA, your infusion may be stopped.
   Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion, and after you have left the healthcare facility:
   - swelling in your mouth or throat
   - trouble breathing
   - weakness
   - fast, slow, or irregular heart beat
   - chest pain
   - rash

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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To lower your chances of getting a serious infusion reaction, your healthcare provider will give you a medicine called corticosteroids before your first 3 infusions of a treatment course. You may also be given other medicines before or after the infusion to try reduce your chances of these reactions or to treat them after they happen.

3. **Certain cancers.** Receiving LEMTRADA may increase your chance of getting some kinds of cancers, including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:
   - new lump
   - swelling in your neck
   - pain in the front of your neck
   - hoarseness or other voice changes that do not go away
   - trouble swallowing or breathing
   - cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA and each year while you are receiving treatment to monitor symptoms of skin cancer.

Because of your risk of autoimmunity, infusion reactions and the risk of some kinds of cancers, LEMTRADA is only available through a restricted program called the LEMTRADA Risk Evaluation and Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the LEMTRADA REMS Program.

- You and your healthcare provider must be enrolled in the LEMTRADA REMS Program.
- LEMTRADA can only be given at a certified healthcare facility that participates in the LEMTRADA REMS Program. Your healthcare provider can give you information on how to find a certified healthcare facility.
- Read the LEMTRADA REMS "What You Need to Know About LEMTRADA Treatment: A Patient Guide" and "What you Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide" after you are enrolled in the program.
- Carry your LEMTRADA REMS Patient Safety Information Card with you in case of an emergency.

What is LEMTRADA?

LEMTRADA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). Because of its risks, LEMTRADA is generally used in people who have tried 2 or more MS medicines that have not worked well enough. It is not known if LEMTRADA is safe and effective for use in children under 17 years of age.

Who should not receive LEMTRADA?

Do not receive LEMTRADA if you are infected with human immunodeficiency virus (HIV).

What should I tell my healthcare provider before receiving LEMTRADA?

Before receiving LEMTRADA, tell your healthcare provider if you:

- are taking a medicine called Campath®. Alemtuzumab the active ingredient in LEMTRADA is the same drug as Campath.
- have bleeding problems
- have thyroid problems
- have kidney problems
- have a recent history of infection
- have HIV
- have received a live vaccine in the past 6 weeks before receiving LEMTRADA or plan to receive any live vaccines. Ask your healthcare provider if you are not sure if your vaccine is a live vaccine.
- are pregnant or plan to become pregnant. LEMTRADA may harm your unborn baby. You should use birth control while receiving LEMTRADA and for 4 months after your course of treatment.
- are breastfeeding or plan to breastfeed. It is not known if LEMTRADA passes into your breast milk. You and your healthcare provider should decide if you should receive LEMTRADA or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

LEMTRADA and other medicines may affect each other causing side effects. Especially tell your healthcare provider if you take medicines that increase your chance of getting infections, including medicines used to treat cancer or to control your immune system.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How will I receive LEMTRADA?

- LEMTRADA is given through a needle placed in your vein (IV infusion).
- It takes about 4 hours to receive a full dose of LEMTRADA each day.
- You will receive LEMTRADA over 2 treatment courses.
- You will receive LEMTRADA for 5 days in a row (consecutive) for the first treatment course and then for 3 days in a row (consecutive) about 1 year later for your second treatment course.

What are the possible side effects of LEMTRADA?

LEMTRADA may cause serious side effects including:

- See **"What is the most important information I should know about LEMTRADA?"**
- **thyroid problems.** Some people who receive LEMTRADA may get thyroid problems including an overactive thyroid (hyperthyroidism) or an underactive thyroid (hypothyroidism). Your healthcare provider will do blood tests to check how your thyroid is working. Call your healthcare provider if you have any of the symptoms of thyroid problems.

Symptoms of **hyperthyroidism** may include:

- excessive sweating
- unexplained weight loss
- eye swelling
- nervousness
- fast heartbeat

Symptoms of **hypothyroidism** may include:

- unexplained weight gain
- feeling cold
- worsening tiredness
- constipation

- **low blood counts (cytopenias).** LEMTRADA may cause a decrease in some types of blood cells. Some people with these low blood counts have increased infections. Symptoms of cytopenias may include:
  - weakness
  - chest pain
  - yellowing of the skin or whites of eyes (jaundice)
  - dark urine
  - fast heartbeat

  Your healthcare provider will do blood tests to check for cytopenias. Call your healthcare provider right away if you have symptoms listed above.
- **serious infections.** LEMTRADA may cause you to have serious infections while you receive and after receiving a treatment course. Serious infections may include:
  - **herpes viral infections.** Some people taking LEMTRADA have an increased chance of getting herpes viral infections. Your healthcare provider will prescribe medicines to reduce your chances of getting these infections. Take these medicines exactly as your healthcare provider tells you to.
  - **human papilloma virus (HPV).** Females have an increased chance of getting a cervical HPV infection. If you are a female, you should have an HPV screening each year.
  - **tuberculosis.** Your healthcare provider should check you for tuberculosis before you receive LEMTRADA.
  - **fungal infections.**
  - **listeria.** People who receive LEMTRADA have an increased chance of getting an infection caused by the bacteria, listeria. Avoid foods that may be a source for listeria (for example, deli meat, unpasteurized milk and cheese products, or undercooked meat, seafood or poultry) or make sure that the food you eat which may contain listeria is heated well if you receive treatment with LEMTRADA.

  Call your healthcare provider right away if you have symptoms of a serious infection, such as fever or swollen glands. You may need to go to the hospital for treatment if you get a serious infection. It is

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If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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important to tell the healthcare providers that you have received LEMTRADA.
Talk to your healthcare provider before you get vaccinations after receiving LEMTRADA. Certain vaccinations may increase your chances of getting infections.

- **swelling of lung tissue (pneumonitis).** Some people have had swelling of the lung tissue while receiving LEMTRADA. Call your healthcare provider right away if you have the following symptoms:
  - shortness of breath
  - cough
  - wheezing
  - chest pain or tightness
  - coughing up blood

The most common side effects of LEMTRADA include:

- rash
- headache
- thyroid problems
- fever
- swelling of your nose and throat (nasopharyngitis)
- nausea
- urinary tract infection
- feeling tired
- trouble sleeping
- upper respiratory tract infection
- herpes viral infection
- hives
- itching
- fungal infection
- joint pain
- pain in your arms or legs
- back pain
- diarrhea
- sinus infection
- mouth pain or sore throat
- tingling sensation
- dizziness
- stomach pain
- sudden redness in face, neck, or chest
- vomiting

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.
These are not all the possible side effects of LEMTRADA. For more information, ask your healthcare provider or pharmacist.
Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

General information about the safe and effective use of LEMTRADA.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use LEMTRADA for a condition for which it was not prescribed. Do not give LEMTRADA to other people, even if they have the same symptoms that you have. It may harm them. This Medication Guide summarizes the most important information about LEMTRADA. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about LEMTRADA that is written for health professionals.
For more information, go to www.LemtradaREMS.com or call Genzyme at 1-855-676-6326.

What are the ingredients in LEMTRADA?
Active ingredient: alemtuzumab
Inactive ingredients: sodium chloride, dibasic sodium phosphate, potassium chloride, potassium dihydrogen phosphate, polysorbate 80, disodium edetate dihydrate, and water for injection.
This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured and distributed by:

Genzyme Corporation

500 Kendall Street

Cambridge, MA 02142

US License Number: 1596

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LEMTRADA REMS Program Training

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LEMTRADA REMS PROGRAM OVERVIEW

What is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug. It is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions, and malignancies, LEMTRADA® (alemtuzumab) is only available through a restricted program called the LEMTRADA REMS Program.

LEMTRADA REMS Program Requirements

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

PRESCRIBER ENROLLMENT INSTRUCTIONS

1. Complete the training program, which includes reviewing the following:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - *LEMTRADA REMS Education Program for Prescribers*
2. Successfully complete the 8-question LEMTRADA REMS Knowledge Assessment.
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form.
4. Submit the completed and signed forms to the LEMTRADA REMS Program.

PHARMACY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the pharmacy by reviewing the LEMTRADA REMS Program Overview and completing the LEMTRADA REMS Pharmacy Enrollment Form, which acknowledges that the pharmacy agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All relevant staff at the pharmacy who will be involved with the dispensing of LEMTRADA must be educated and trained.
   - The pharmacy will verify that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
   - The pharmacy will verify that prescribers and healthcare facilities are certified and patients are authorized to receive LEMTRADA prior to dispensing LEMTRADA.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.
2. Submit the completed and signed LEMTRADA REMS Pharmacy Enrollment Form to the LEMTRADA REMS Program.

(Continued on next page)

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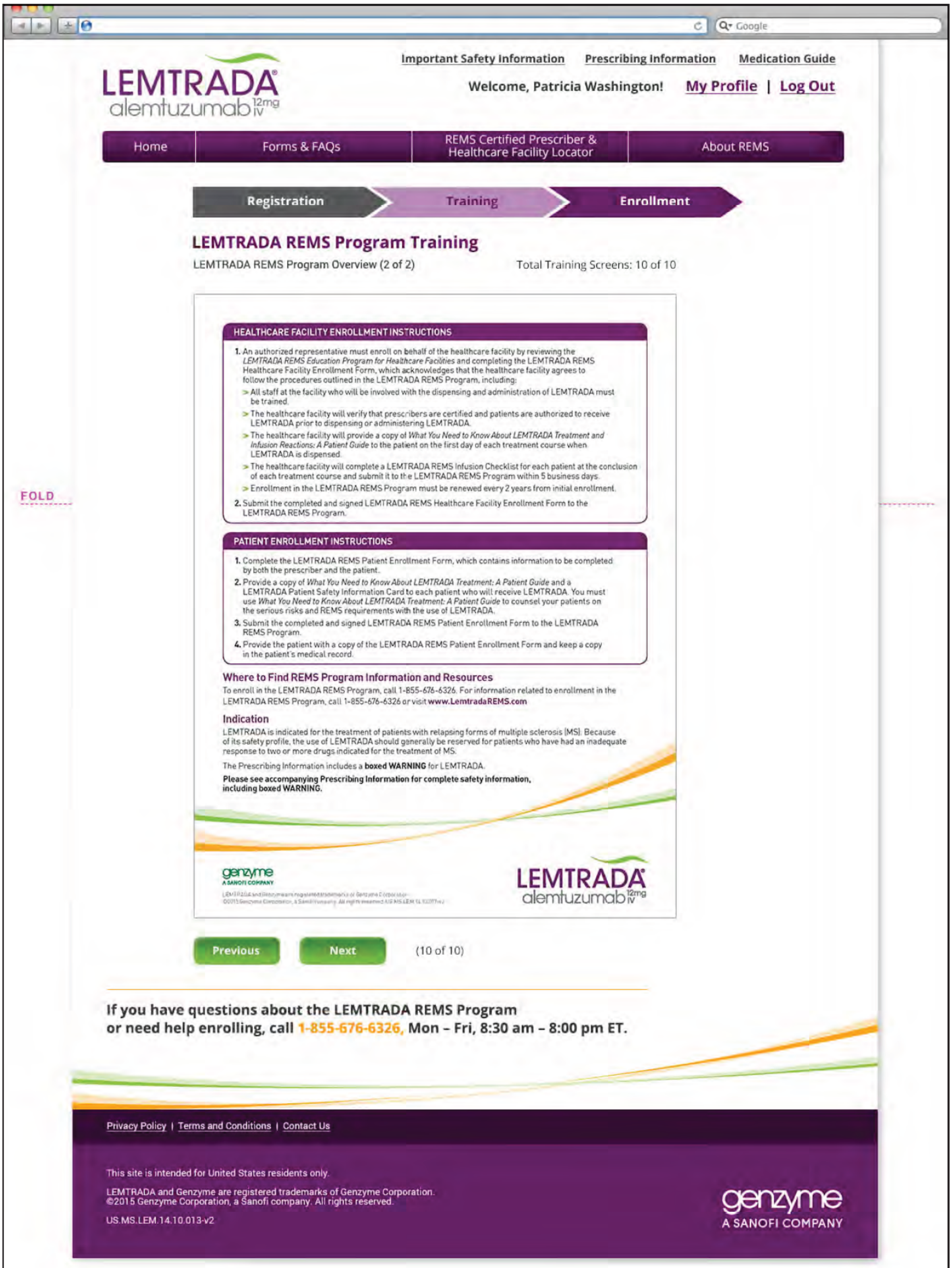

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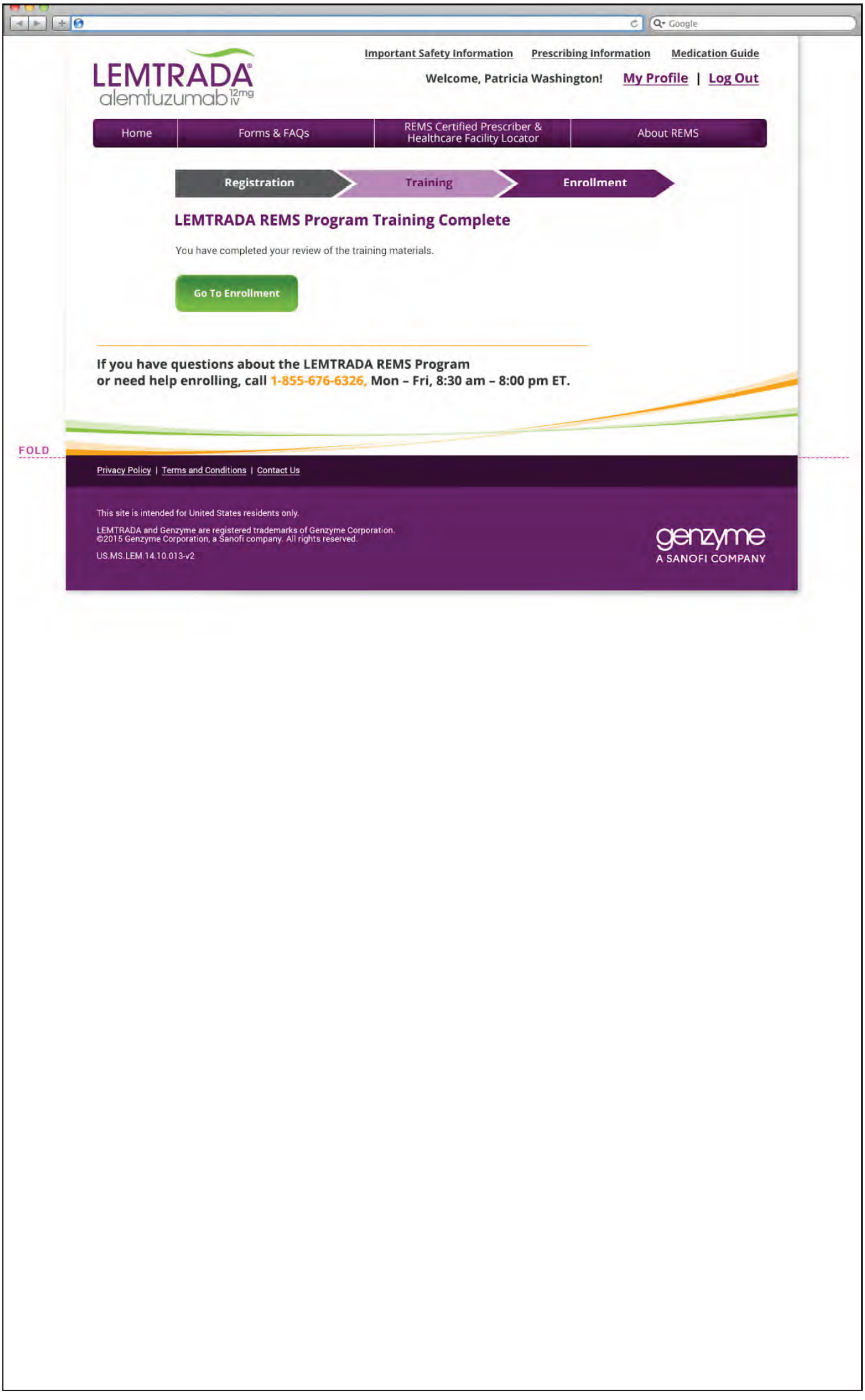

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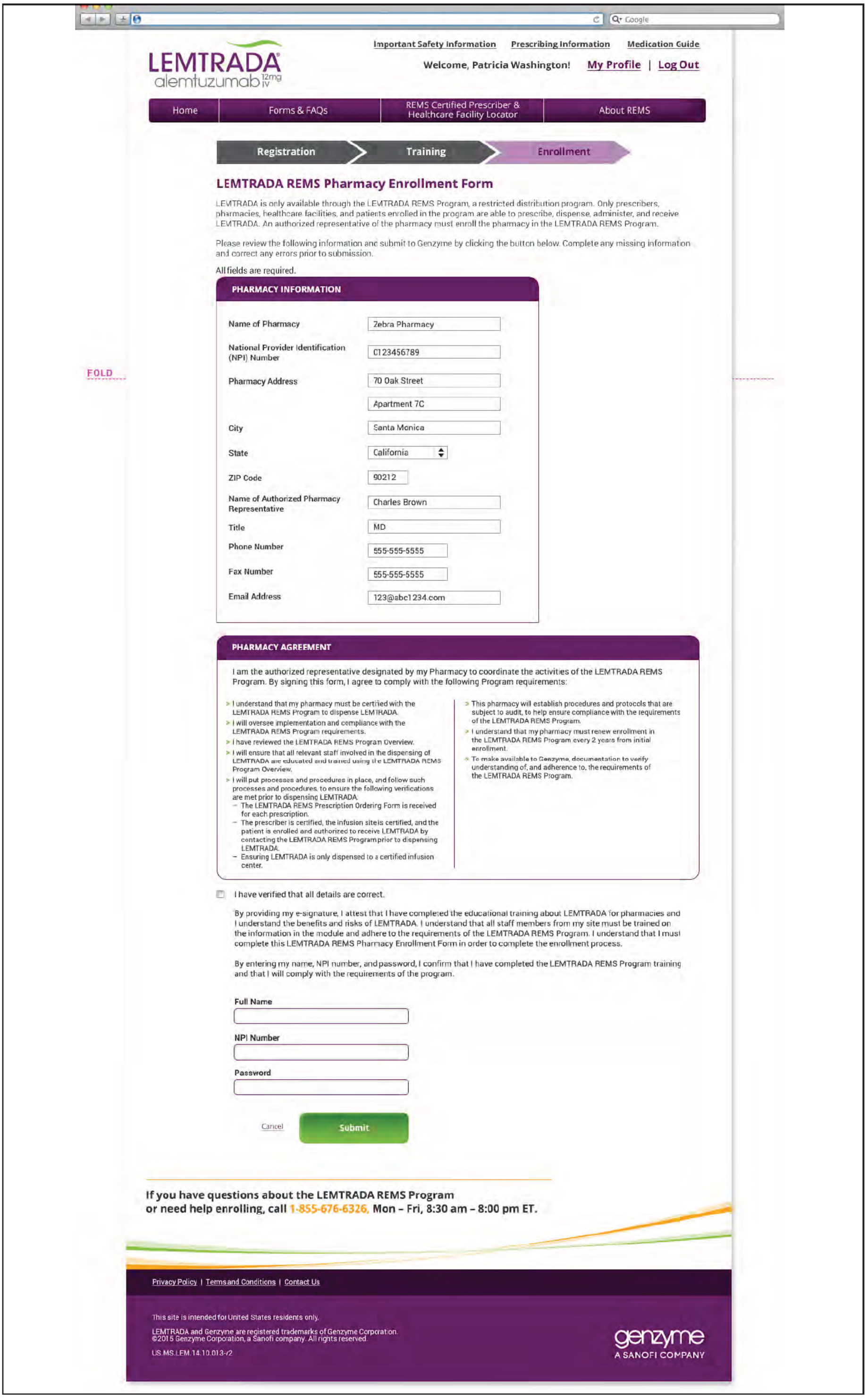

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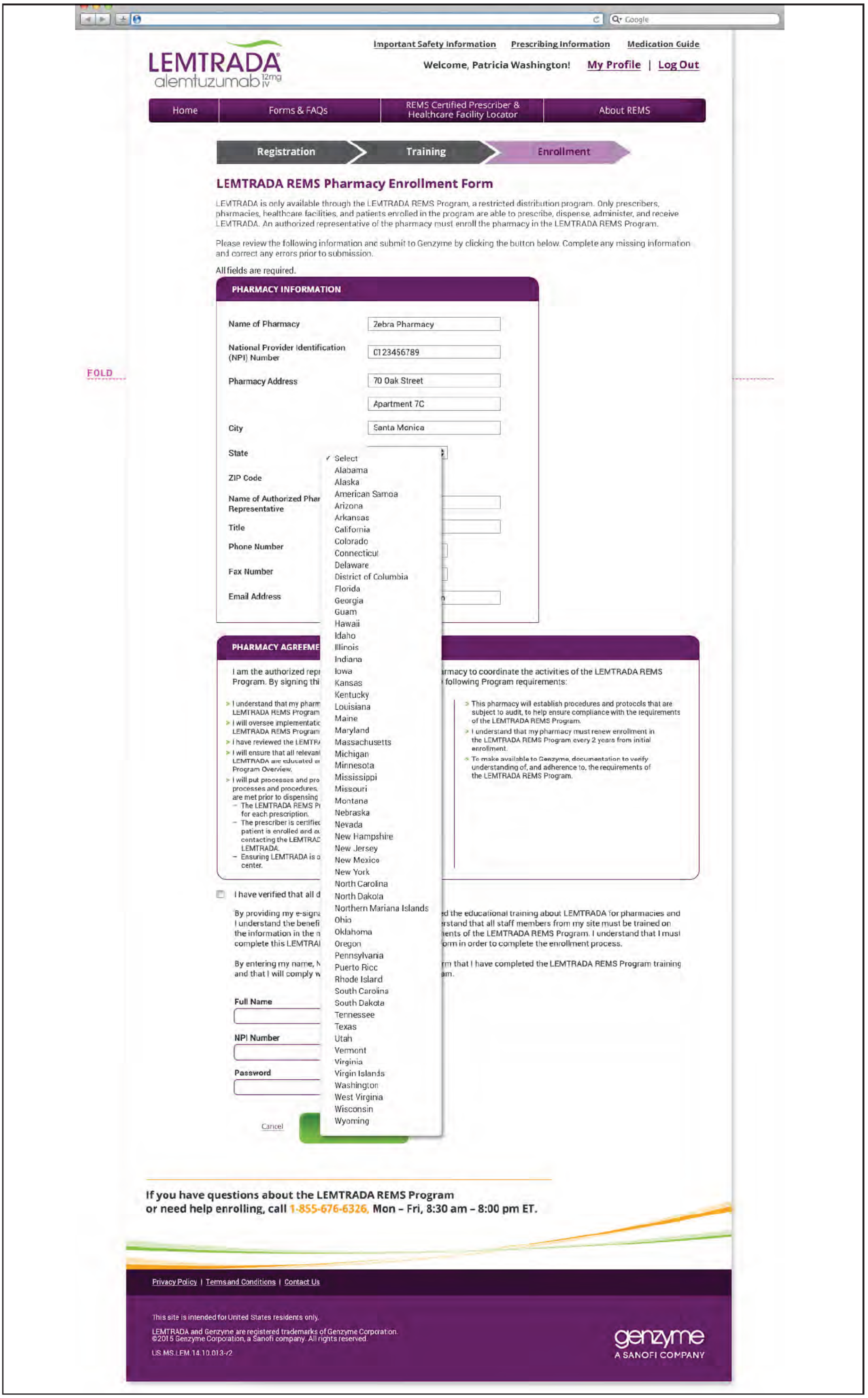

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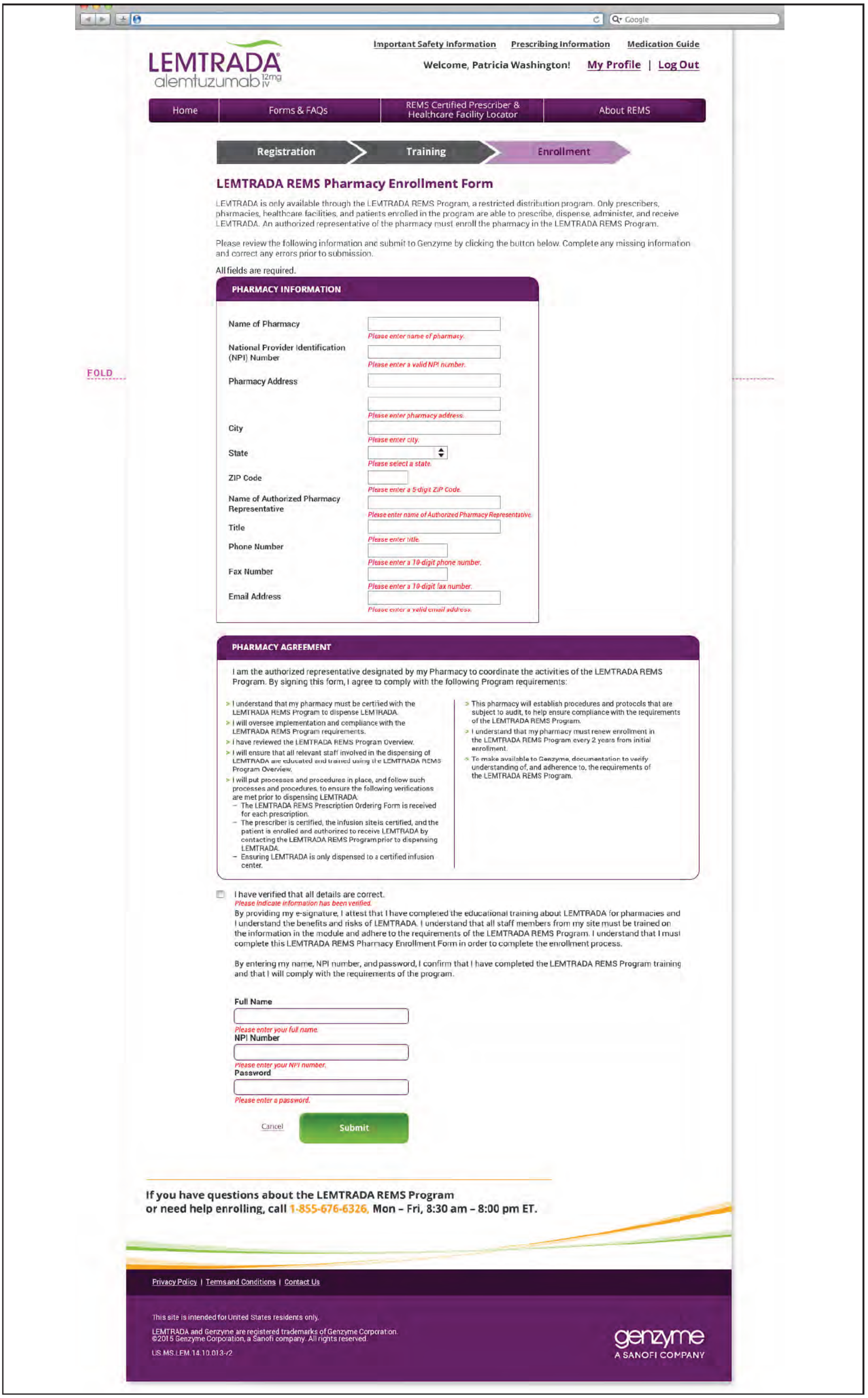

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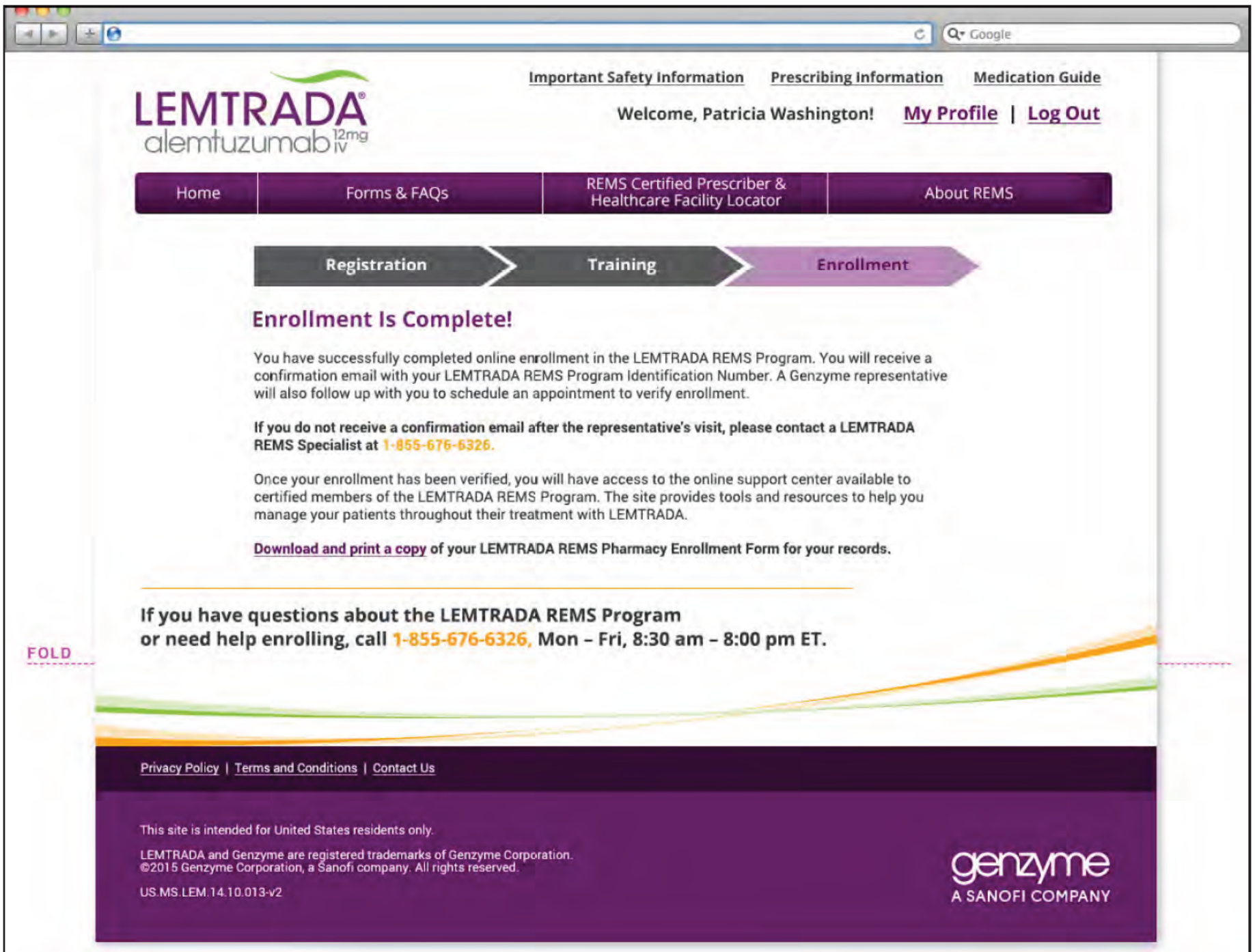

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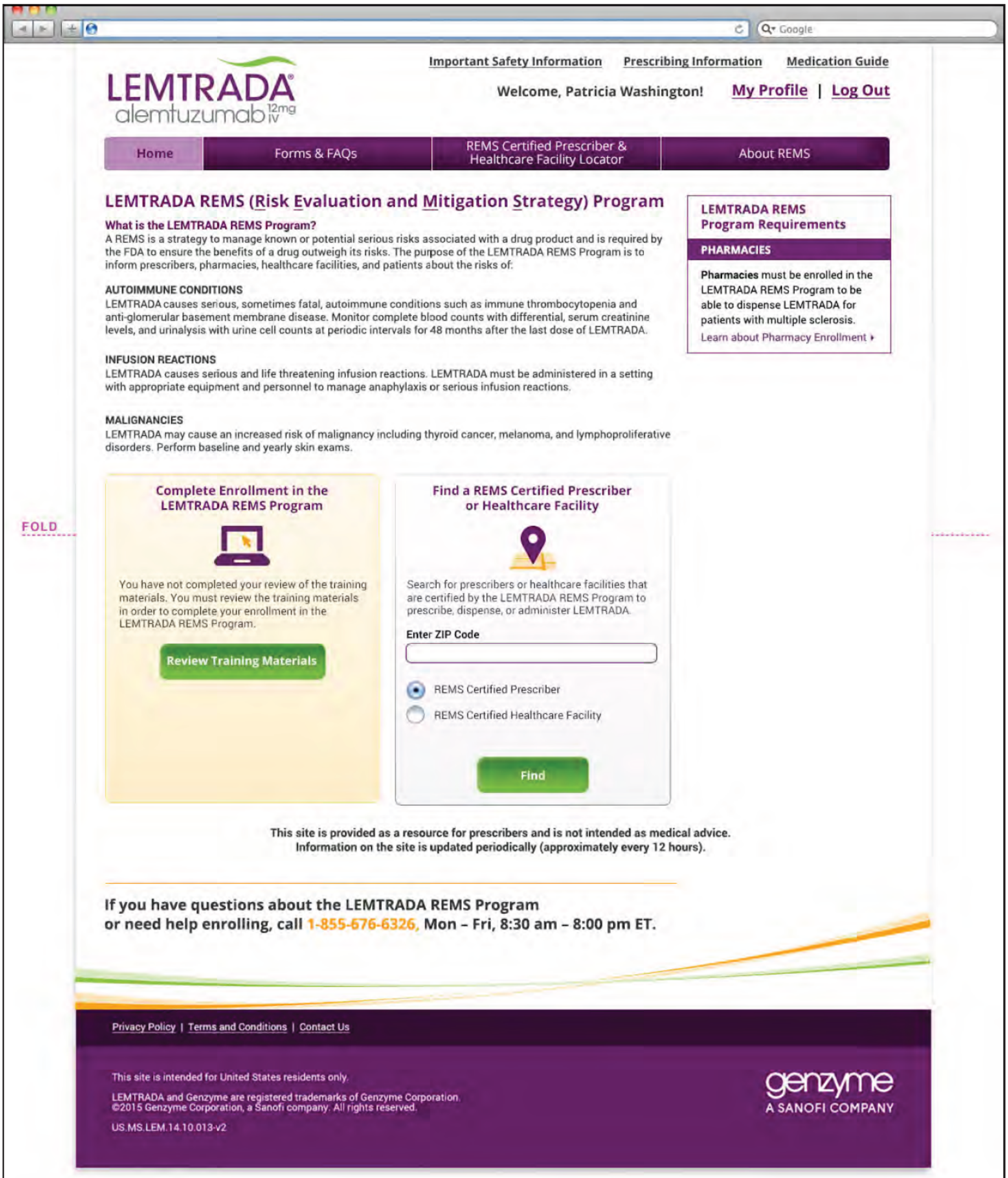

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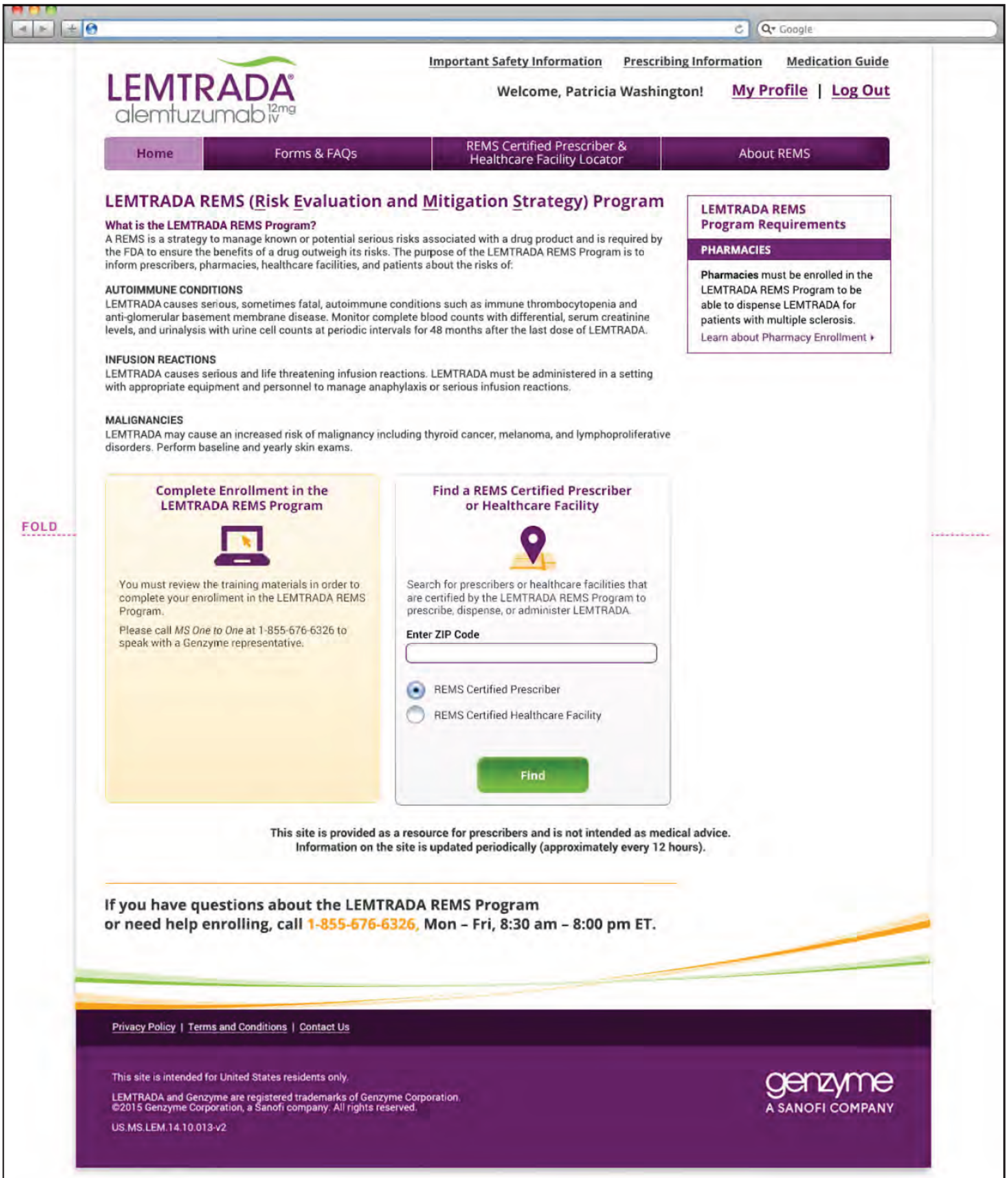

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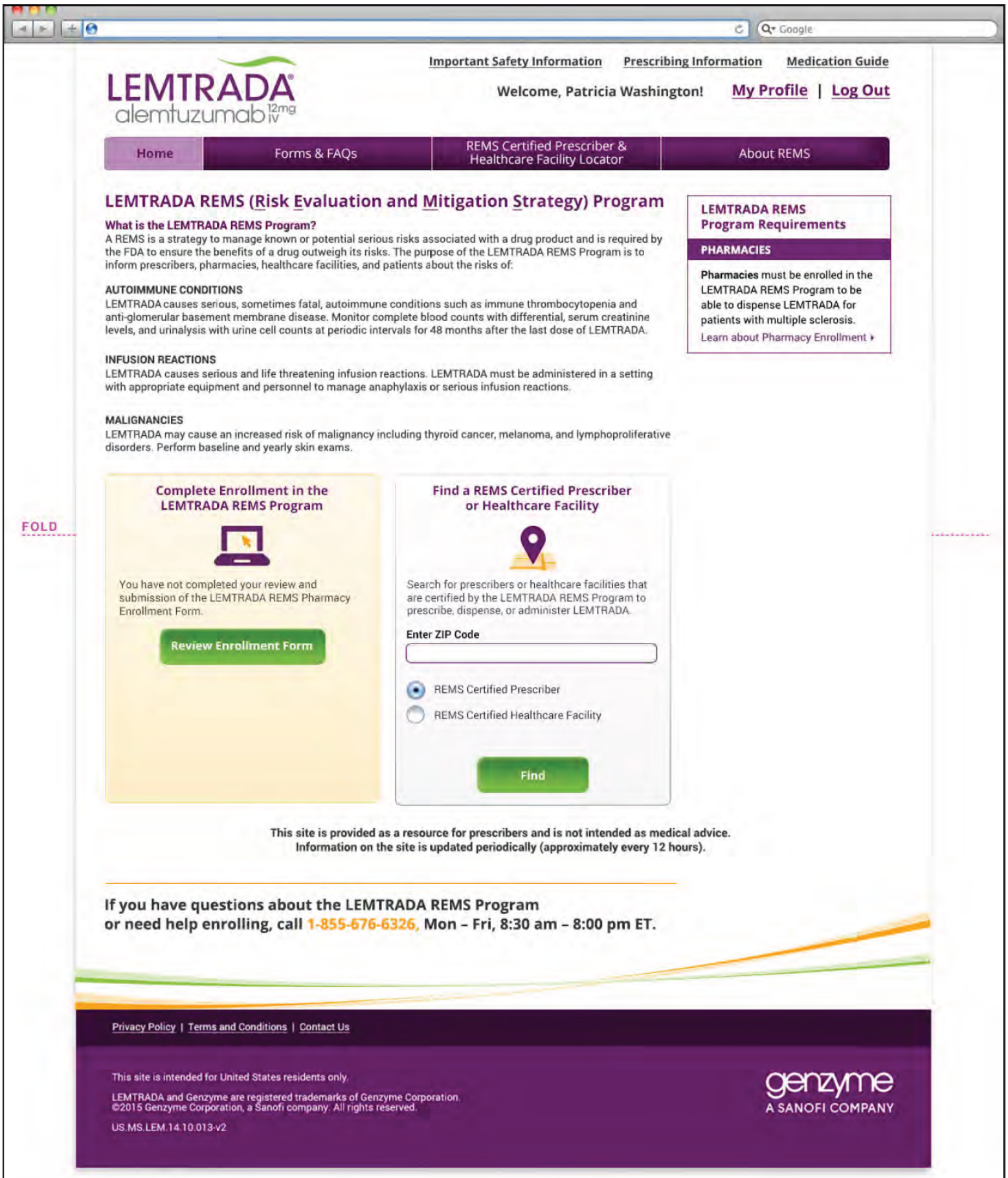

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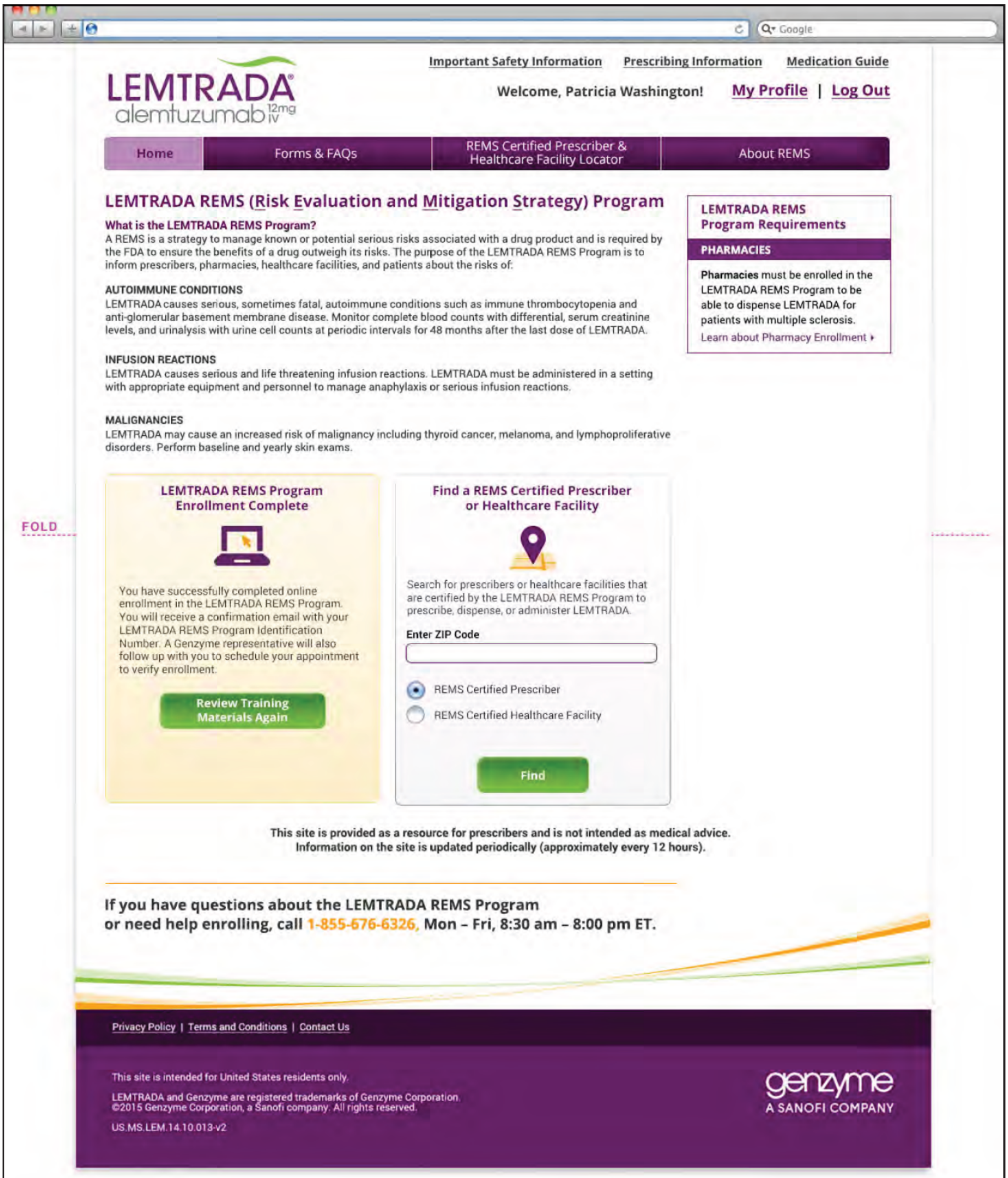

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEMTRADA safely and effectively. See full prescribing information for LEMTRADA.

LEMTRADA™ (alemtuzumab) injection, for intravenous use

Initial U.S. Approval: 2001

WARNING: AUTOIMMUNITY, INFUSION REACTIONS, AND MALIGNANCIES

See full prescribing information for complete boxed warning.

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose. (5.1)
- LEMTRADA causes serious and life-threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2 hour monitoring period. (5.2)
- LEMTRADA may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. (5.3)
- LEMTRADA is available only through a restricted distribution program. (5.4)

INDICATIONS AND USAGE

- LEMTRADA is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. (1)

DOSAGE AND ADMINISTRATION

- Administer LEMTRADA by intravenous infusion over 4 hours for 2 treatment courses:
  - First course: 12 mg/day on 5 consecutive days. (2.1)
  - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. (2.1)
- Premedicate with corticosteroids prior to LEMTRADA infusion for the first 3 days of each treatment course. (2.3)
- Administer antiviral agents for herpetic prophylaxis starting on the first day of LEMTRADA dosing and continuing for a minimum of two months after completion of LEMTRADA dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later. (2.3)
- Must be diluted prior to administration. (2.4)

DOSAGE FORMS AND STRENGTHS

Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial. (3)

CONTRAINDICATIONS

Infection with Human Immunodeficiency Virus. (4)

WARNINGS AND PRECAUTIONS

- Thyroid Disorders: Obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion. (5.7)
- Other Autoimmune Cytopenias: Monitor complete blood counts monthly until 48 months after the last infusion. (5.8)
- Consider delaying initiation of LEMTRADA in patients with active infections until the infection is fully controlled. Do not administer live viral vaccines following a course of LEMTRADA. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 10% and > interferon beta-1a): rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 11/2014

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- 2.2 Vaccinations
- 2.3 Recommended Premedication and Concomitant Medication
- 2.4 Preparation Instructions
- 2.5 Infusion Instructions
- 2.6 Laboratory Testing and Monitoring to Assess Safety

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4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
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17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

Next

(1 of 10)

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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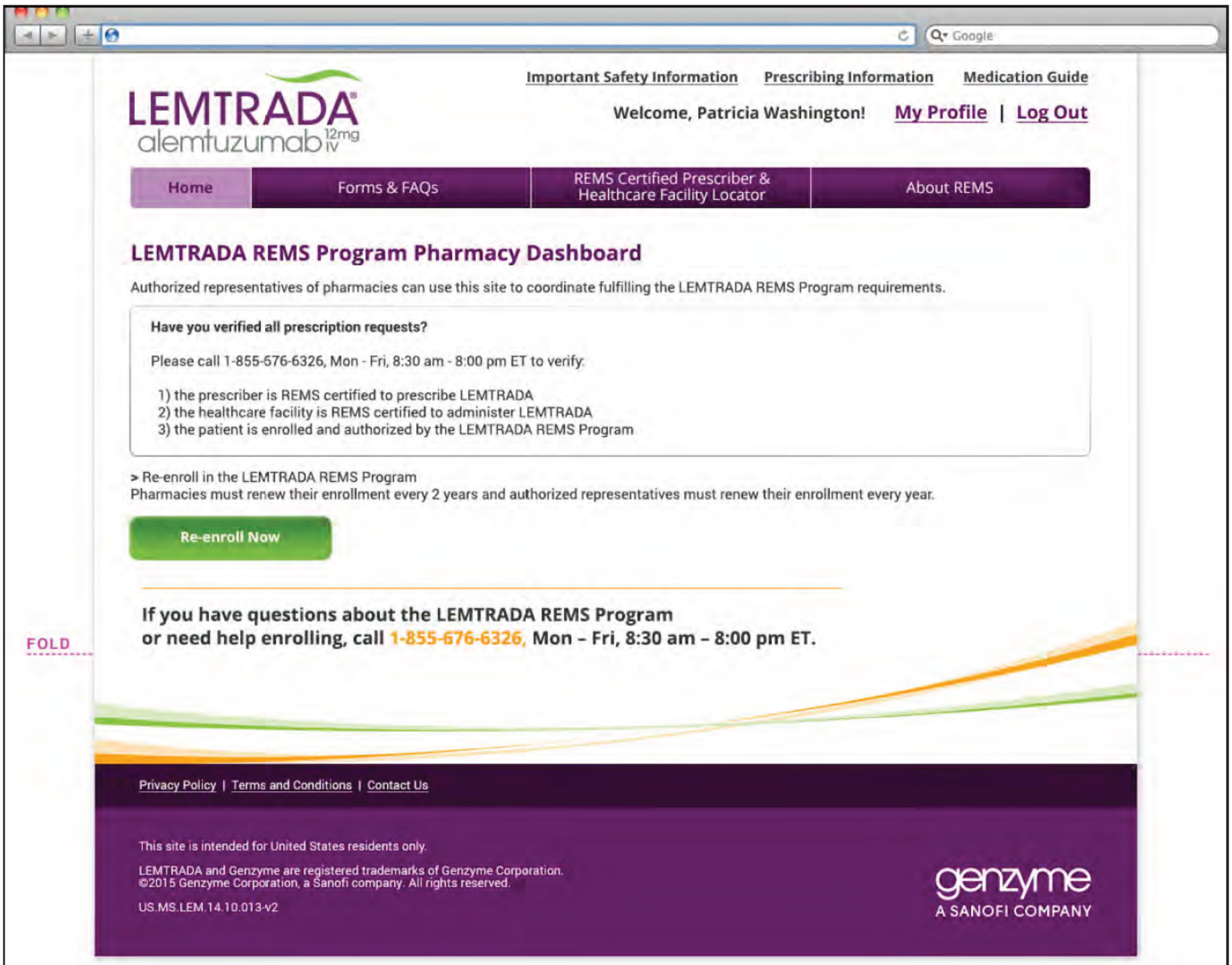
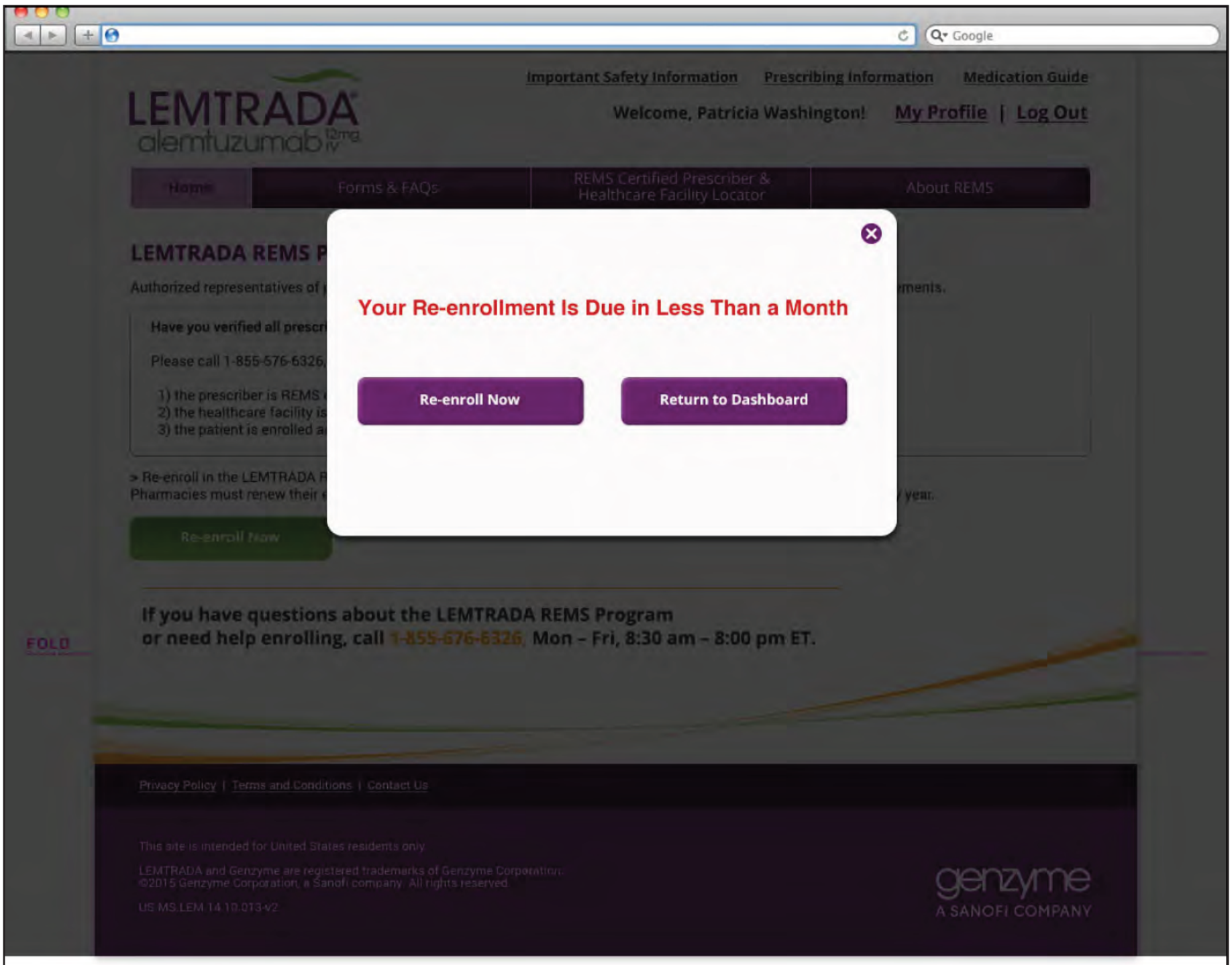
PHARMACY DASHBOARD PAGES

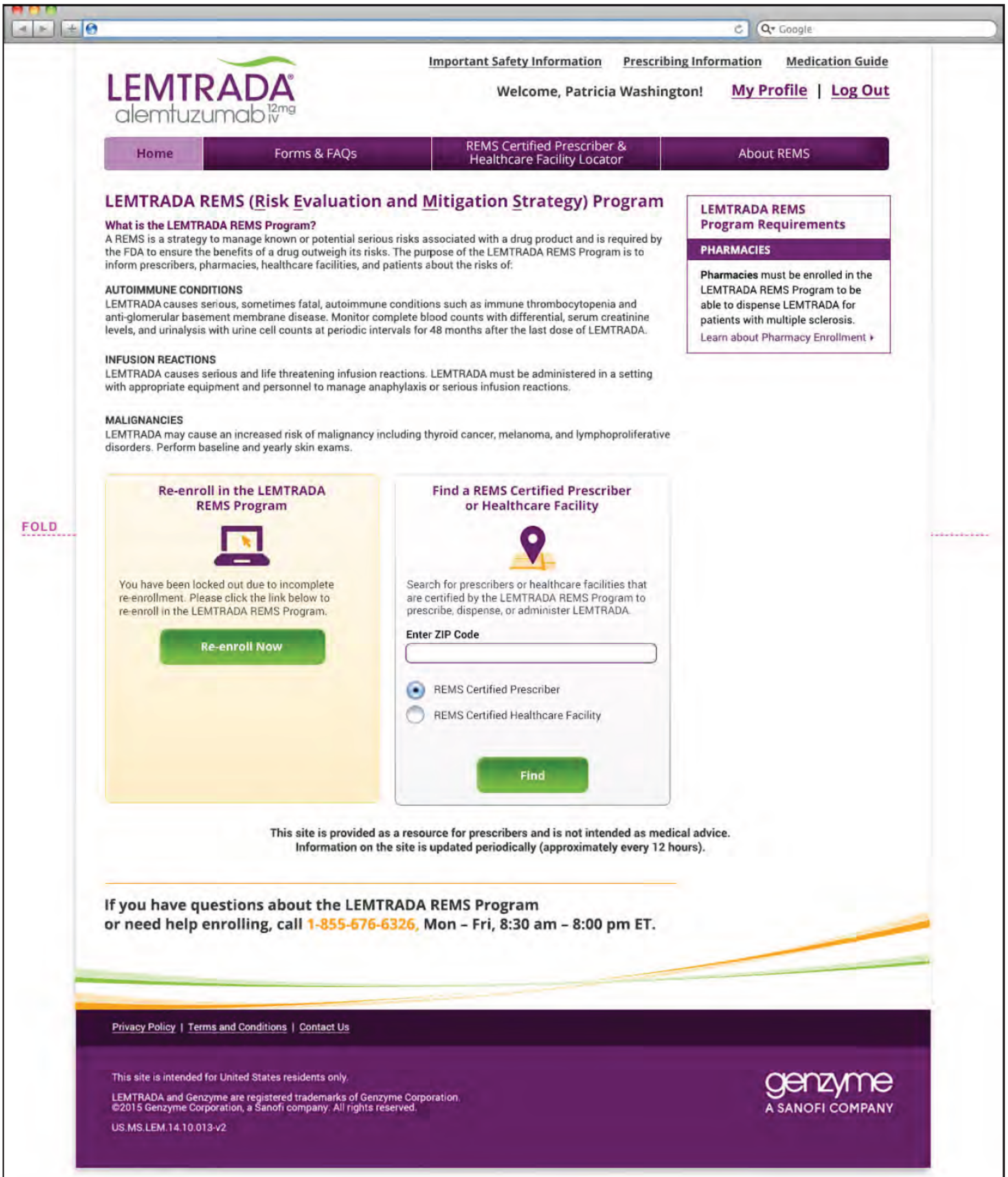
LEMTRADA REMS Desktop - Pharmacy Dashboard



LEMTRADA REMS Desktop - Pharmacy Dashboard, Re-enrollment Overlay

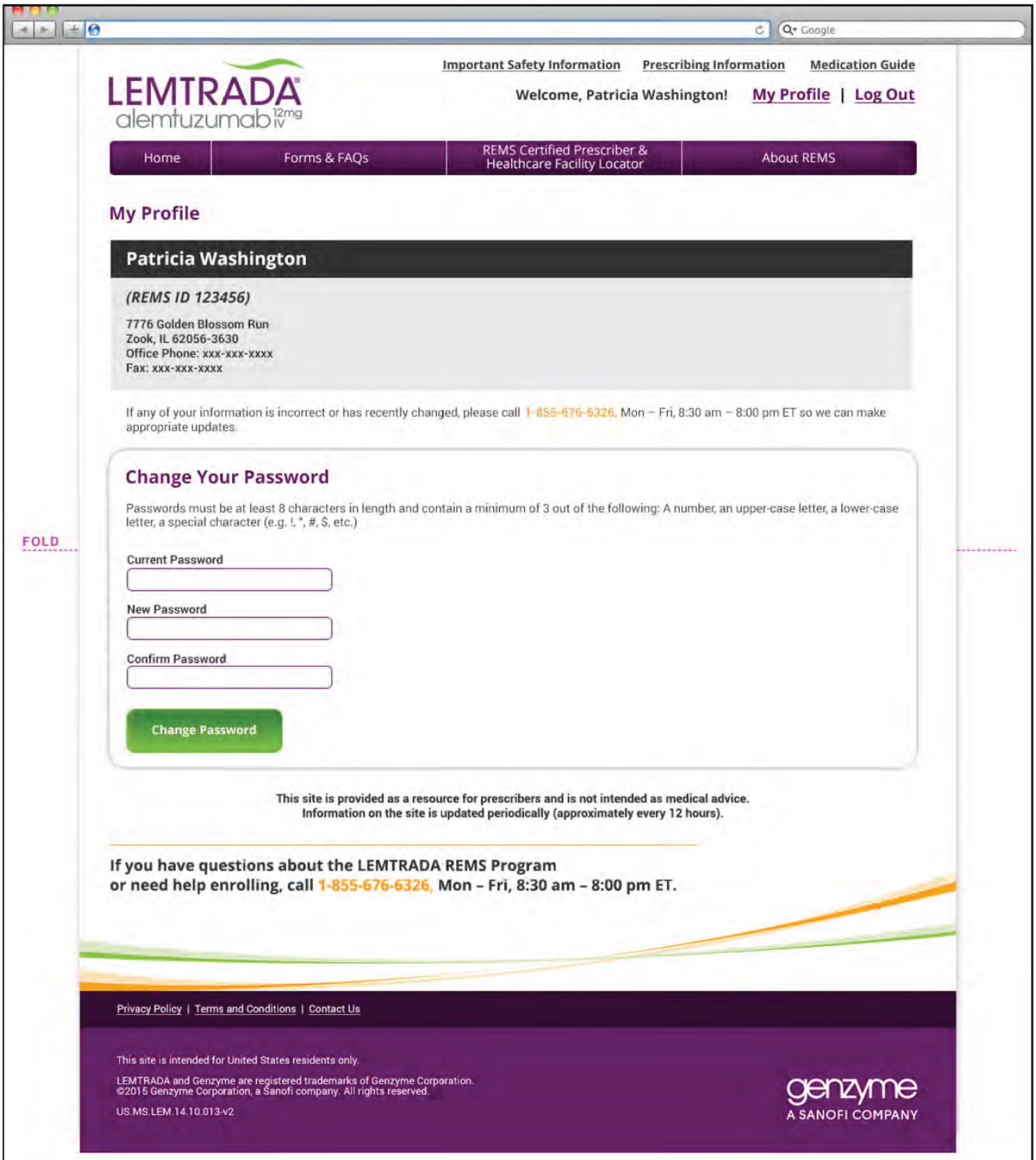


LEMTRADA REMS Desktop - Pharmacy Dashboard - Re-enrollment Lockout

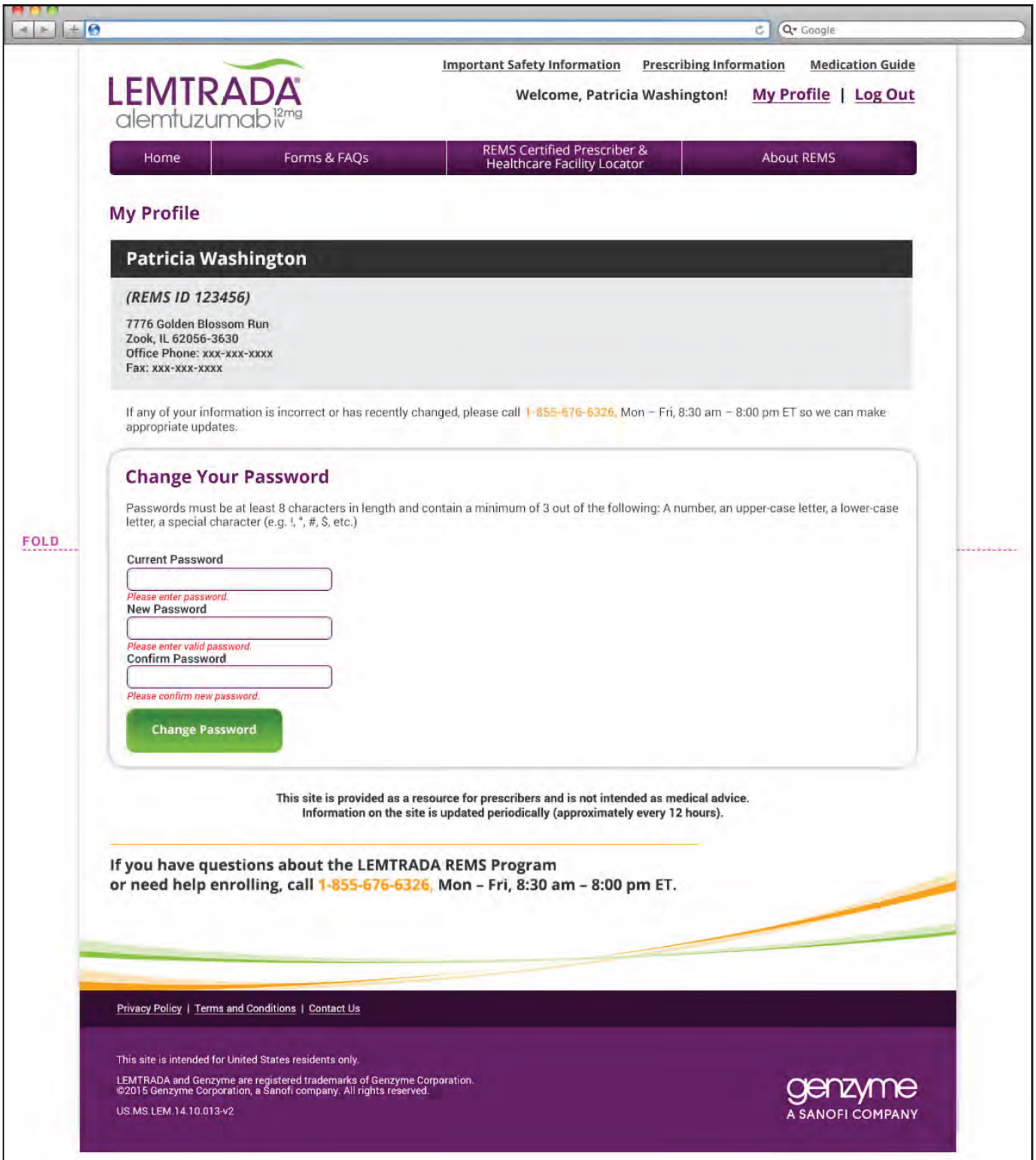


FOLD

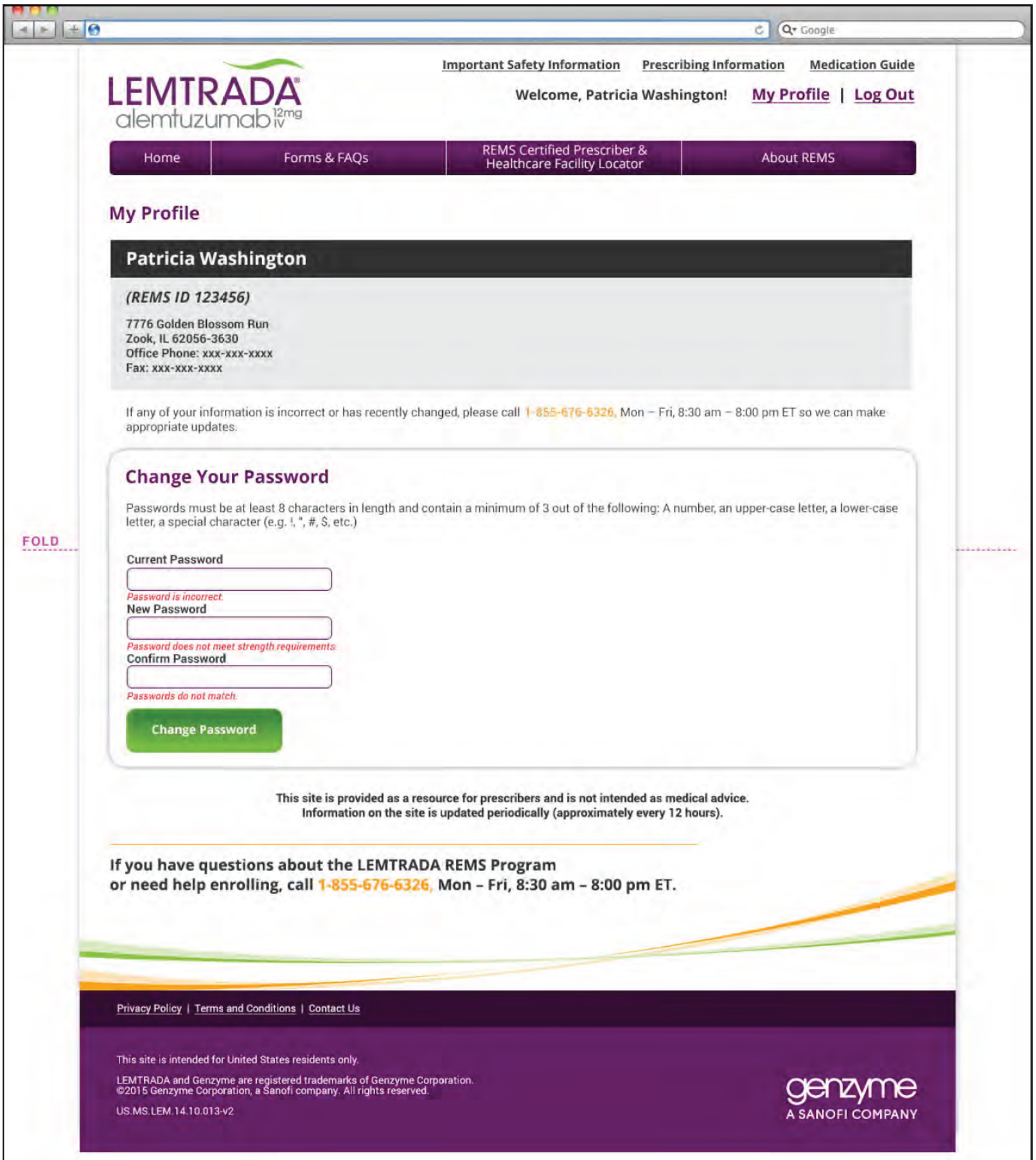
LEMTRADA REMS Desktop - Pharmacy Dashboard - My Profile



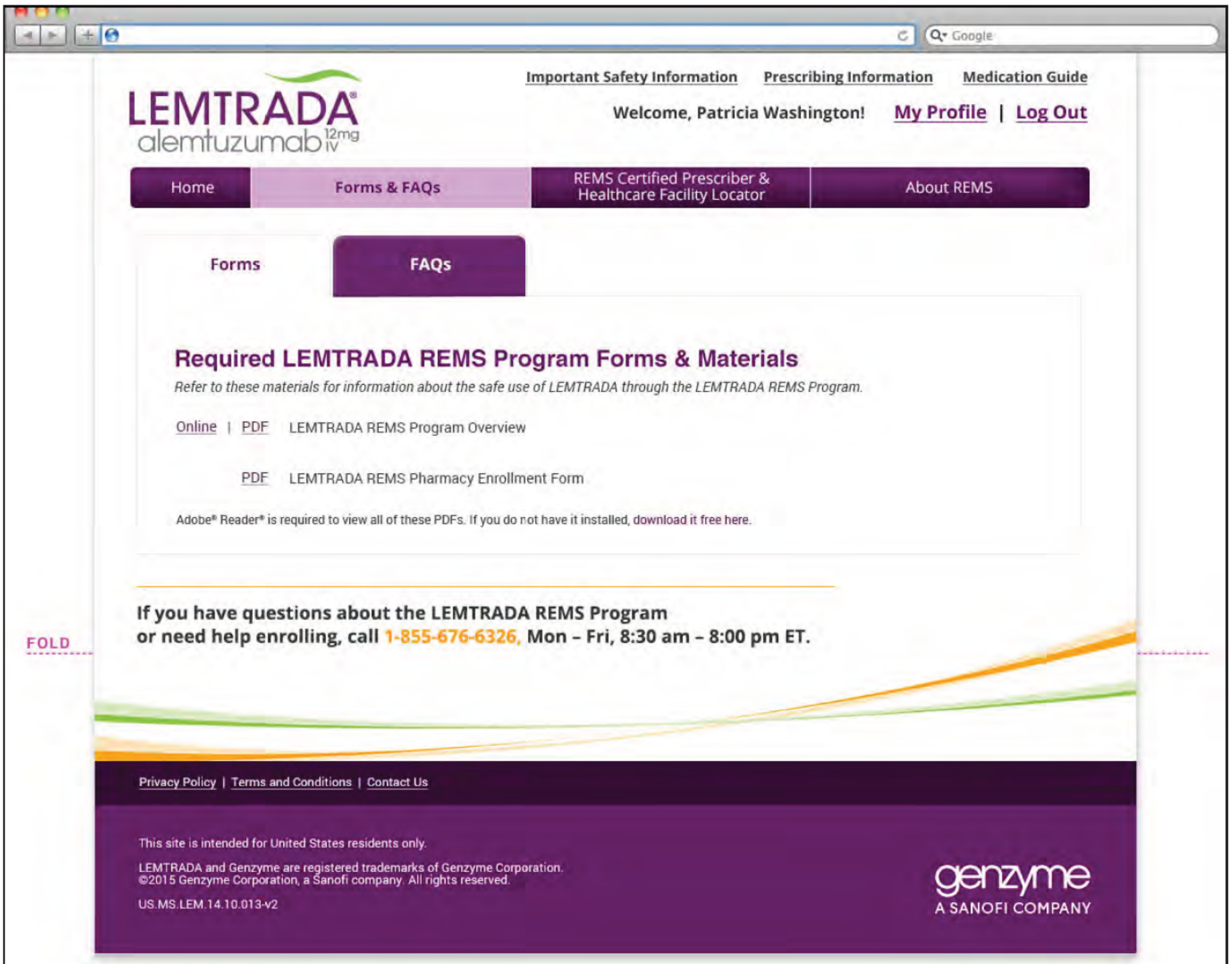
LEMTRADA REMS Desktop - Pharmacy Dashboard - My Profile, Error



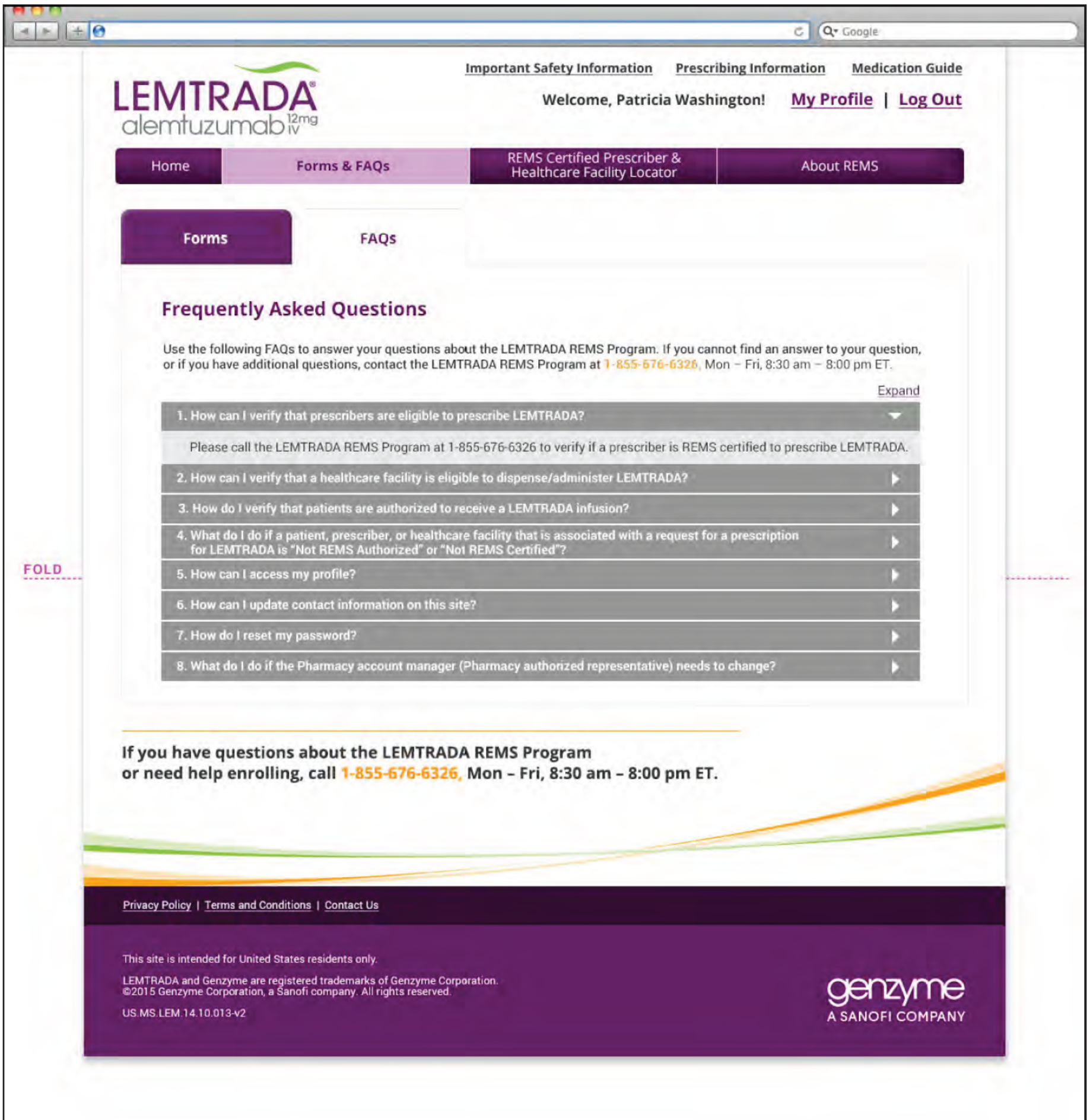
LEMTRADA REMS Desktop - Pharmacy Dashboard - My Profile, Password Strength Error



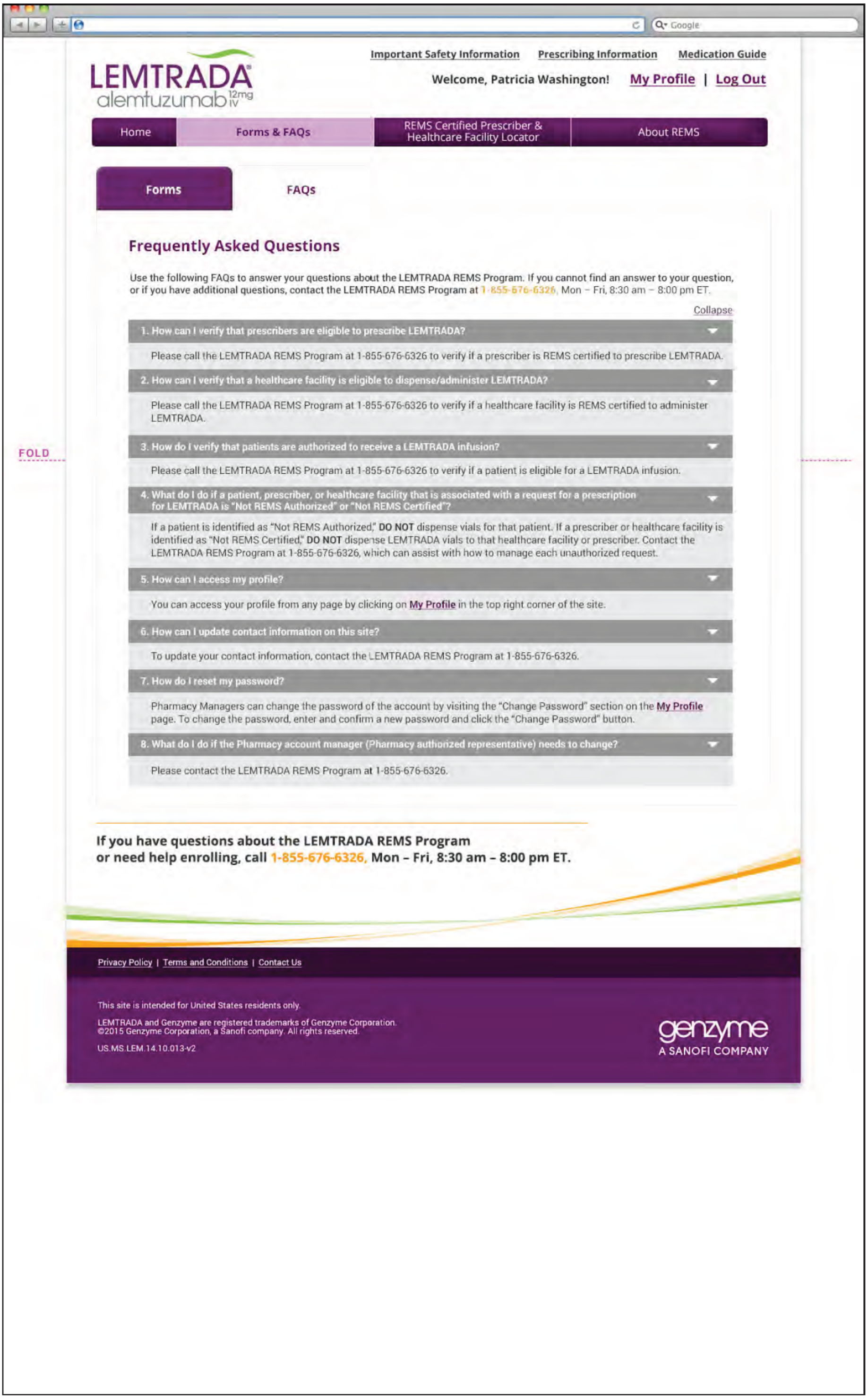
LEMTRADA REMS Desktop - Pharmacy Dashboard - Support, Forms



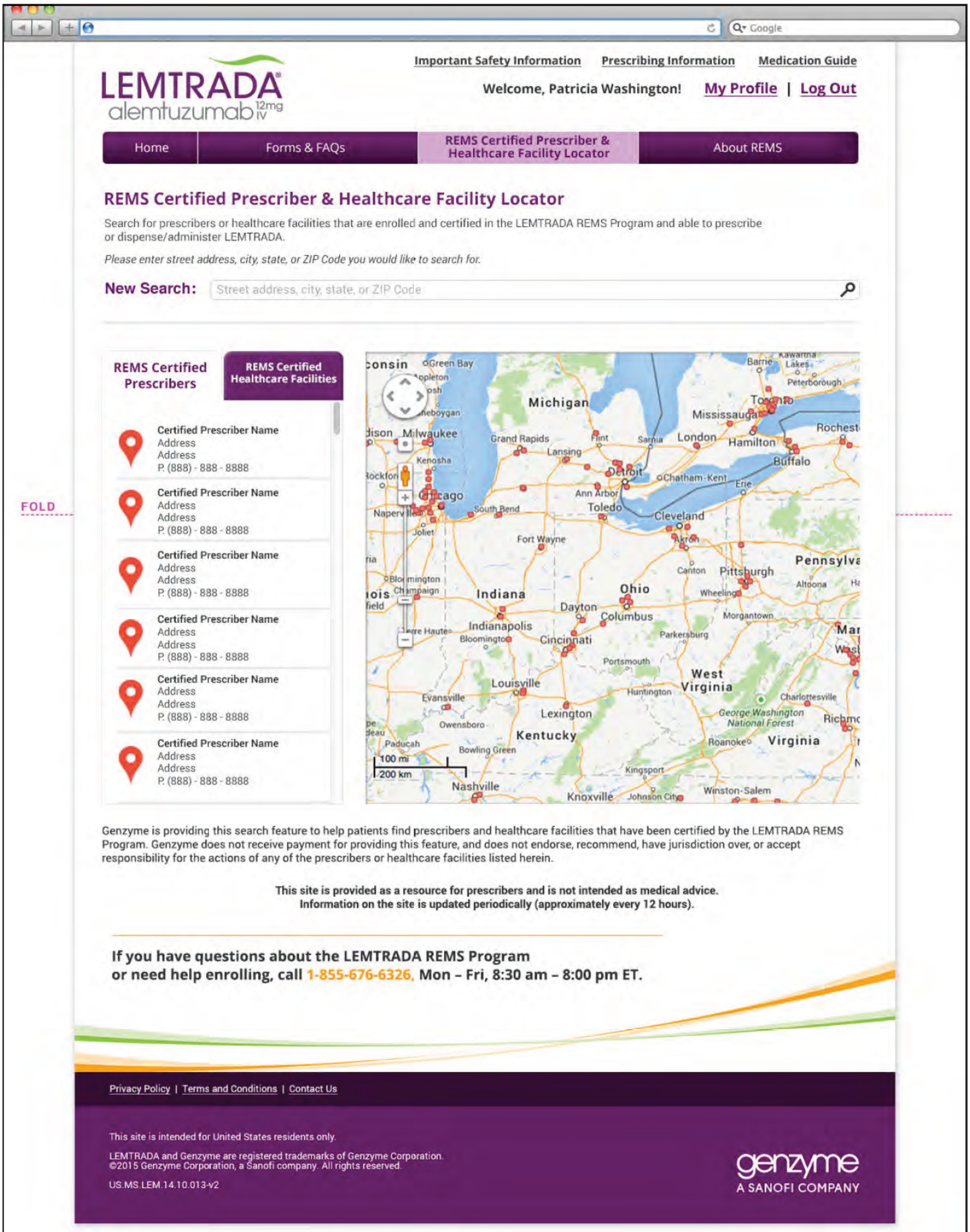
LEMTRADA REMS Desktop - Pharmacy Dashboard - Support, FAQs



LEMTRADA REMS Desktop - Pharmacy Dashboard - Support, FAQs Expanded



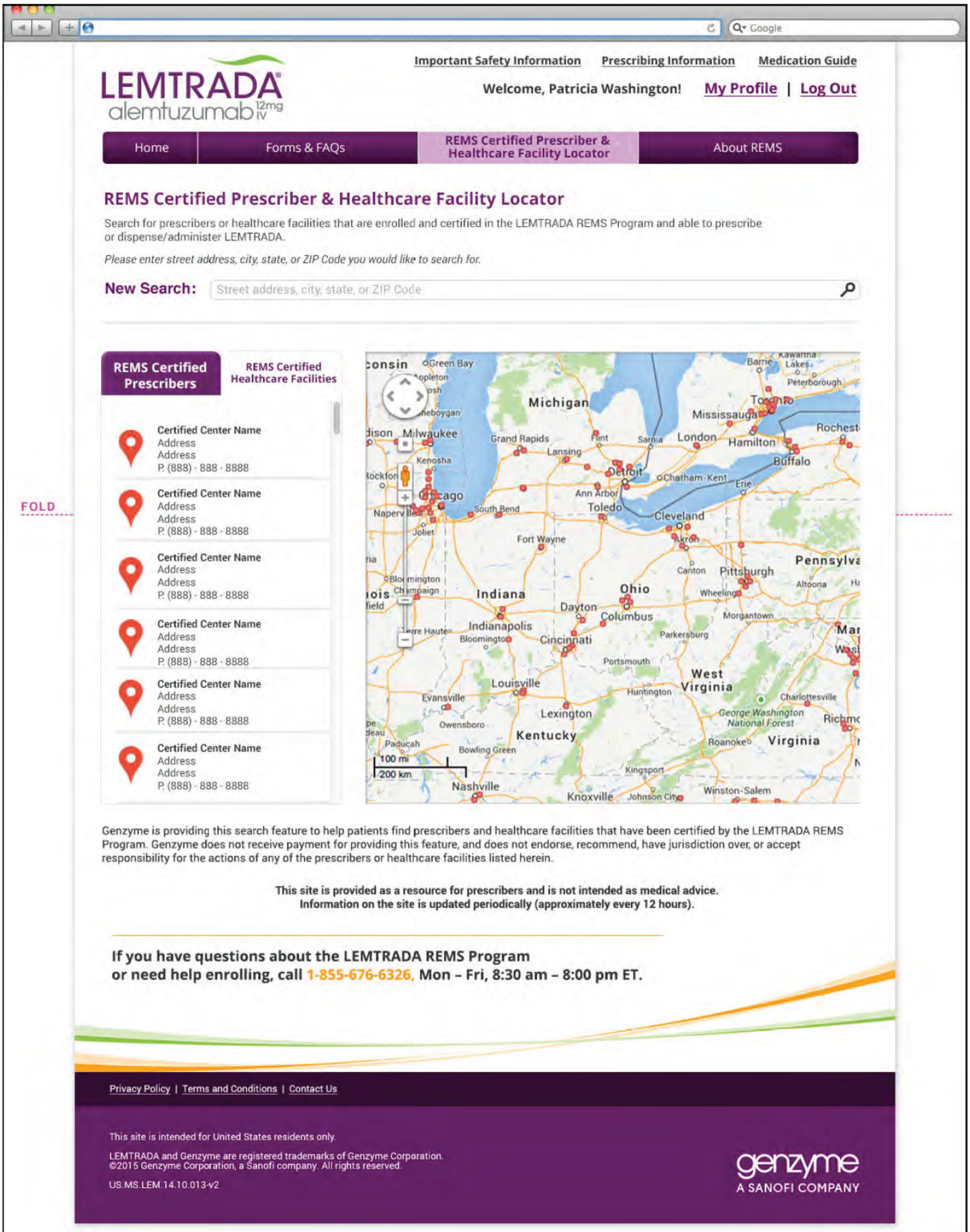
LEMTRADA REMS Desktop - Pharmacy Dashboard - REMS Certified Prescriber and Healthcare Facility Locator



FOLD

Reference ID: 3821900

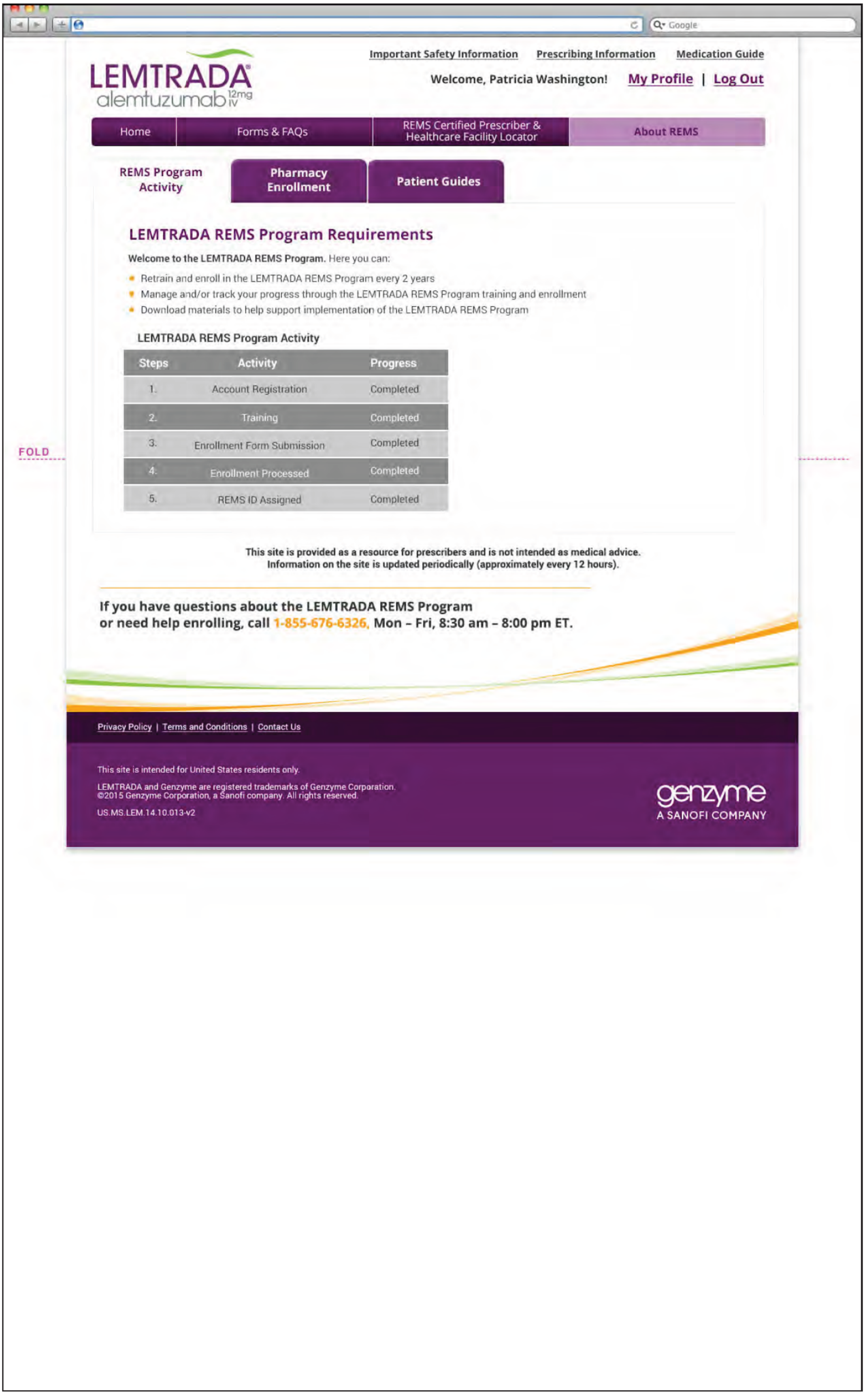
LEMTRADA REMS Desktop - Pharmacy Dashboard - REMS Certified Prescriber and Healthcare Facility Locator



FOLD

Reference ID: 3821900

LEMTRADA REMS Desktop - Pharmacy Dashboard - About REMS, REMS Program Activity



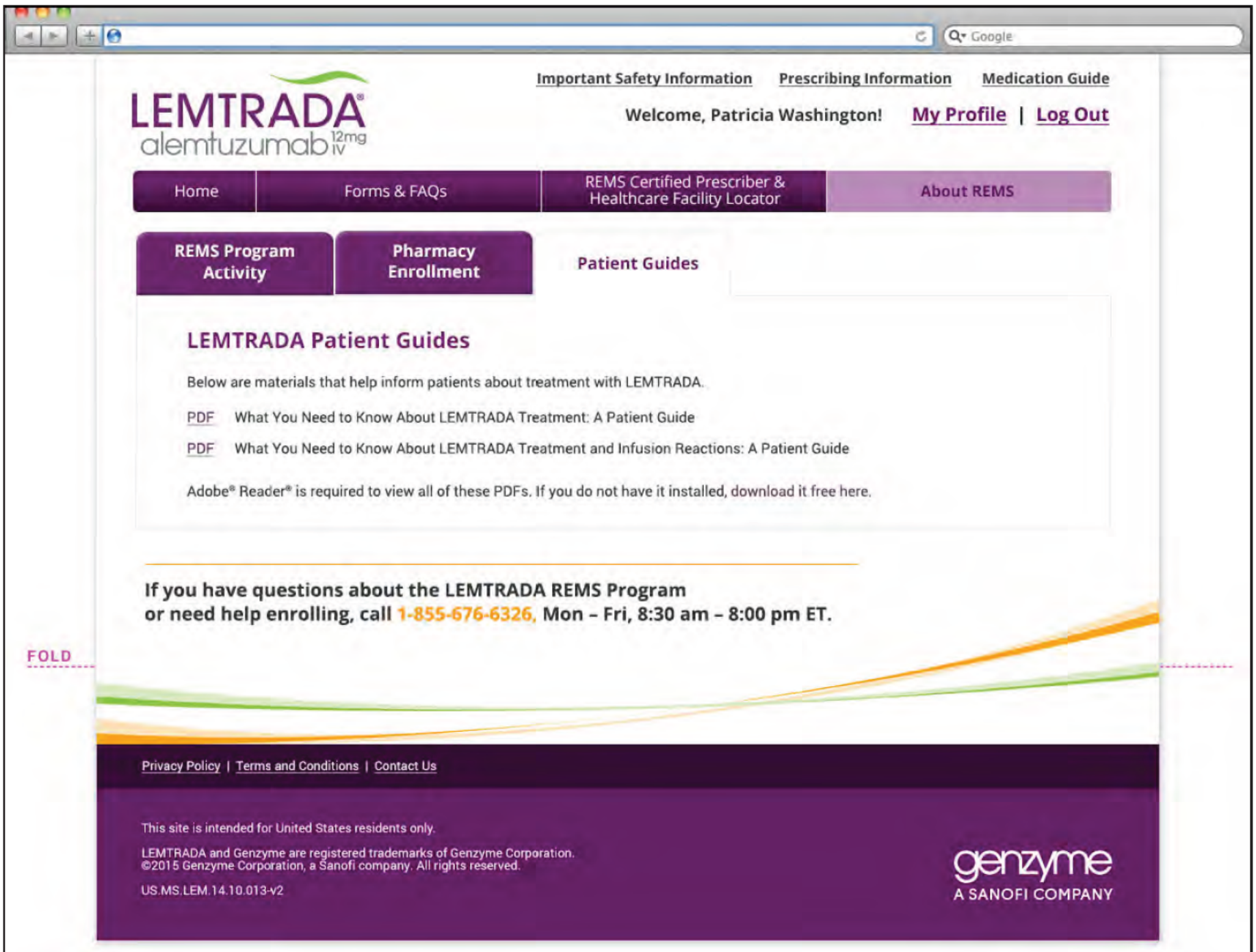
LEMTRADA REMS Desktop - Pharmacy Dashboard - About REMS, Pharmacy Enrollment



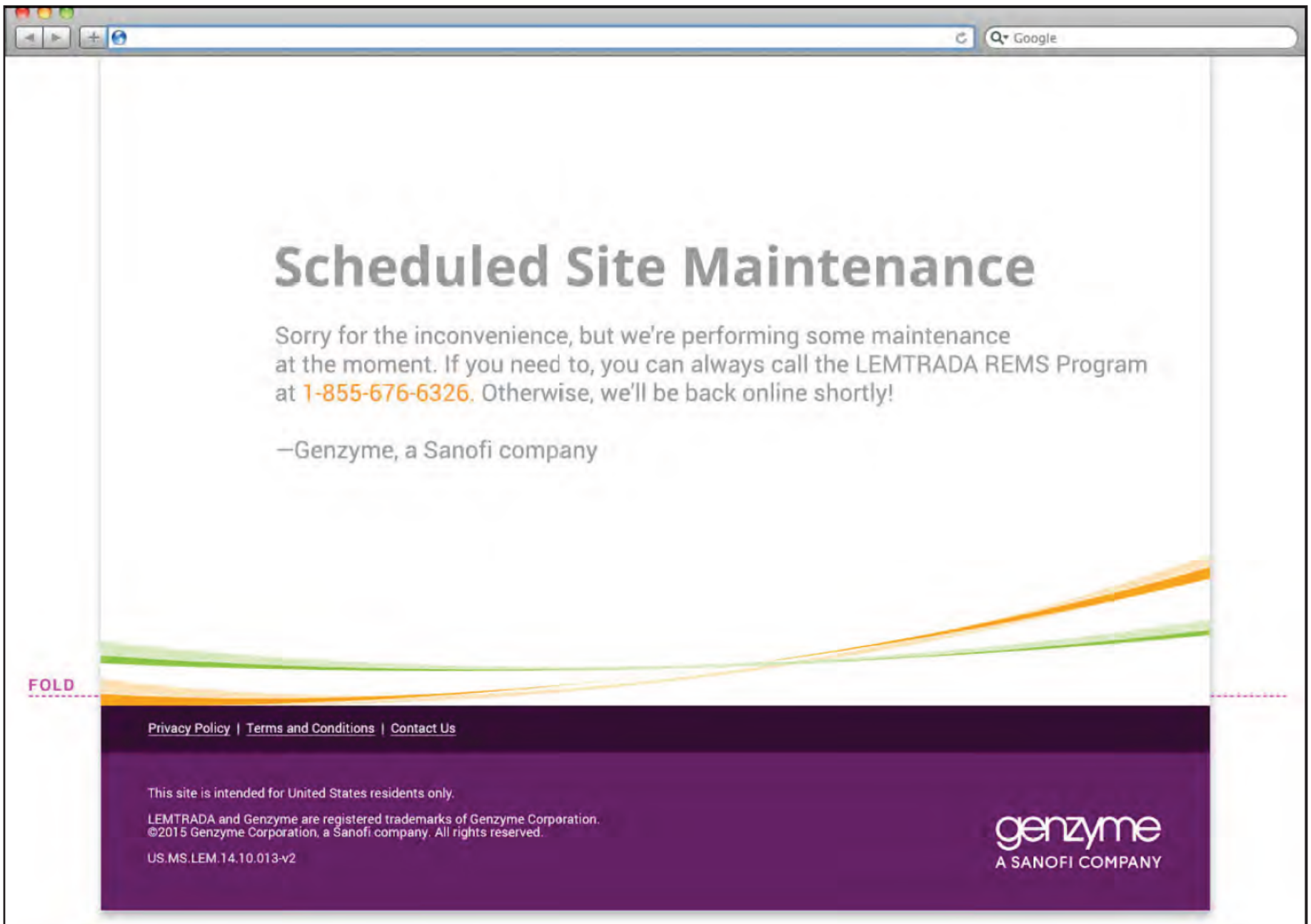
FOLD

FOLD

LEMTRADA REMS Desktop - Pharmacy Dashboard - About REMS, Patient Guide



LEMTRADA REMS Desktop - Scheduled Site Maintenance



LEMTRADA REMS

User Emails

A Registration Confirmation [All Users]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Thank You for Registering!
Sent: Thu 04/20/2012 4:00 PM

Registration confirmation of your LEMTRADA REMS Program account. Log in

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Thank You for Registering With the LEMTRADA REMS Program Online Training Center!

Dear [First Name] [Last Name],

You are now registered with the LEMTRADA REMS Program Online Training Center. You can use your email address and password to access your account and complete your enrollment in the LEMTRADA REMS Program. Follow these steps to complete your enrollment:

- **Review** the LEMTRADA REMS Program training materials
- **Verify** your understanding of the LEMTRADA REMS Program requirements
- **Complete and sign** the LEMTRADA REMS Enrollment Form

Log in to Complete Enrollment

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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B Password Reset Request [All Users]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Password Reset Request
Sent: Thu 04/20/2012 4:00 PM

Reset your password.

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Password Reset Request Received

Dear [First Name] [Last Name],

We received a request to reset the password for your LEMTRADA REMS Program Account.

Click the link below to reset your password using our secure server:

[http://urltoresetpasswordgoeshereloremipsumdolor.com/@1562162t1]

If clicking the link doesn't seem to work, copy and paste the link into your browser's address window, or retype it there. If you did not request a password reset, you may safely disregard this email.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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C Password Reset Confirmation [All Users]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Your Password Has Been Reset
Sent: Thu 04/20/2012 4:00 PM

Your password for LemtradaREMS.com has been reset. Log in

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Your Password Has Been Reset

Dear [First Name] [Last Name],

The password for your LEMTRADA REMS Program account has been reset. You may now access your account with your new password. You do not need to reply to this email.

Log in to My Account

If you did not request a password change, or have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist to help manage your account at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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D Incomplete Training [All Users]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Complete Your Review of the LEMTRADA REMS Program Training Materials
Sent: Thu 04/20/2012 4:00 PM

Continue your enrollment in the LEMTRADA REMS Program. Log in

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Continue LEMTRADA REMS Program Training

Dear [First Name] [Last Name],

Our records indicate that you have not completed your review of the LEMTRADA REMS Program online training materials. In order to complete your enrollment in the LEMTRADA REMS Program and be certified to prescribe, dispense, or administer LEMTRADA, you must review all of the required materials.

Continue Review of Training Materials

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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E Incomplete Knowledge Assessment [HCP Only]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Complete the LEMTRADA REMS Knowledge Assessment
Sent: Thu 04/20/2012 4:00 PM

Continue your enrollment in the LEMTRADA REMS Program. Log in

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Please Complete the LEMTRADA REMS Knowledge Assessment

Dear [First Name] [Last Name],

Our records indicate that you have not successfully completed the LEMTRADA REMS Knowledge Assessment. In order to become enrolled in the LEMTRADA REMS Program and be certified to prescribe LEMTRADA, prescribers must successfully complete all questions in the Knowledge Assessment.

Continue the Knowledge Assessment

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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The Genzyme Support Team

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F Training Complete [HCP]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Your Enrollment in the LEMTRADA REMS Program is Almost Complete
Sent: Thu 04/20/2012 4:00 PM

Your enrollment in the LEMTRADA REMS Program is almost complete. Log in

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LEMTRADA REMS Program Training Complete

Dear [First Name] [Last Name],

You have successfully reviewed the LEMTRADA REMS Program prescriber training materials! You may log in to review the training materials again at any time.

Please note that you must complete the Knowledge Assessment and LEMTRADA REMS Prescriber Enrollment Form to complete your enrollment.

Complete the Knowledge Assessment

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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G Training Complete [HCF, Pharmacy]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Your Enrollment in the LEMTRADA REMS Program Is Almost Complete

Sent: Thu 04/20/2012 4:00 PM

Your enrollment in the LEMTRADA REMS Program is almost complete. Log in

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LEMTRADA REMS Program Training Complete

Dear [First Name] [Last Name],

You have successfully completed the required training for the LEMTRADA REMS Program! You may log in to review the training materials again at any time.

Please ensure that all staff members involved with the dispensing/administering of LEMTRADA also understand the content in the training materials. Note that you must complete the LEMTRADA REMS Enrollment Form to complete your enrollment.

Complete the Enrollment Form

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
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H Knowledge Assessment Complete [HCP only]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Your Enrollment in the LEMTRADA REMS Program is Almost Complete
Sent: Thu 04/20/2012 4:00 PM

Your enrollment in the LEMTRADA REMS Program is almost complete. Log in

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LEMTRADA REMS Program Knowledge Assessment Complete

Dear [First Name] [Last Name],

You have successfully completed the Knowledge Assessment for the LEMTRADA REMS Program! Please note that you need to verify your information on the LEMTRADA REMS Prescriber Enrollment Form in order to complete your certification.

Complete the Enrollment Form

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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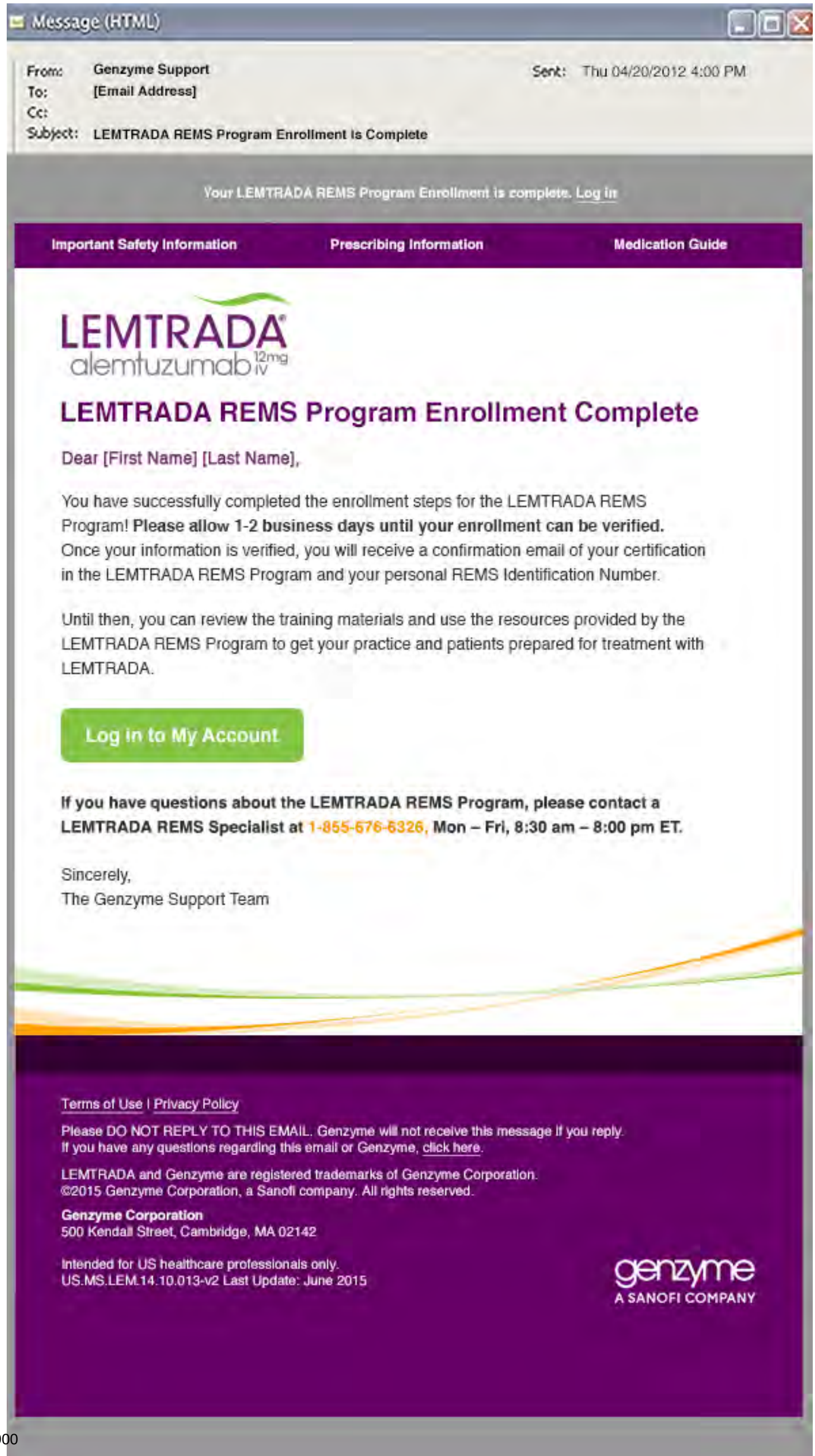
I Enrollment Complete [All Users]



Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: LEMTRADA REMS Program Enrollment is Complete
Sent: Thu 04/20/2012 4:00 PM

Your LEMTRADA REMS Program Enrollment is complete. Log in

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LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS Program Enrollment Complete

Dear [First Name] [Last Name],

You have successfully completed the enrollment steps for the LEMTRADA REMS Program! **Please allow 1-2 business days until your enrollment can be verified.** Once your information is verified, you will receive a confirmation email of your certification in the LEMTRADA REMS Program and your personal REMS Identification Number.

Until then, you can review the training materials and use the resources provided by the LEMTRADA REMS Program to get your practice and patients prepared for treatment with LEMTRADA.

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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J Certification Confirmation [HCF]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Congratulations! You Are Certified by the LEMTRADA REMS Program
Sent: Thu 04/20/2012 4:00 PM

You are now certified by the LEMTRADA REMS Program. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

Welcome to the LEMTRADA REMS Program!

Dear [First Name] [Last Name],

Congratulations! You are now certified by the LEMTRADA REMS Program to dispense/administer LEMTRADA. Your LEMTRADA REMS Identification Number is [xxxxxxxxx]. This number will be used to verify your activity in the LEMTRADA REMS Program. Please ensure that all staff members of your facility receive the necessary training to comply with the LEMTRADA REMS Program requirements. Use LemtradaREMS.com to:

- **View** patient and prescriber information, including REMS status, REMS ID number, and eligibility to receive or prescribe LEMTRADA
- **Download** forms and materials to support you in implementing the requirements of the program
- **Access** educational materials about LEMTRADA for you and your staff

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Message (HTML)

From: Genzyme Support
To: [Email Address]
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You are now certified by the LEMTRADA REMS Program. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

Welcome to the LEMTRADA REMS Program!

Dear [First Name] [Last Name],

Congratulations! You are now certified by the LEMTRADA REMS Program to dispense/administer LEMTRADA. Your LEMTRADA REMS Identification Number is [xxxxxxxxx]. This number will be used to verify your activity in the LEMTRADA REMS Program. Please ensure that all staff members of your facility receive the necessary training to comply with the LEMTRADA REMS Program requirements. Use LemtradaREMS.com to:

- **Download** forms and materials to support you in implementing the requirements of the program
- **Access** educational materials about LEMTRADA for you and your staff

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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If you have any questions regarding this email or Genzyme, click here.

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Genzyme Corporation
500 Kendall Street, Cambridge, MA 02142

Intended for US healthcare professionals only.
US.MS.LEM.14.10.013-v2 Last Update: June 2015

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K Certification Confirmation [HCP]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Congratulations! You Are Certified by the LEMTRADA REMS Program

Sent: Thu 04/20/2012 4:00 PM

You are now certified by the LEMTRADA REMS Program. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

Welcome to the LEMTRADA REMS Program!

Dear [First Name] [Last Name],

Congratulations! You are now certified by the LEMTRADA REMS Program to prescribe LEMTRADA. Your LEMTRADA REMS Identification Number is [xxxxxxxxxxx]. This number will be used to verify your activity in the LEMTRADA REMS Program. As a member of the LEMTRADA REMS Program, you can now access personal online tools to help you manage your LEMTRADA patients. This site will allow you to:

- **View** patient and healthcare facility information, including REMS status, REMS ID number, and eligibility to receive or dispense/administer LEMTRADA
- **Complete** required authorization forms, including the LEMTRADA REMS Patient Status Form and the LEMTRADA REMS Patient Authorization and Baseline Lab Form
- **Download** forms to sign patients up for the LEMTRADA Central Lab Program
- **Access** educational materials about LEMTRADA for you and your staff

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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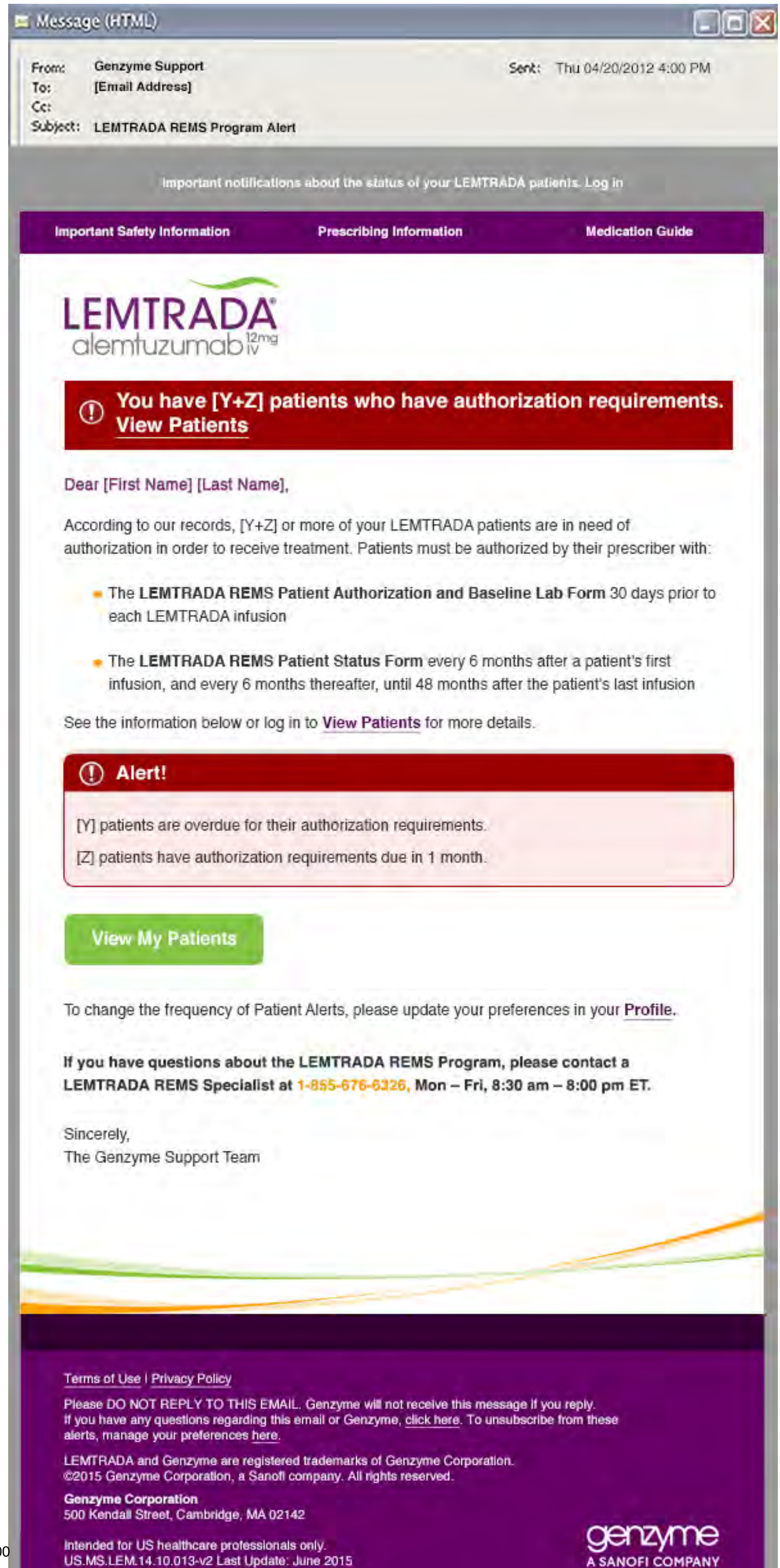
L Authorization Alert [HCP, HCF]



Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: LEMTRADA REMS Program Alert
Sent: Thu 04/20/2012 4:00 PM

Important notifications about the status of your LEMTRADA patients. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

You have [Y+Z] patients who have authorization requirements. View Patients

Dear [First Name] [Last Name],

According to our records, [Y+Z] or more of your LEMTRADA patients are in need of authorization in order to receive treatment. Patients must be authorized by their prescriber with:

- The **LEMTRADA REMS Patient Authorization and Baseline Lab Form** 30 days prior to each LEMTRADA infusion
- The **LEMTRADA REMS Patient Status Form** every 6 months after a patient's first infusion, and every 6 months thereafter, until 48 months after the patient's last infusion

See the information below or log in to View Patients for more details.

Alert!

[Y] patients are overdue for their authorization requirements.

[Z] patients have authorization requirements due in 1 month.

View My Patients

To change the frequency of Patient Alerts, please update your preferences in your Profile.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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La Authorization Alert [HCP, HCF]

Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: LEMTRADA REMS Program Alert
Sent: Thu 04/20/2012 4:00 PM

Important notifications about the status of your LEMTRADA patients. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

You have [Y+Z] patient who has authorization requirements. View Patient

Dear [First Name] [Last Name],

According to our records, [Y+Z] of your LEMTRADA patients is in need of authorization in order to receive treatment. Patients must be authorized by their prescriber with:

- The **LEMTRADA REMS Patient Authorization and Baseline Lab Form** 30 days prior to each LEMTRADA infusion
- The **LEMTRADA REMS Patient Status Form** every 6 months after a patient's first infusion, and every 6 months thereafter, until 48 months after the patient's last infusion

See the information below or log in to **View Patients** for more details.

View My Patients

To change the frequency of Patient Alerts, please update your preferences in your **Profile**.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Message (HTML)

From: Genzyme Support
To: [Email Address]
Cc:
Subject: Your LEMTRADA REMS Training Was Invalid
Sent: Thu 04/20/2012 4:00 PM

Your LEMTRADA REMS training was invalid.

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

Your LEMTRADA REMS Training Was Invalid

Dear [First Name] [Last Name],

Thank you for completing your LEMTRADA REMS Training. Unfortunately, your training was deemed invalid. In order to proceed with training, please contact *MS One to One*® at 1-855-676-6326.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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LEMTRADA REMS

Online Forms

Printed for User Records

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is available only through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA.

Instructions:

1. Review the LEMTRADA REMS Education Program for Prescribers, including the Prescribing Information
2. Successfully complete the LEMTRADA REMS Knowledge Assessment
3. Complete and submit this LEMTRADA REMS Prescriber Enrollment Form
4. Send your patient to a healthcare facility that is enrolled in the LEMTRADA REMS Program

Please complete all required fields on this form and fax it to 1-855-557-2478. You will receive enrollment confirmation via your preferred method of communication (email or fax) within 2 business days.

*Indicates a mandatory field.

LEMTRADA PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)/Degree* Doe, Dr. John/Doctor Of Osteopathy			
Name of Institution or Healthcare Facility* TheBestHCF			
Street Address* 1234 Intouch DriveSuite 400			
City* Overland Park		State* KS	ZIP Code* 12345
Office Phone Number* 9131112222	Fax Number* 9132223333	Email Address john.doe@gmail.com	Mobile Phone Number 9135551234
National Provider Identification (NPI) Number* 1234567893			

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

PRESCRIBER AGREEMENT

By completing this form, I attest that:

- I understand that LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- I understand that LEMTRADA is only available through the LEMTRADA REMS Program and that I must comply with the program requirements in order to prescribe LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Prescribers*, including a review of the LEMTRADA Prescribing Information, and successfully completed the LEMTRADA REMS Knowledge Assessment.
- I understand that by completing the training program and signing this LEMTRADA REMS Prescriber Enrollment Form, I will be enrolled in the LEMTRADA REMS Program and can prescribe LEMTRADA.
- I understand that I am responsible for reviewing *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with each patient, and counseling each patient on an ongoing basis about the serious risks associated with the use of LEMTRADA and how to mitigate these risks through periodic monitoring.
- I understand that I must enroll all patients being treated with LEMTRADA into the LEMTRADA REMS Program prior to initiating the patient on treatment with LEMTRADA. I am responsible for completing a LEMTRADA REMS Patient Enrollment Form with the patient (or patient's legal representative), obtaining the patient's (or patient's legal representative's) signature on the form, and submitting the signed form to the LEMTRADA REMS Program. A completed copy should be provided to the patient and another copy should be stored in the patient's records.
- I will provide enrolled patients with a LEMTRADA Patient Safety Information Card and instruct patients to carry this card with them at all times in case of an emergency.
- I understand that I must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription. I understand that I am responsible for completing baseline lab monitoring within 30 days prior to infusion of LEMTRADA.

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PRESCRIBER AGREEMENT (CONTINUED)

- I understand that I must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form indicating completion of each patient's baseline labs within 30 days prior to the patient's infusion date.
- I understand the risks of autoimmune conditions and malignancies associated with the use of LEMTRADA, and the need for periodic monitoring in order to identify and mitigate these risks:
  - Complete blood counts with differential obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Serum creatinine levels obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Urinalysis with urine cell counts obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Thyroid function tests, such as thyroid stimulating hormone (TSH) level, obtained within 30 days prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion.
  - Baseline and yearly skin examinations.
- I will report any adverse events of autoimmune conditions, infusion reactions, or malignancies to Genzyme.
- I will complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the Program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

WEBSITE CONSENT

I understand that the LEMTRADA REMS Program will publish my name, business address, and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-800-557-2478.

(●) Yes ( ) No

SIGNATURE

6/24/2015

Prescriber Signature* Date*

Dr. John Doe

Print Name*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:12:14 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT STATUS FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed every 6 months for each LEMTRADA® (alemtuzumab) patient under your care. Please complete this form 6 months after your patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the patient's last infusion.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Dr. John

Office Phone Number* 9135551234

Address* 1234 Intouch Drive Suite 400

City* Los Angeles

State* CA

ZIP Code* 90210

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Jane

Patient LEMTRADA REMS Program Identification Number* 1122334455

Date of Birth (MM/DD/YYYY)* 08/18/1969

Date of Last LEMTRADA Infusion (MM/DD/YYYY)* 03/21/2015

Is the above-named patient still under your care?* (Check one) ■ **Yes** ☐ **No**

IF NO, please indicate the name of the healthcare provider now responsible for this patient's care

Healthcare Provider Name

Healthcare Provider Phone Number

Patient's Current Healthcare Provider Is Unknown ☐

IF YES, please complete the following information

The patient has completed the periodic monitoring within the last 6 months. ■ Yes ☐ No

Since submitting the last LEMTRADA REMS Patient Status Form, has the patient been diagnosed with any of the following?

a. Autoimmune conditions ☐ Yes ■ No

b. Infusion reactions ■ Yes ☐ No

c. Malignancies ☐ Yes ■ No

☑ This adverse event has already been reported to Genzyme (specify date of report): 06/04/2015

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

In signing this form, I acknowledge that I have reviewed *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with this patient and counseled the patient about the serious risks associated with the use of LEMTRADA, and how to mitigate these risks through periodic monitoring.

PRESCRIBER'S SIGNATURE

Prescriber Signature*

Date* 6/24/2015

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:08:23 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT AUTHORIZATION AND BASELINE LAB FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed within 30 days prior to the first infusion date of each LEMTRADA® (alemtuzumab) patient's treatment course.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Dr. John

Office Phone Number* 9135551234

Address* 1234 Intouch Drive Suite 400

City* Overland Park

State* KS

ZIP Code* 12345

Prescriber LEMTRADA REMS Program Identification Number* 1234567893

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Jane

Patient LEMTRADA REMS Program Identification Number* 1122334455

Date of Birth (MM/DD/YYYY)* 08/18/1969

AUTHORIZATION AND BASELINE LABS

Do you authorize LEMTRADA treatment for the above-referenced patient?* (●) Yes ( ) No

Do you attest that required baseline laboratory testing has been completed prior to LEMTRADA treatment and within 30 days of the patient's first infusion?* (●) Yes ( ) No

PRESCRIPTION INFORMATION

Check one*

(●) Initial course (1 vial [12 mg/day]) X 5 consecutive days — Total number of vials: 10

( ) Subsequent course (1 vial [12 mg/day]) X 3 consecutive days — Total number of vials: _____

SIGNATURE

Prescriber Signature*

Date* 6/24/2015

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:13:56 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS HEALTHCARE FACILITY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the healthcare facility must enroll the facility in the LEMTRADA REMS Program.

- ○ New Enrollment
- ◉ Re-enrollment (every 2 years)

*Indicates a mandatory field.

Please complete a separate Healthcare Facility Enrollment Form for each facility site, if applicable.

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Name of Institution or Healthcare Facility* TheBestHCF		NPI Number* 1122334455	
Infusion Facility Address* 1234 Intouch Drive Suite 400			
City* Overland Park		State* KS	ZIP Code* 12345
Ship-to Street Address (if different)* 1234 Shipping St.			
City* Leawood		State* KS	ZIP Code* 55555
Phone Number* 9135551234	Fax Number* 9135558888	Email Address thebestHCF@gmail.com	
Name of Authorized Healthcare Facility Representative* John Doe		Title* TheBest	

Site Affiliation

○ Academic ○ Government ○ Ambulatory/Freestanding ◉ Hospital Based ○ Private Practice (in office)

HEALTHCARE FACILITY AGREEMENT

I am the authorized representative designated by my healthcare facility to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following Program requirements:

- I understand that my healthcare facility must be certified with the LEMTRADA REMS Program to receive or administer LEMTRADA.
- I have completed the review of the *LEMTRADA REMS Education Program for Healthcare Facilities* and the LEMTRADA REMS Program Overview.
- I understand that my healthcare facility must confirm that the patient is authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program or verifying online at www.LemtradaREMS.com prior to initiation of each treatment course.
- I understand the risk of serious infusion reactions during and following the administration of LEMTRADA.
- I understand the need to monitor patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
  - To include the monitoring of patient vital signs before the infusion and periodically during the infusion.
- I understand that my healthcare facility must be equipped with the necessary on-site equipment and personnel to manage anaphylaxis or serious infusion reactions.
- I understand that my healthcare facility must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

Reference ID: 3821900

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HEALTHCARE FACILITY AGREEMENT (CONTINUED)

- This healthcare facility will establish procedures and protocols that are subject to audit, to help ensure compliance with the safe use conditions required in the LEMTRADA REMS Program, including the following:
  - Ensure that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - Ensure that the prescriber is certified and the patient is enrolled and authorized by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website prior to dispensing and administering LEMTRADA.
  - Ensure that the infusion site is equipped to manage infusion reactions.
  - Ensure that LEMTRADA is not dispensed outside of the authorized representative's certified healthcare facility.
  - Prior to the first day of each treatment course, counsel and provide a copy of *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* to each patient to inform them about the risk of serious infusion reactions.
  - Observe each patient administered LEMTRADA at my healthcare facility during and for at least 2 hours after each LEMTRADA infusion, in order to provide appropriate medical treatment in the event of serious infusion reactions following LEMTRADA infusion.
  - For each patient, complete and return the LEMTRADA REMS Infusion Checklist to the LEMTRADA REMS Program within 5 business days from the patient's last infusion of LEMTRADA within a specific treatment course.
  - Renew enrollment into the LEMTRADA REMS Program every 2 years from the initial enrollment.
- To make available to Genzyme documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.
- To return to Genzyme any unused vials of LEMTRADA within 50 days from the date of receipt of the LEMTRADA REMS Patient Authorization Baseline Lab Form.
- To ensure that a LEMTRADA REMS Patient Authorization and Baseline Lab Form is received for each prescription by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website.
- To ensure that all non-prescribing HCPs who administer LEMTRADA in my healthcare setting are trained using the LEMTRADA REMS Program Overview and the *LEMTRADA REMS Education Program for Healthcare Facilities*, and a record regarding such training must be maintained.

SIGNATURE

	6/24/2015
Authorized Healthcare Facility Representative Signature*	Date*
John Doe	TheBest
Print Name*	Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:04:04 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS INFUSION CHECKLIST

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and submitted within **5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

All fields on this form are mandatory.

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First) Doe, Jane

DOB (MM/DD/YYYY) 08/18/1969

Patient LEMTRADA REMS Program Identification Number 1122334455

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (Last, First) Doe, Dr. John

Prescriber LEMTRADA REMS Program Identification Number 1234567893

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Healthcare Facility Name TheBestHCF

Healthcare Facility LEMTRADA REMS Program Identification Number 1234567893

STEP 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course.

Is the patient authorized to receive LEMTRADA? ☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE.** Refer patient back to the LEMTRADA prescriber.

STEP 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course. Has the patient been counseled and received the guide?

☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP** — provide the patient guide. Proceed to the next question after the patient has received this guide and has been counseled.

STEP 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:

1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available? ☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE** until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information.

Reference ID: 3821900

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First)	DOB (MM/DD/YYYY)
Doe, Jane	08/18/1969

STEP 4: RECORD infusion information

Was the patient infused with LEMTRADA? ■ **Yes** ☐ **No**

Yes Fill in Dates of Infusion below and then proceed to Step 5.

No Proceed to Step 5.

LEMTRADA Infusions

Dates of Infusion:

Date: 03/21/2014

Date: 07/27/2014

Date: 08/14/2014

Date: _____

Date: _____

STEP 5: RETURN unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Baseline Lab Form.

Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

STEP 6: SIGNATURE

	6/24/2015
Signature of staff completing checklist	Date
Dr. John Doe	
Name of staff completing checklist (Please Print)	

STEP 7: Fax the Infusion Checklist to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com within 5 business days

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326.

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genzyme
A SANOFI COMPANY

Reference ID: 3821900

Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:06:36 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Pharmacy

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PHARMACY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the pharmacy must enroll the pharmacy in the LEMTRADA REMS Program.

☒ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

PHARMACY INFORMATION (PLEASE PRINT)

Name of Pharmacy* TheBestSPP		NPI Number* 1234567893	
Pharmacy Address* 1234 Intouch Drive			
City* Overland Park		State* KS	ZIP Code* 64129
Name of Authorized Pharmacy Representative* John Doe		Title* TheBestRep	
Phone Number* 9134441234	Fax Number* 9138881234	Email Address john.doe@gmail.com	

PHARMACY AGREEMENT

I am the authorized representative designated by my Pharmacy to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following program requirements:

- I understand that my pharmacy must be certified with the LEMTRADA REMS Program to dispense LEMTRADA.
- I will oversee implementation and compliance with the LEMTRADA REMS Program requirements.
- I have reviewed the LEMTRADA REMS Program Overview.
- I will ensure that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the LEMTRADA REMS Program Overview.
- I will put processes and procedures in place, and follow such processes and procedures, to ensure the following verifications are met prior to dispensing LEMTRADA:
  - The LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program prior to dispensing LEMTRADA.
  - Ensuring LEMTRADA is only dispensed to a certified infusion center.
- This pharmacy will establish procedures and protocols that are subject to audit, to help ensure compliance with the requirements of the LEMTRADA REMS Program.
- I understand that my pharmacy must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.

SIGNATURE

Authorized Pharmacy Representative Signature* John Doe	Date* 6/24/2015
Print Name*	Title TheBestRep

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

genzyme A SANOFI COMPANY

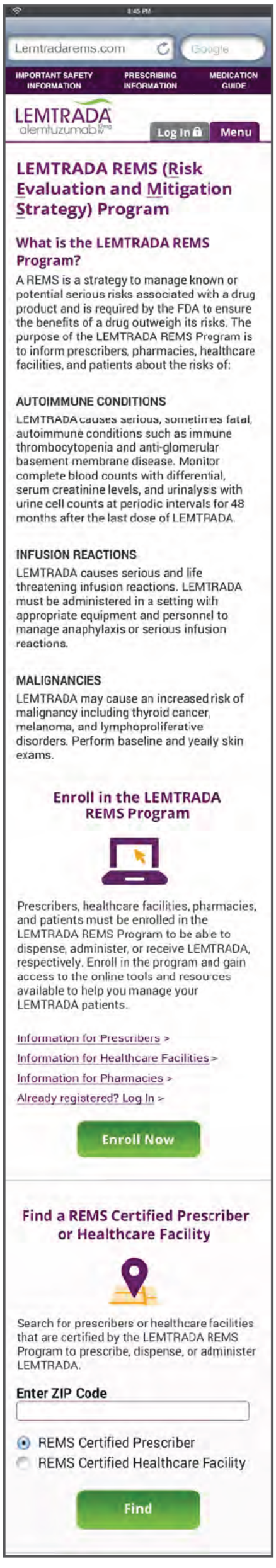
Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:10:10 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

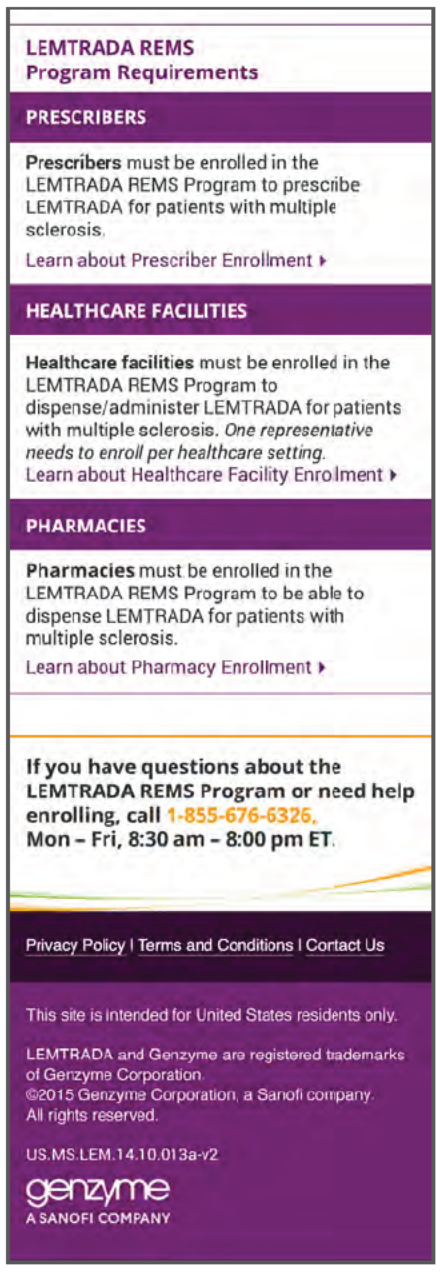
LEMTRADA REMS MOBILE

PUBLIC and Prescriber Pages Only

PUBLIC FACING PAGES

LEMTRADA REMS Mobile - Public Home

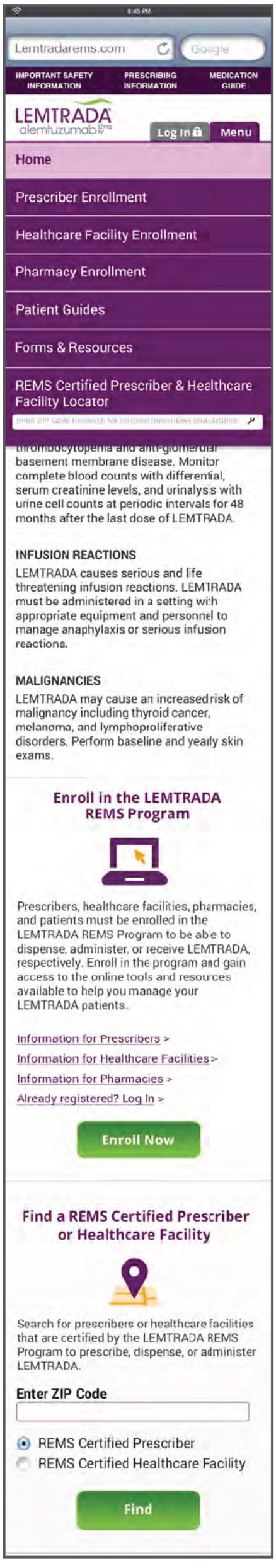


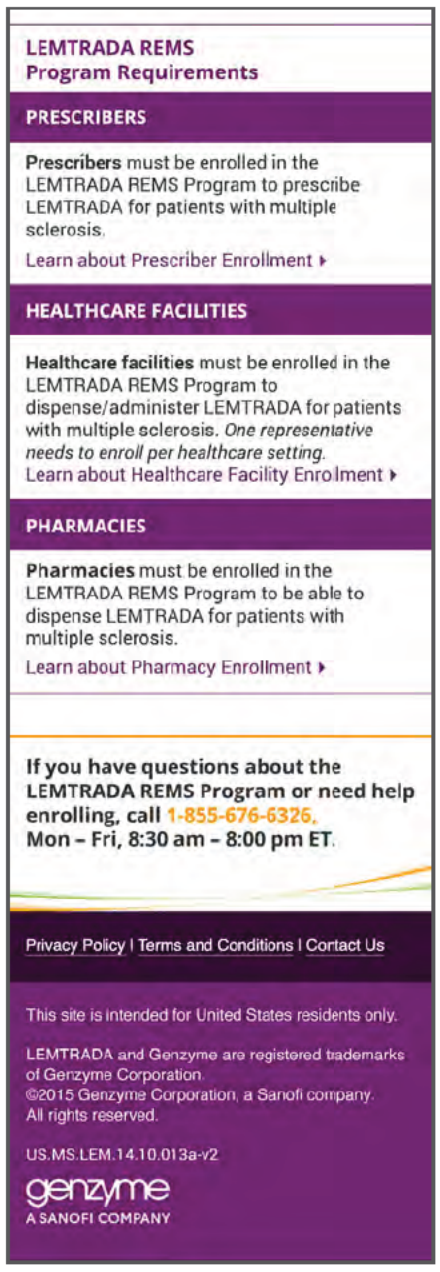


LEMTRADA REMS Mobile - Public Home, Pinned Program Requirements

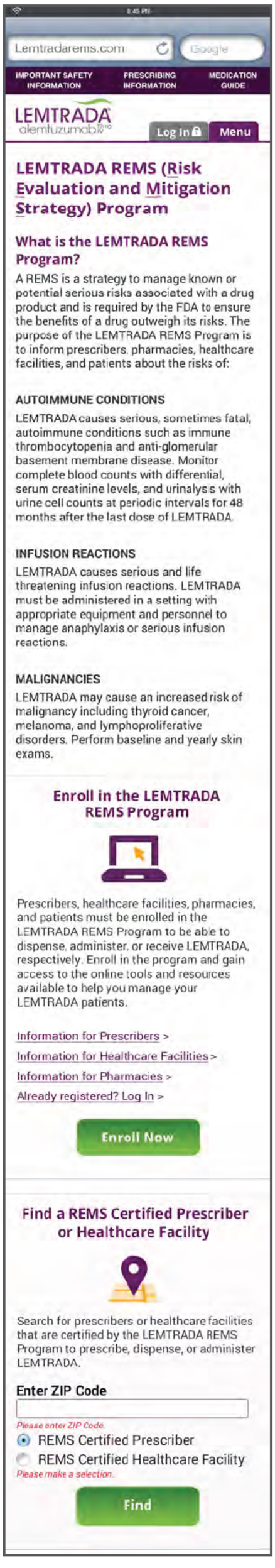


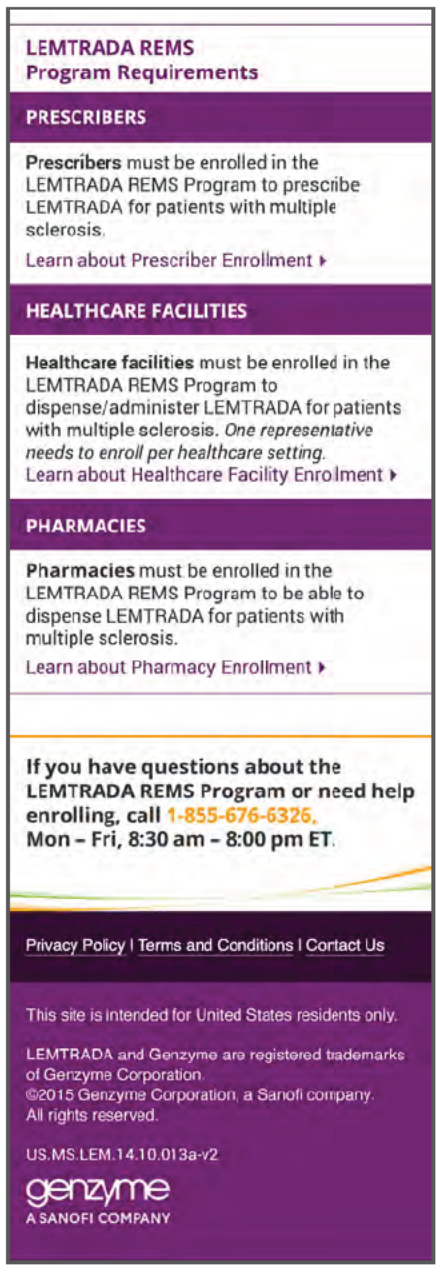
LEMTRADA REMS Mobile - Public Home, Dropdown Navigation



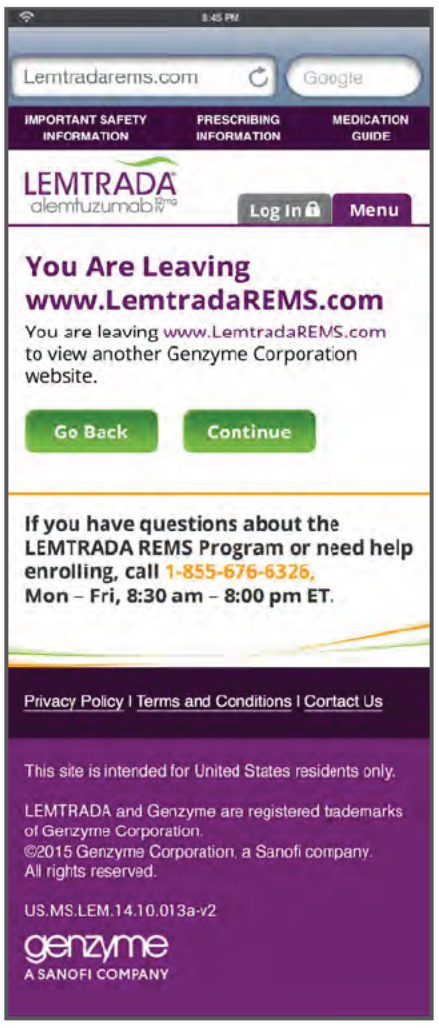


LEMTRADA REMS Mobile - Public Home, Locator Column Error

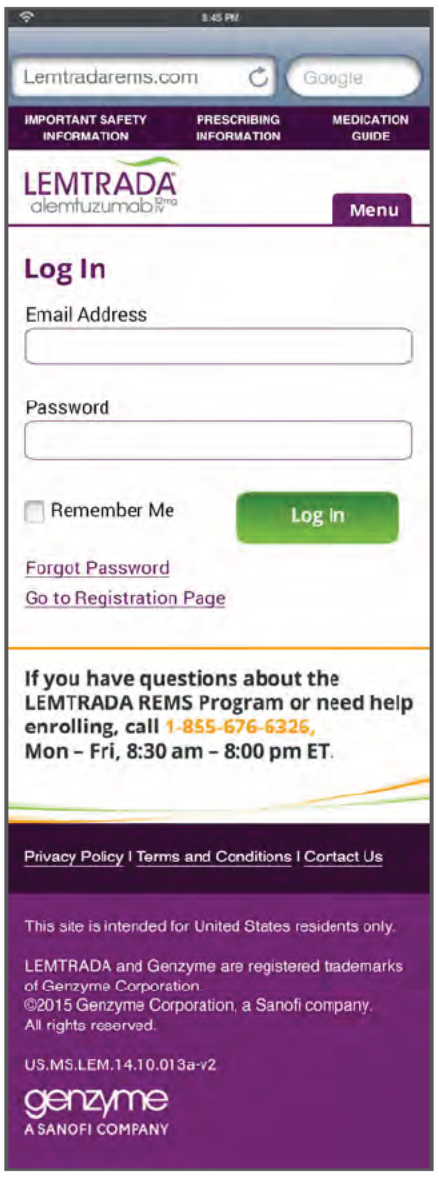




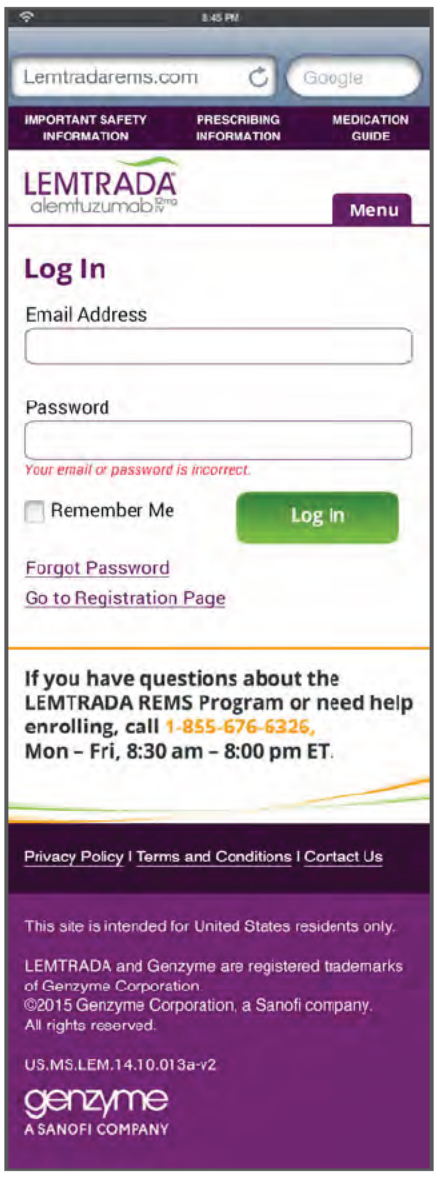
LEMTRADA REMS Mobile - Public Home, 3rd Party Interstitial Page



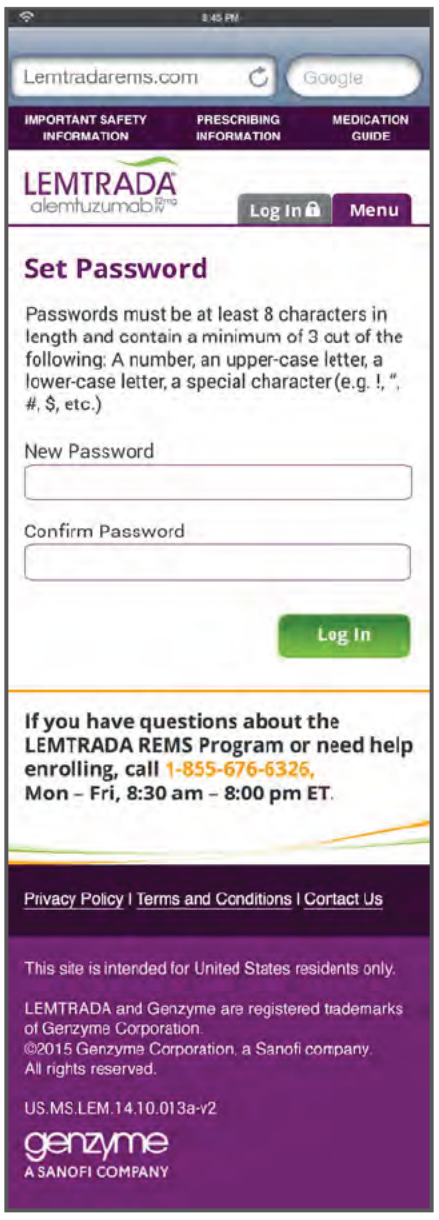
LEMTRADA REMS Mobile - Public Home, Log In



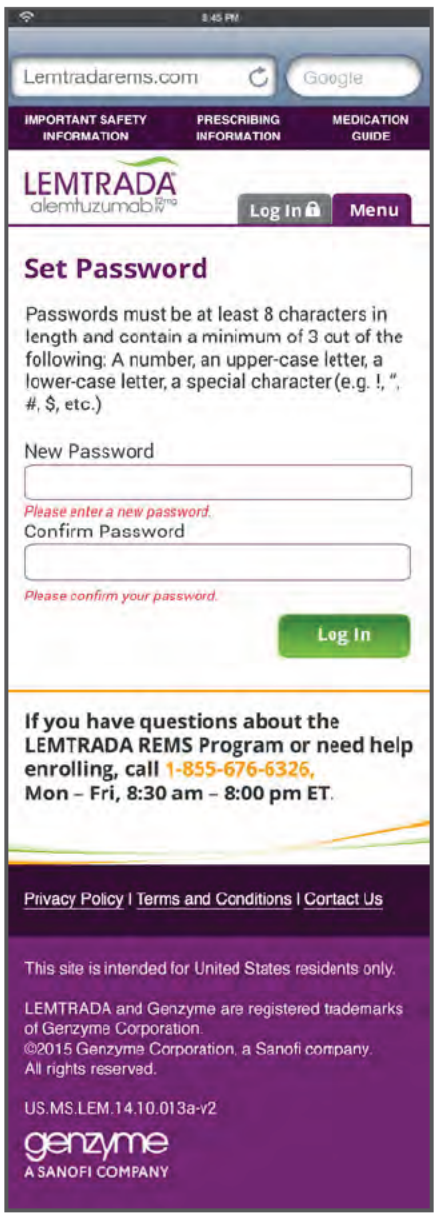
LEMTRADA REMS Mobile - Public Home, Log In, Error



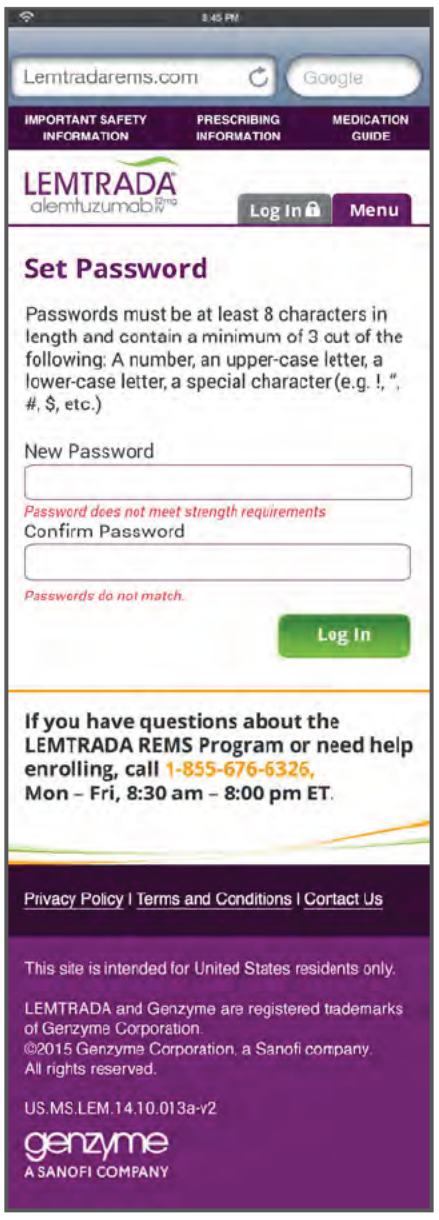
LEMTRADA REMS Mobile - Public Home, Set Password, Log In



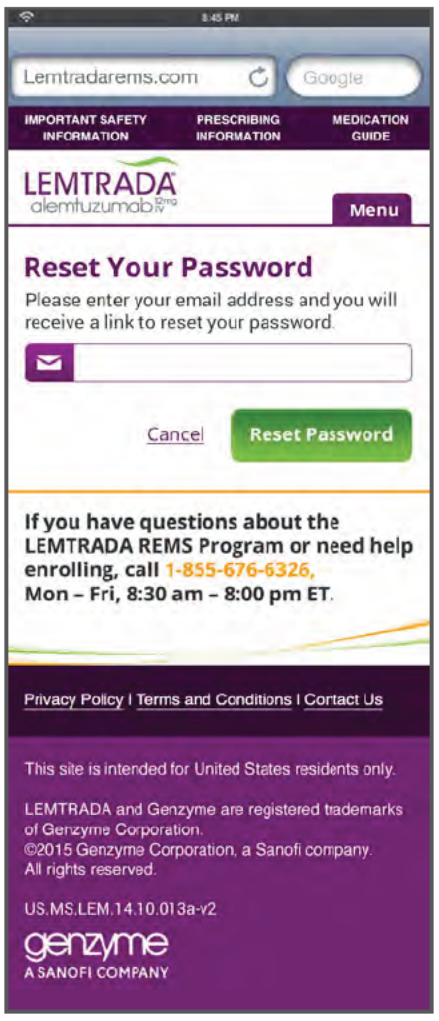
LEMTRADA REMS Mobile - Public Home, Set Password, Error



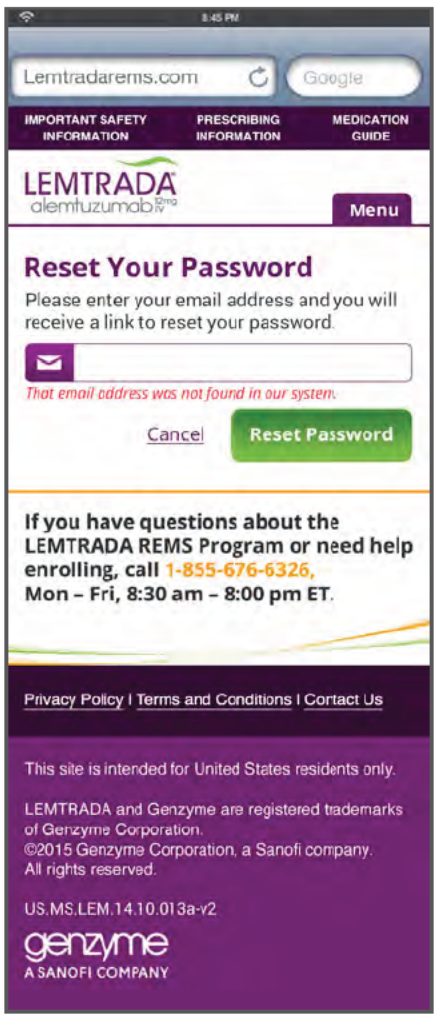
LEMTRADA REMS Mobile - Public Home, Set Password Log In, Password Error



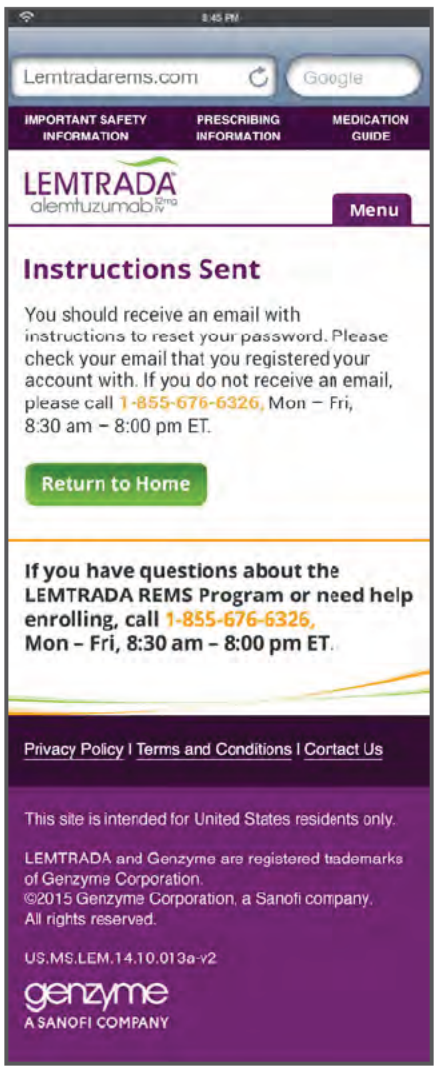
LEMTRADA REMS Mobile - Public Home, Reset Password



LEMTRADA REMS Mobile - Public Home, Reset Password, Error



LEMTRADA REMS Mobile - Public Home, Password Reset



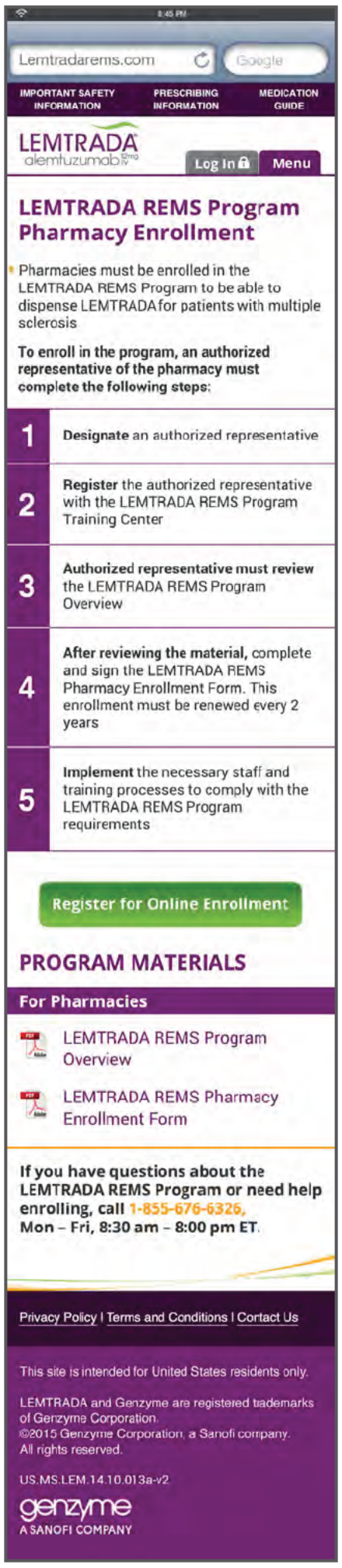
LEMTRADA REMS Mobile - Public Home, Prescriber Enrollment



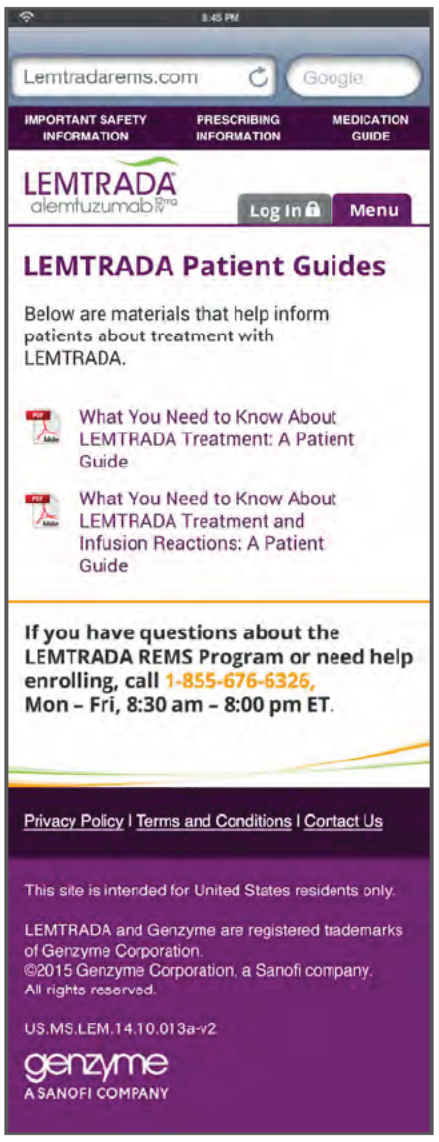
LEMTRADA REMS Mobile - Public Home, HCF Enrollment



LEMTRADA REMS Mobile - Public Home, Pharmacy Enrollment



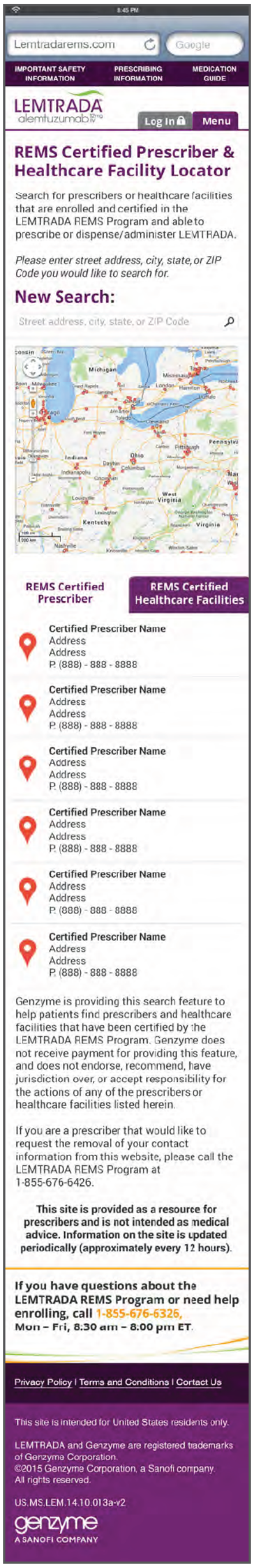
LEMTRADA REMS Mobile - Public Home, Patient Guides



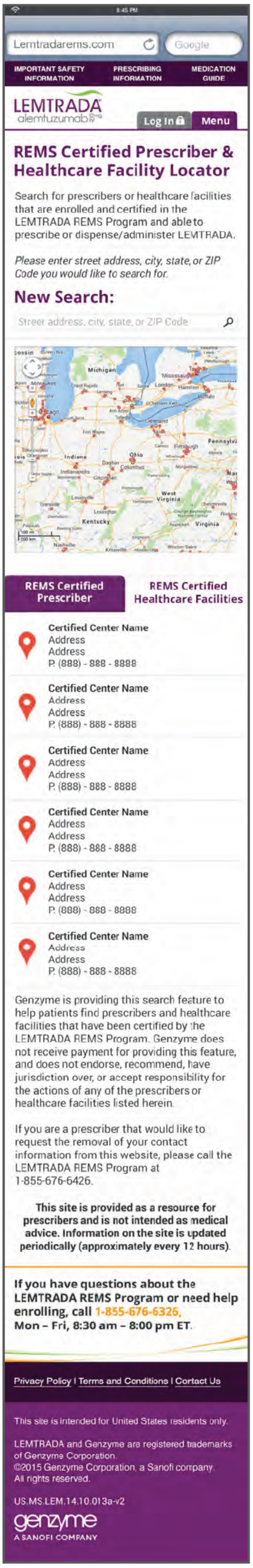
LEMTRADA REMS Mobile - Public Home, Forms and Resources



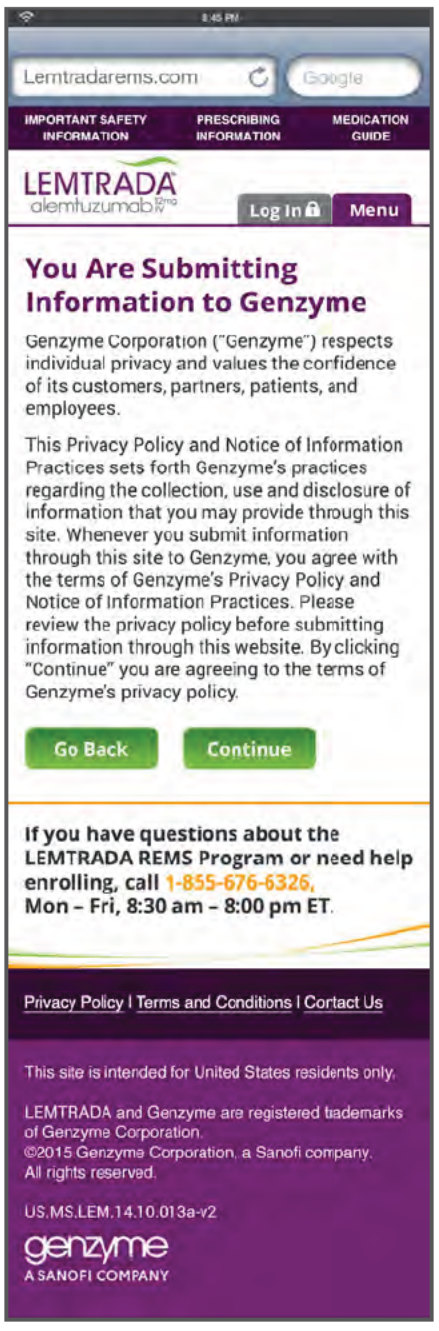
LEMTRADA REMS Mobile - Public / Prescriber Home, REMS Certified Prescriber and Healthcare Facility Locator



LEMTRADA REMS Mobile - Public / Prescriber Home, REMS Certified Prescriber and Healthcare Facility Locator



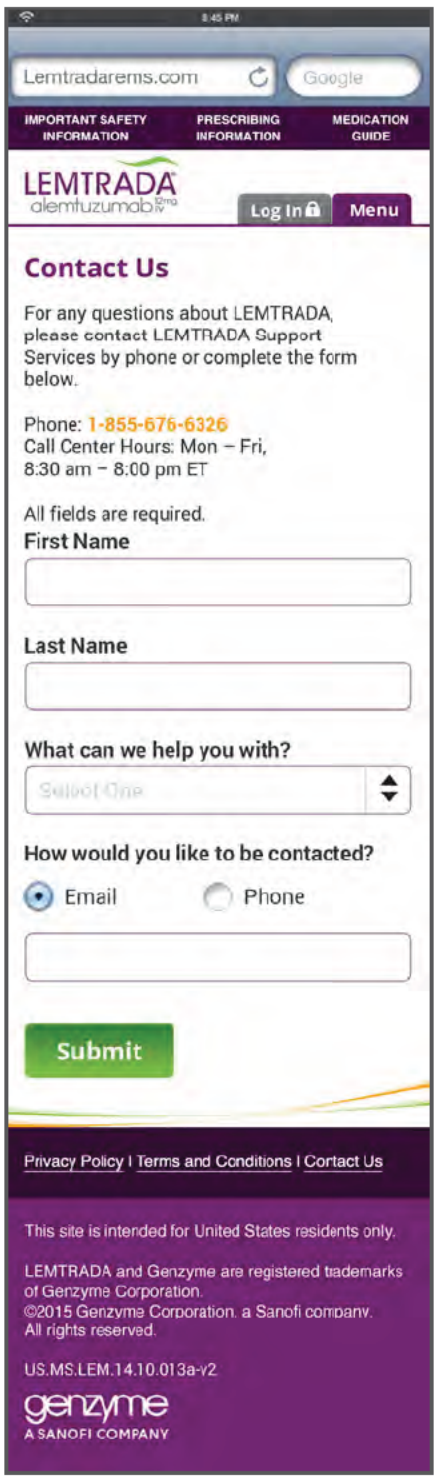
LEMTRADA REMS Mobile - Public Home, Contact Us Interstitial Page



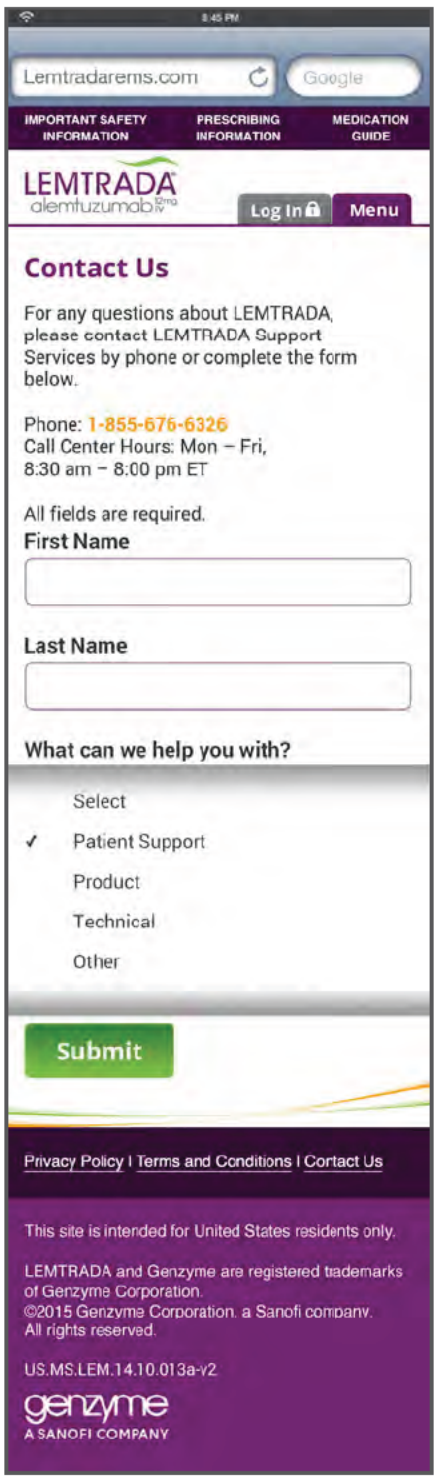
LEMTRADA REMS Mobile - Public Home, Contact Us



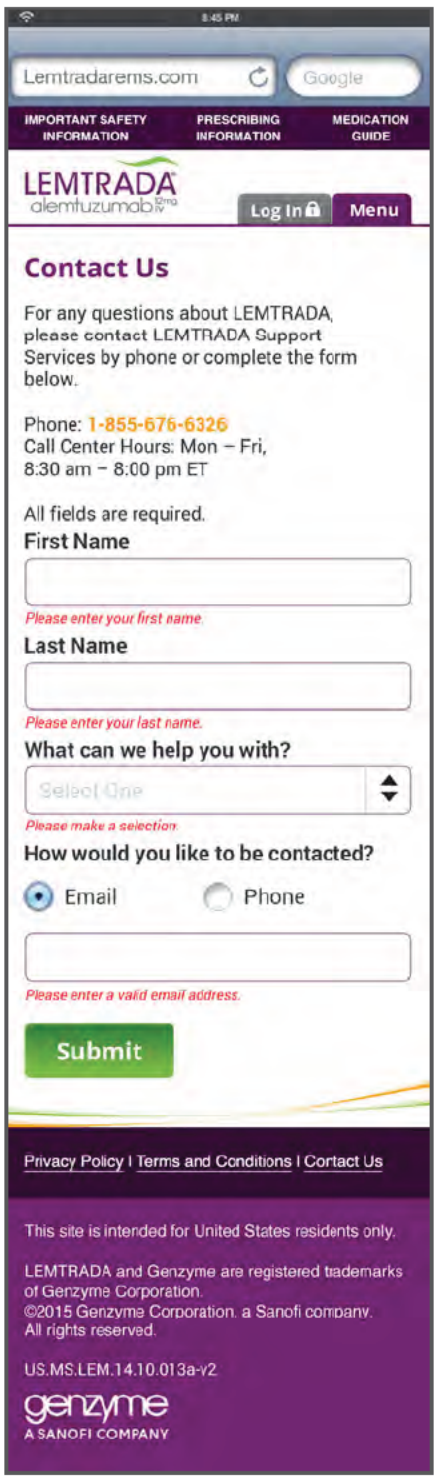
LEMTRADA REMS Mobile - Public Home, Contact Us, Email Selected



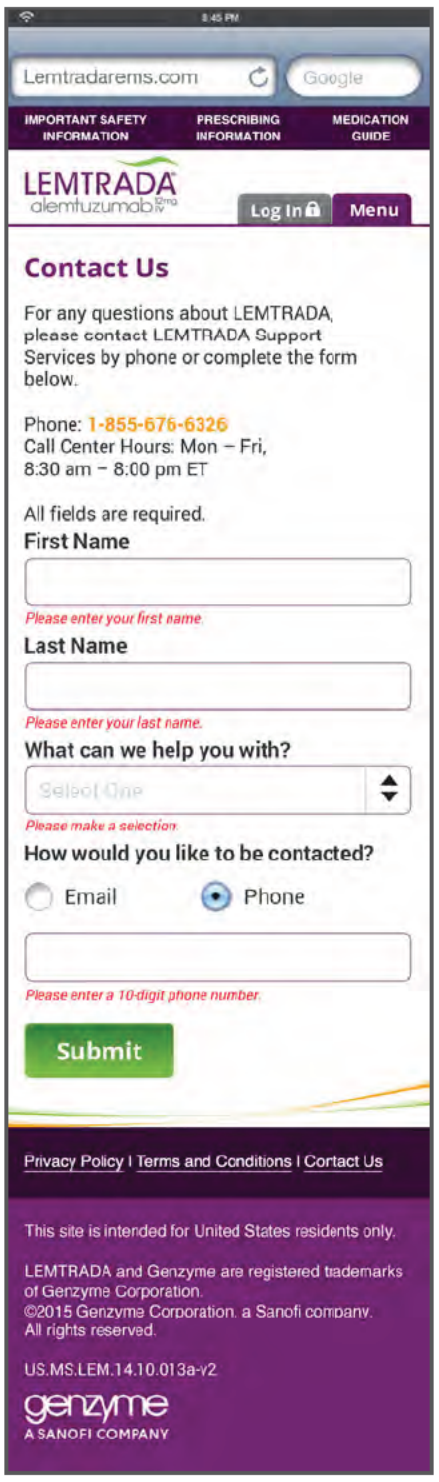
LEMTRADA REMS Mobile - Public Home, Contact Us, Dropdown



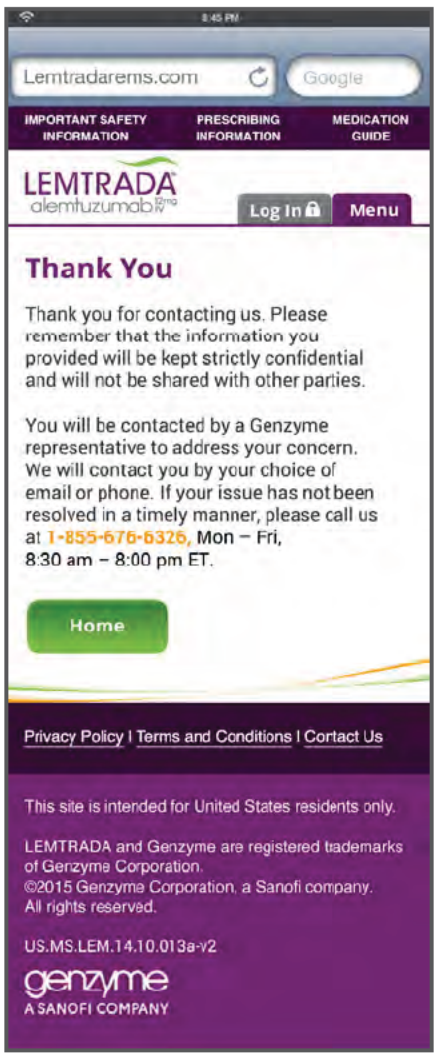
LEMTRADA REMS Mobile - Public Home, Contact Us, Email Error



LEMTRADA REMS Mobile - Public Home, Contact Us, Phone Error

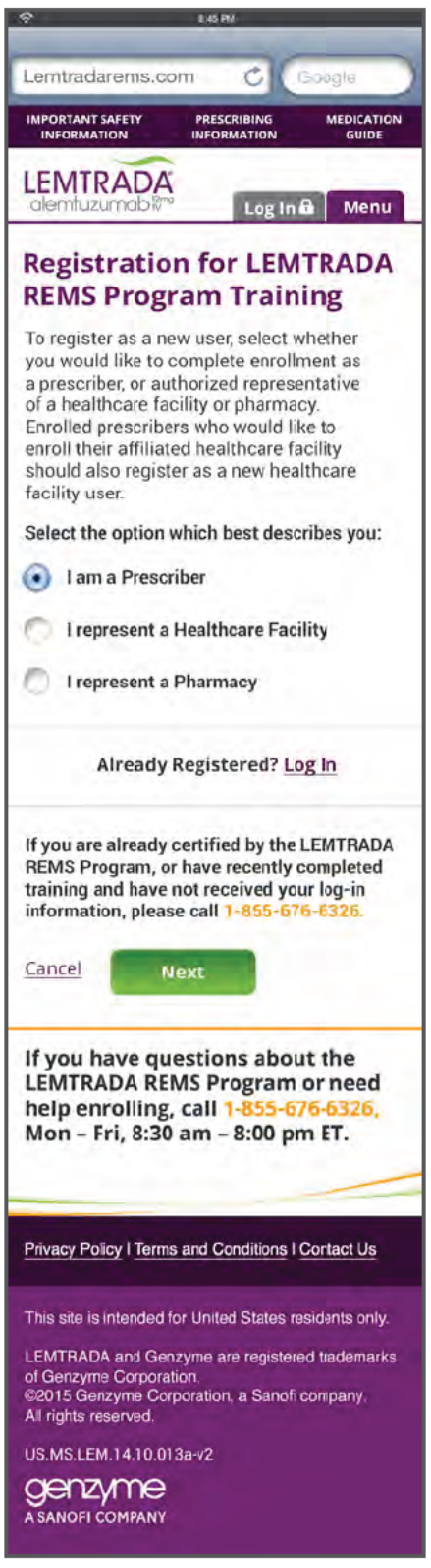


LEMTRADA REMS Mobile - Public Home, Contact Us, Confirmation

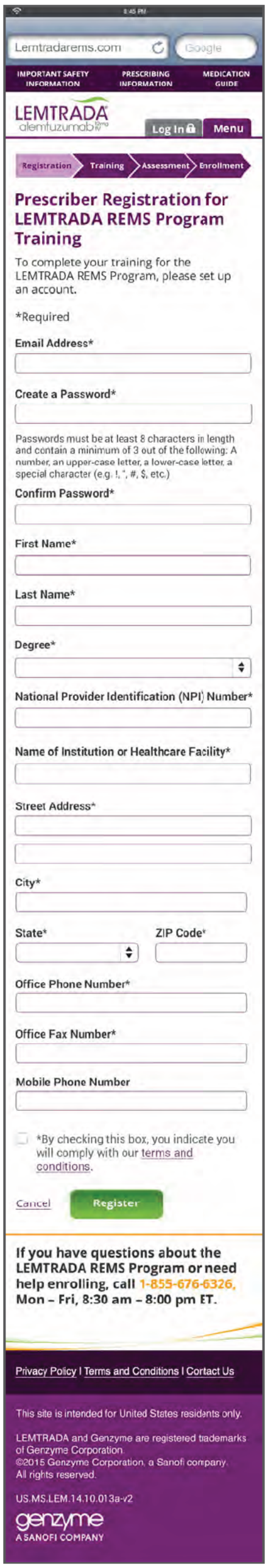


PRESCRIBER TRAINING PAGES

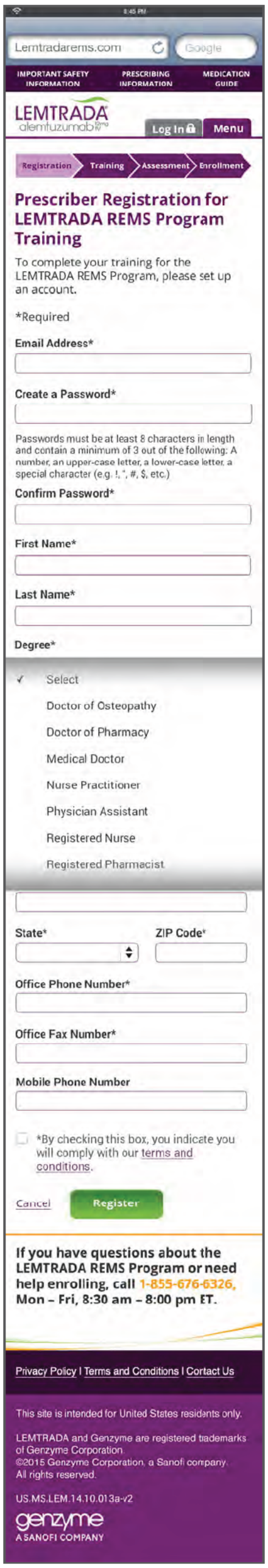
LEMTRADA REMS Mobile - Prescriber Training, Registration Home Selection



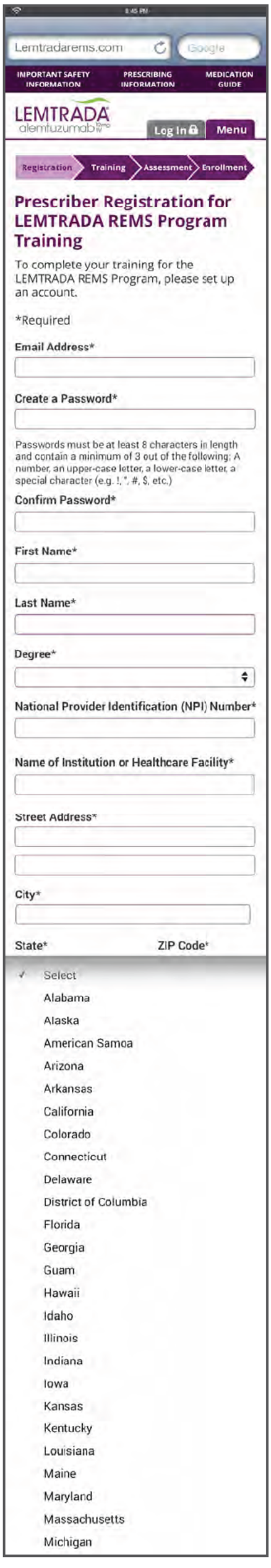
LEMTRADA REMS Mobile - Prescriber Training, Registration



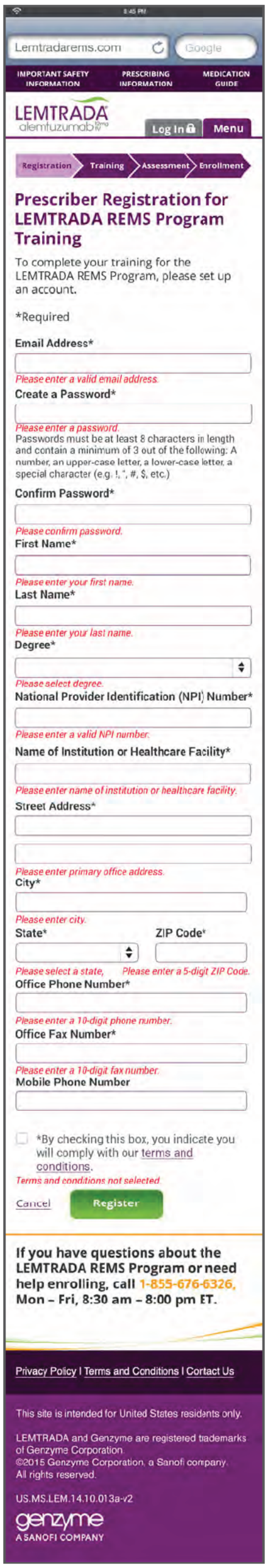
LEMTRADA REMS Mobile - Prescriber Training, Registration, Degree Selection



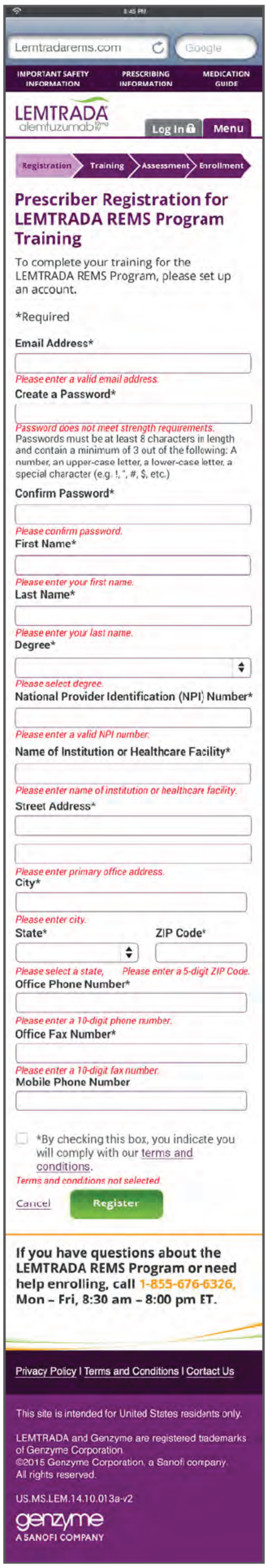
LEMTRADA REMS Mobile - Prescriber Training, Registration, State Selection



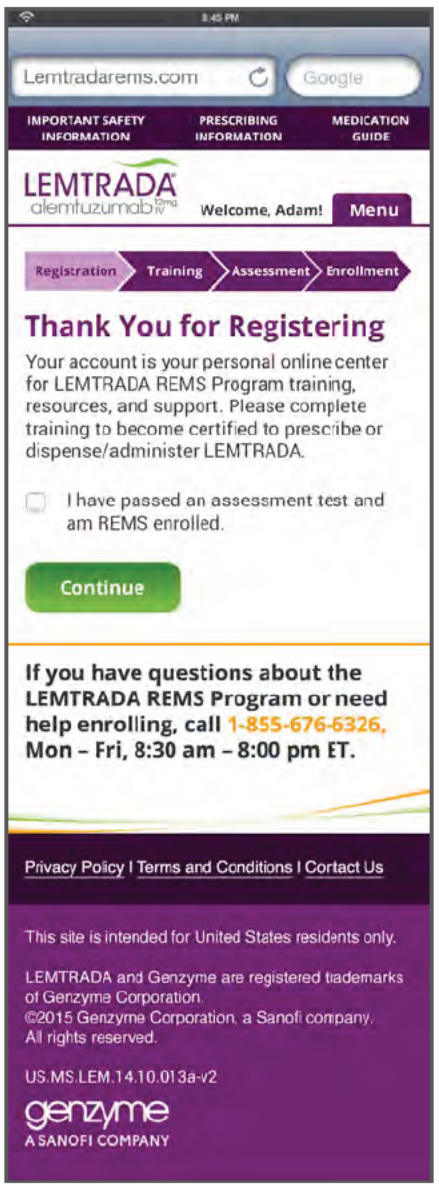
LEMTRADA REMS Mobile - Prescriber Training, Registration, Error



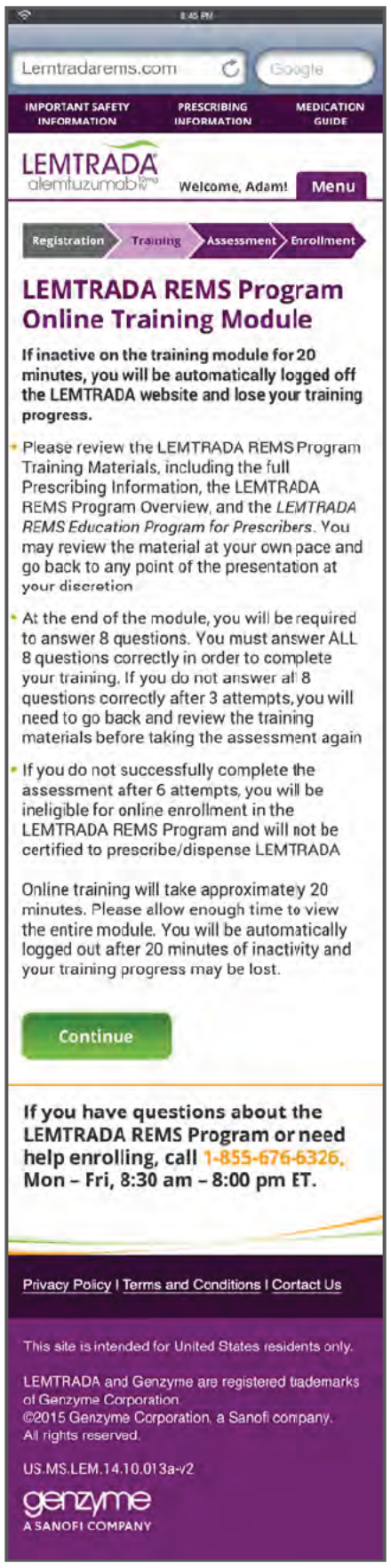
LEMTRADA REMS Mobile - Prescriber Training, Registration, Password Strength Error



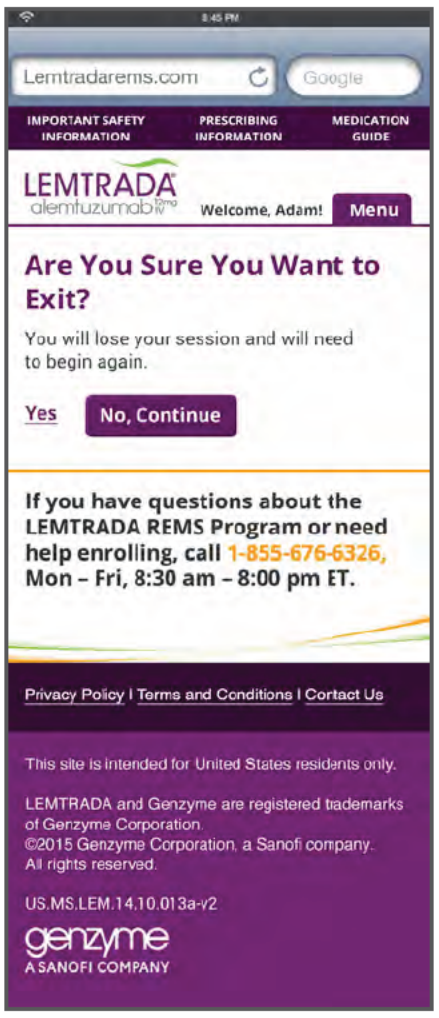
LEMTRADA REMS Mobile - Prescriber Training, Registration, Confirmation



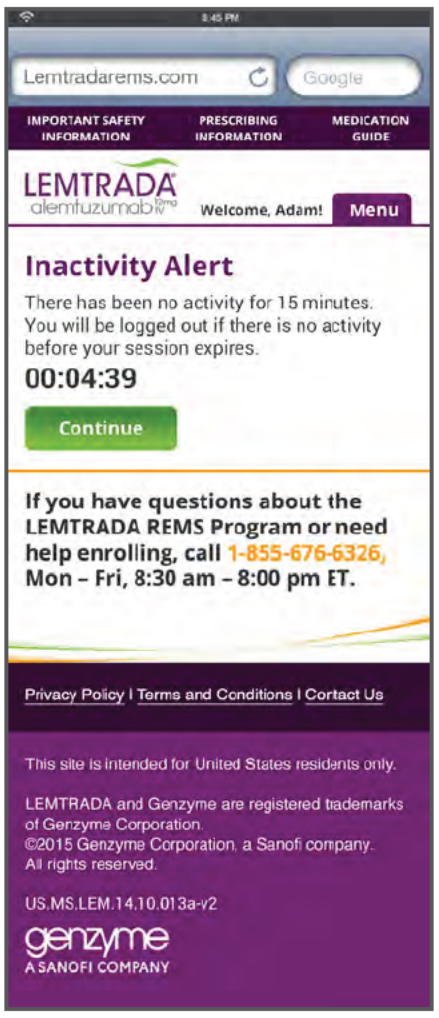
LEMTRADA REMS Mobile - Prescriber Training, Training Module



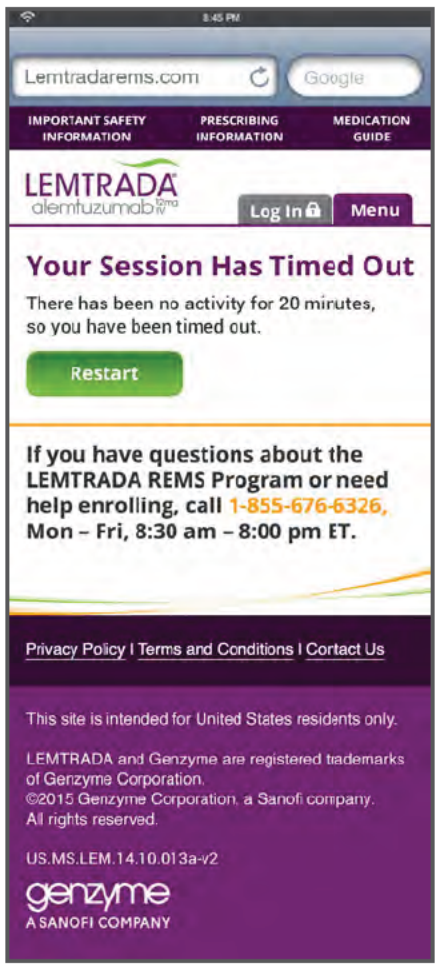
LEMTRADA REMS Mobile - Prescriber Training, Training Module, Exit



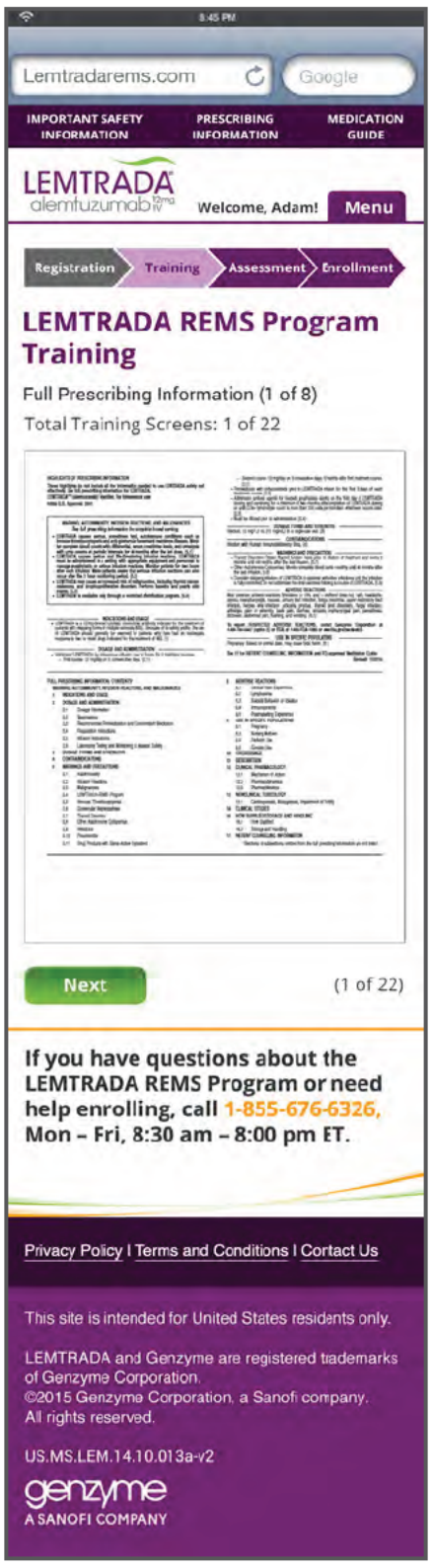
LEMTRADA REMS Mobile - Prescriber Training, Training Module, Timer



LEMTRADA REMS Mobile - Prescriber Training, Training Module, Timed Out



LEMTRADA REMS Mobile - Prescriber Training, PI Page 1



LEMTRADA REMS Mobile - Prescriber Training, PI Page 2



LEMTRADA REMS Mobile - Prescriber Training, PI Page 3



LEMTRADA REMS Mobile - Prescriber Training, PI Page 4



LEMTRADA REMS Mobile - Prescriber Training, PI Page 5



LEMTRADA REMS Mobile - Prescriber Training, PI Page 6



LEMTRADA REMS Mobile - Prescriber Training, PI Page 7



LEMTRADA REMS Mobile - Prescriber Training, PI Page 8



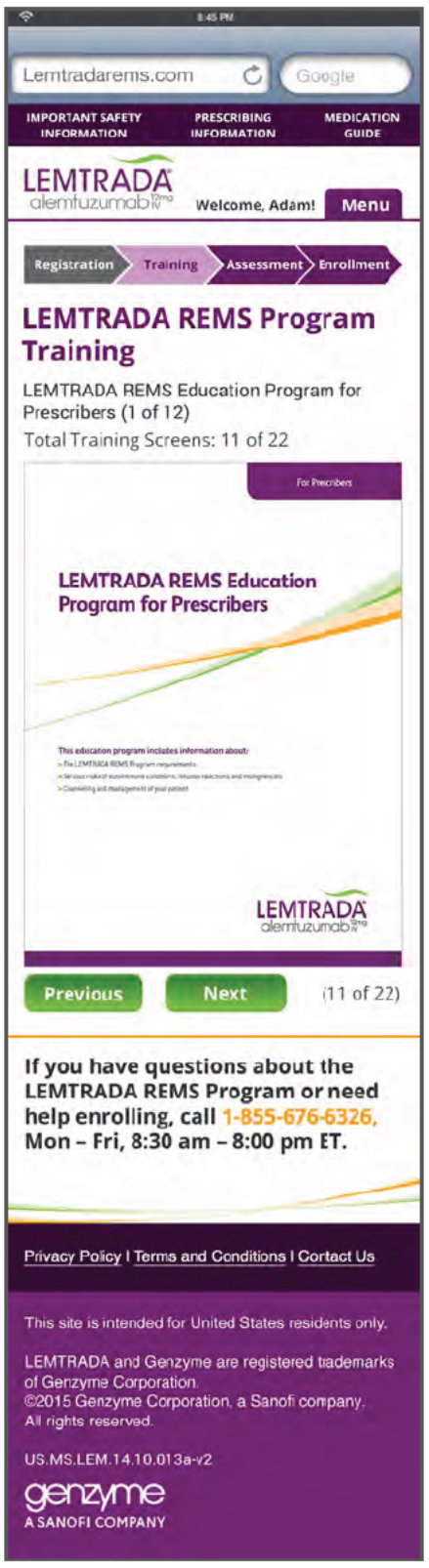
LEMTRADA REMS Mobile - Prescriber Training, Program Over Page 1



LEMTRADA REMS Mobile - Prescriber Training, Program Over Page 2



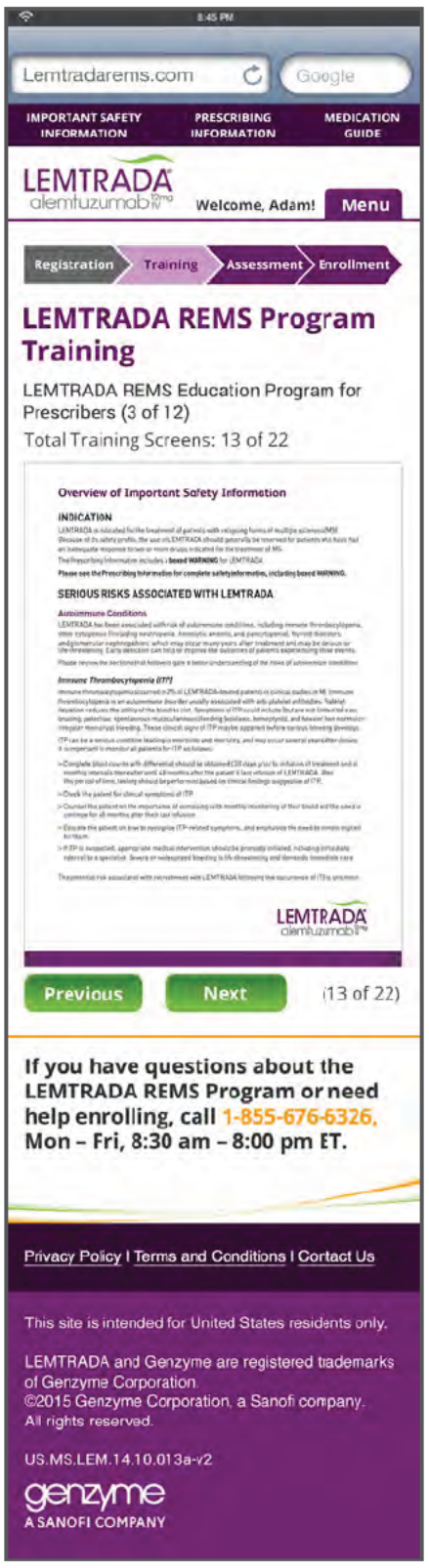
LEMTRADA REMS Mobile - Prescriber Training, Training Page 1



LEMTRADA REMS Mobile - Prescriber Training, Training Page 2



LEMTRADA REMS Mobile - Prescriber Training, Training Page 3



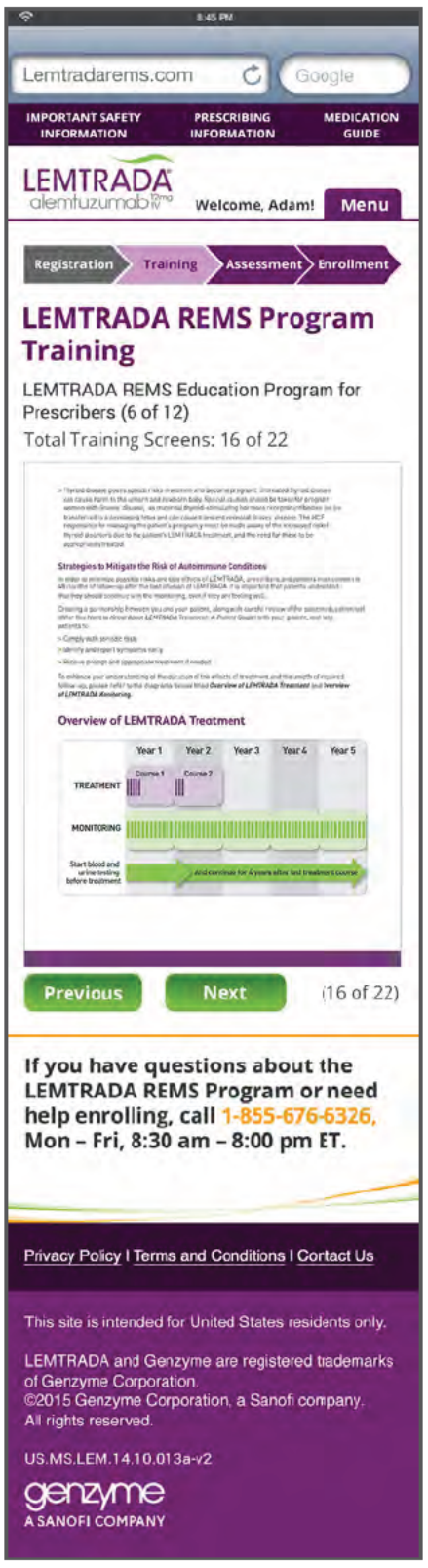
LEMTRADA REMS Mobile - Prescriber Training, Training Page 4



LEMTRADA REMS Mobile - Prescriber Training, Training Page 5



LEMTRADA REMS Mobile - Prescriber Training, Training Page 6



LEMTRADA REMS Mobile - Prescriber Training, Training Page 7



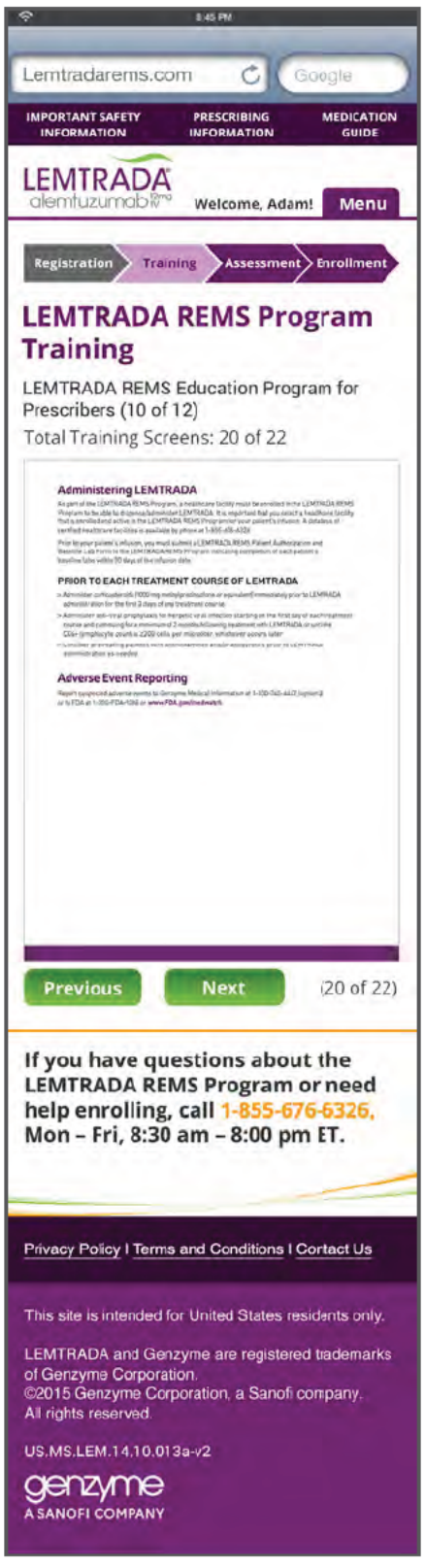
LEMTRADA REMS Mobile - Prescriber Training, Training Page 8



LEMTRADA REMS Mobile - Prescriber Training, Training Page 9



LEMTRADA REMS Mobile - Prescriber Training, Training Page 10

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PRESCRIBING INFORMATION
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alemtuzumab
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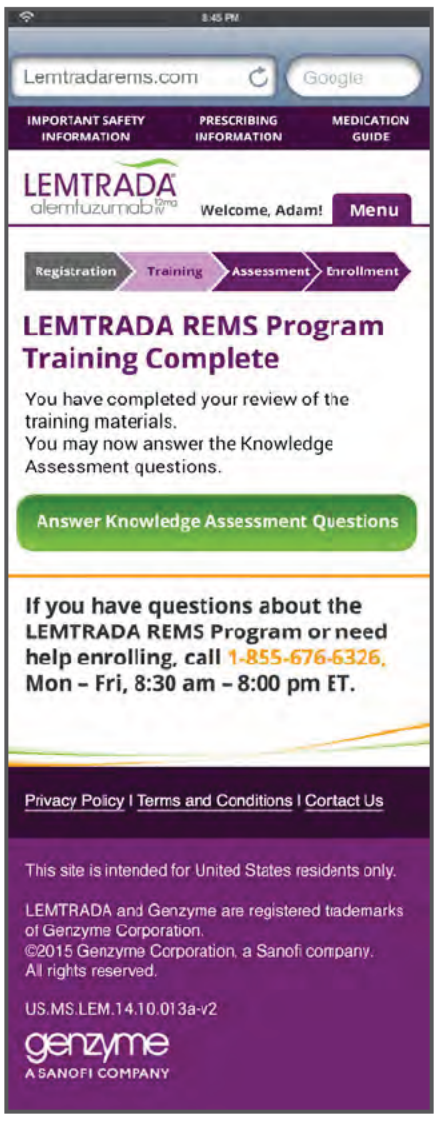
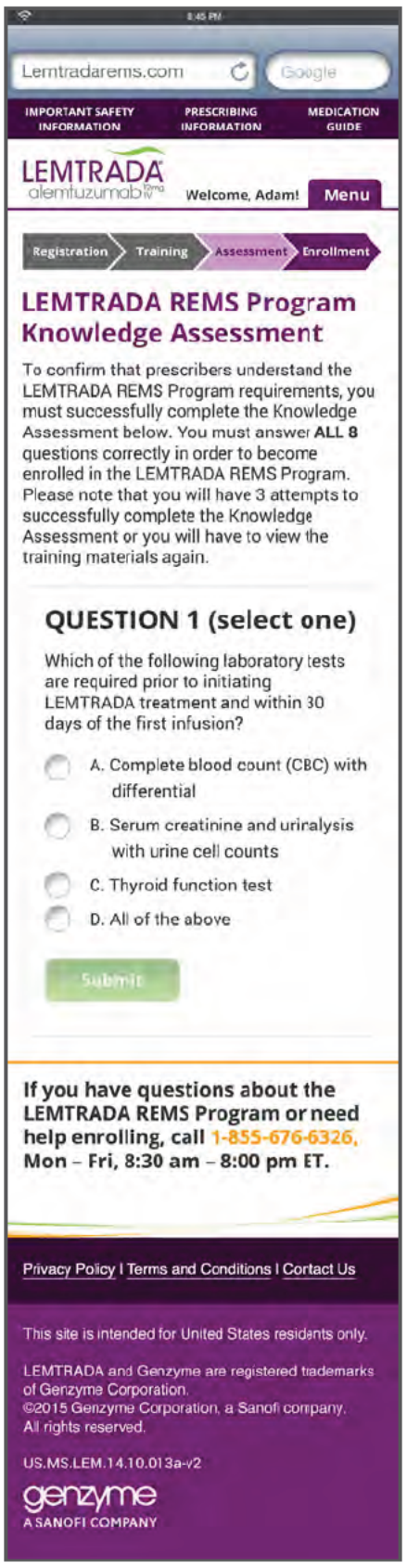
LEMTRADA REMS Mobile - Prescriber Training, Training Page 12



LEMTRADA REMS Mobile - Prescriber Training, Confirmation



LEMTRADA REMS Mobile - Prescriber Training, Assessment Question 1



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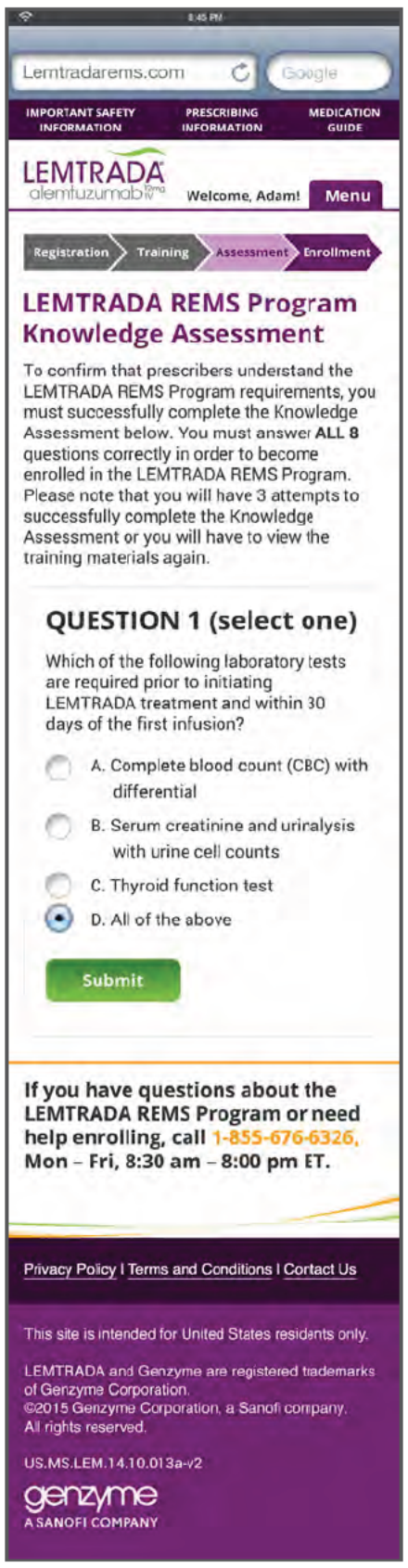

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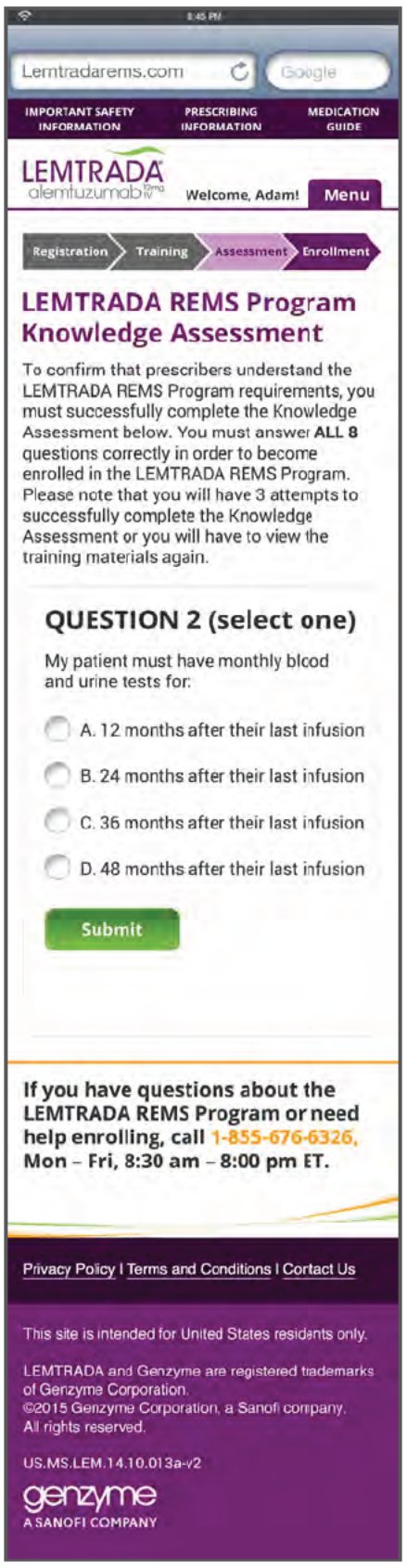

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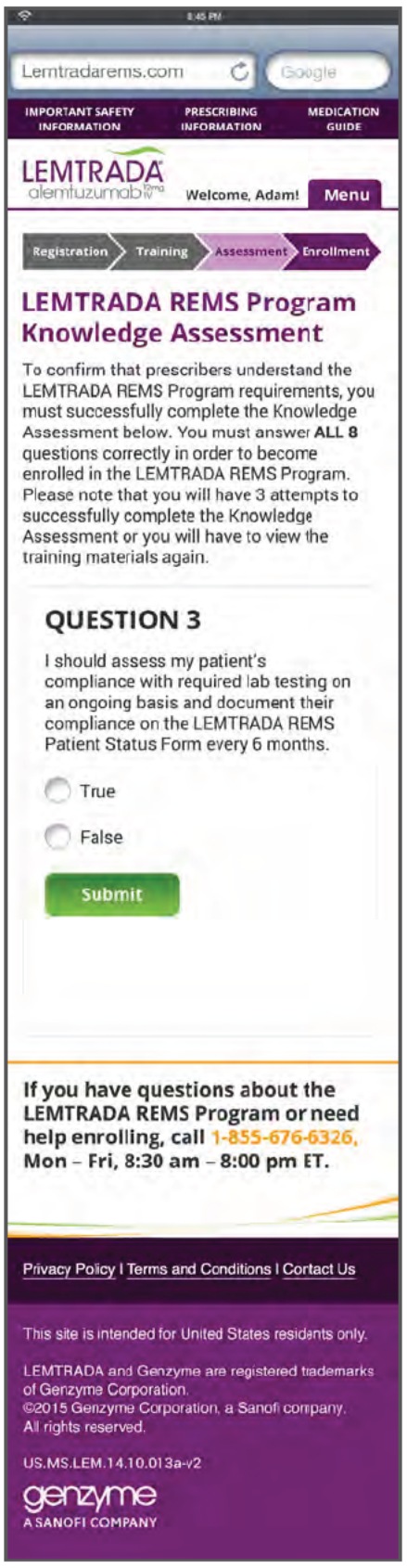

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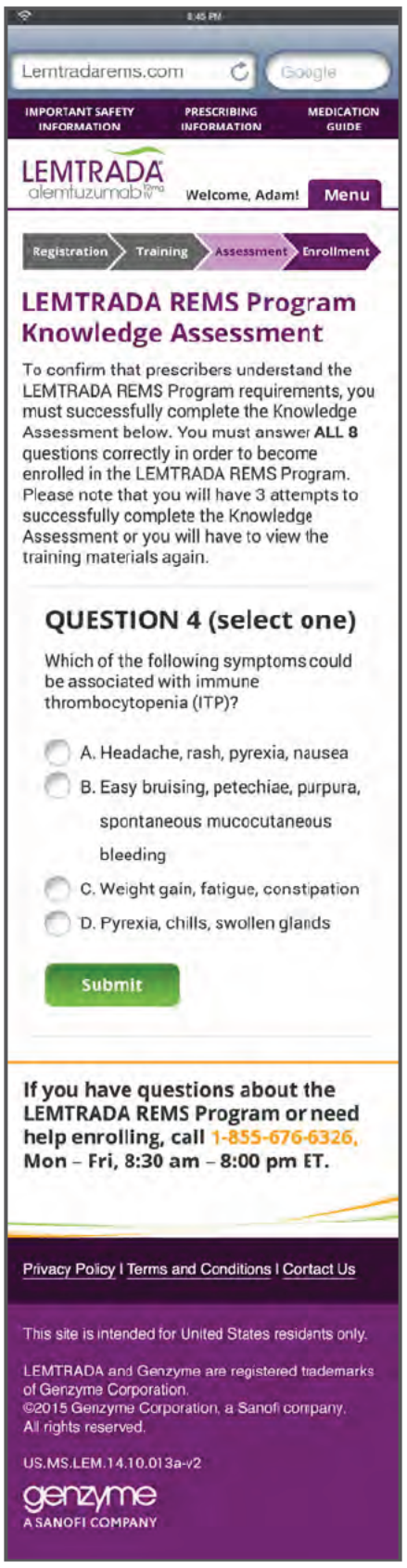

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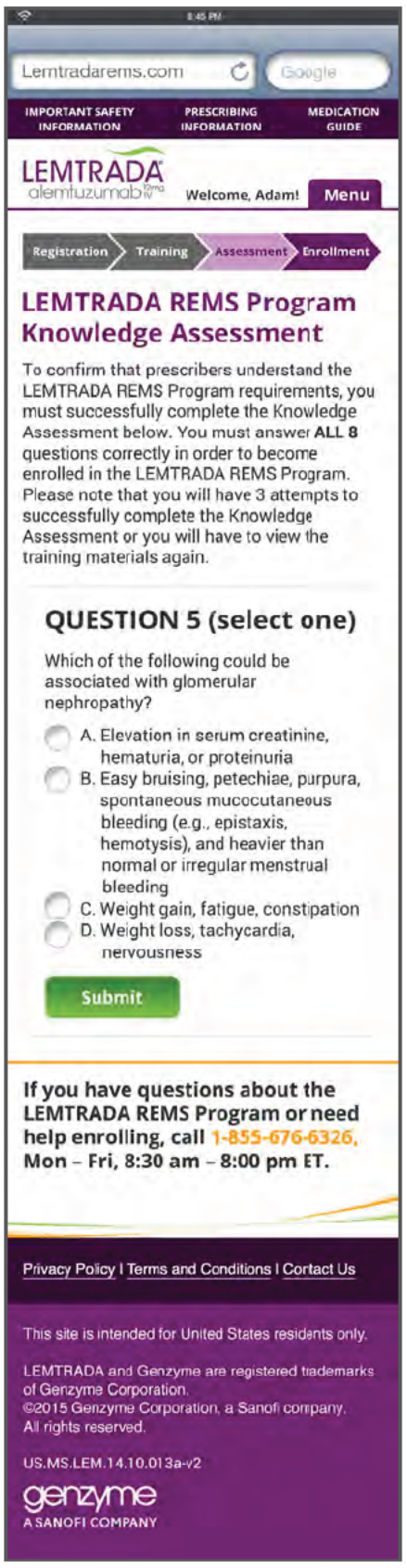

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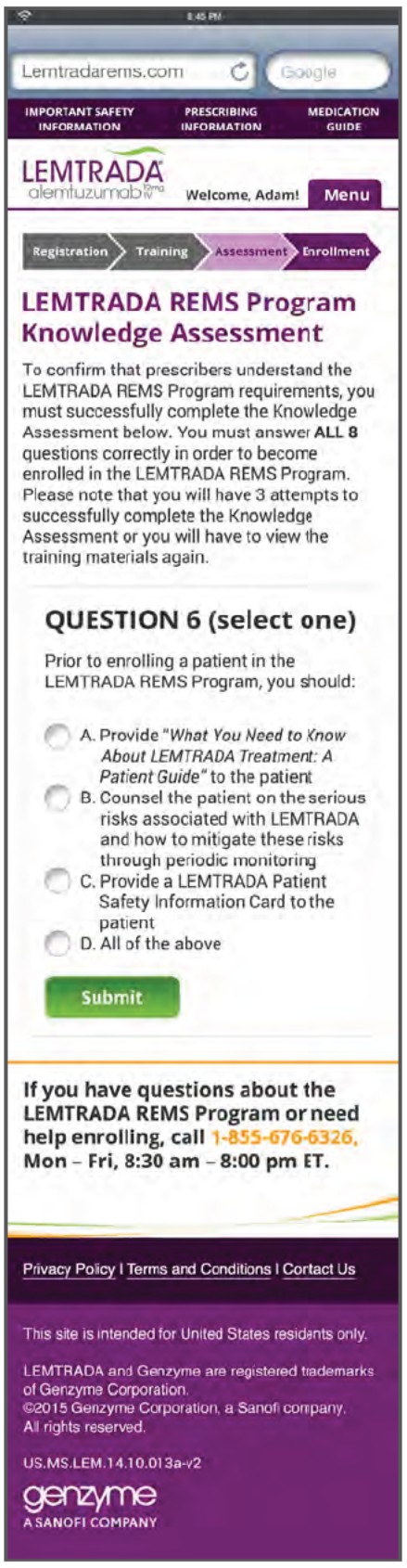

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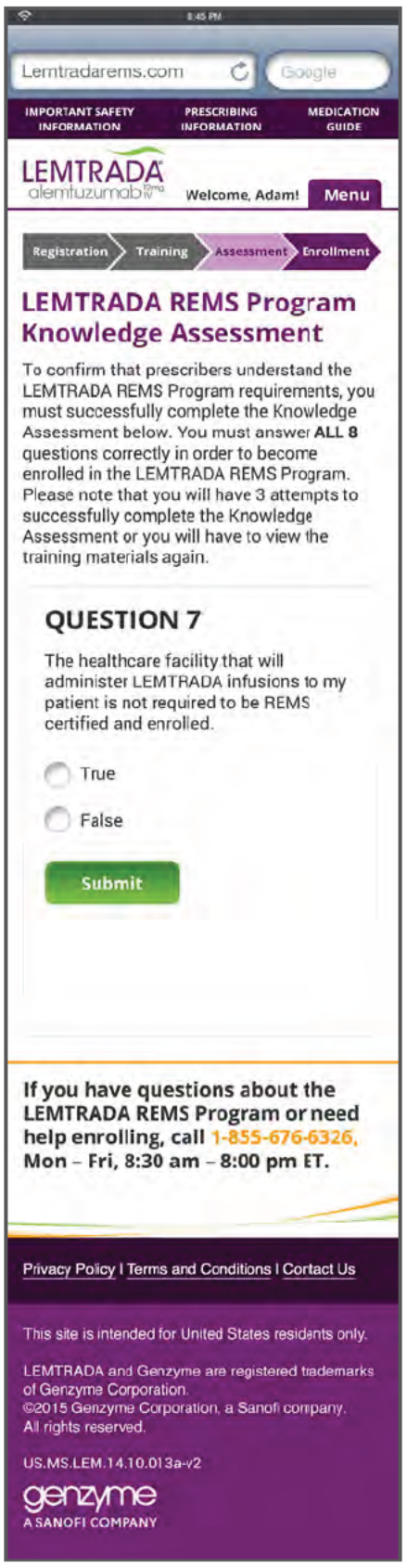
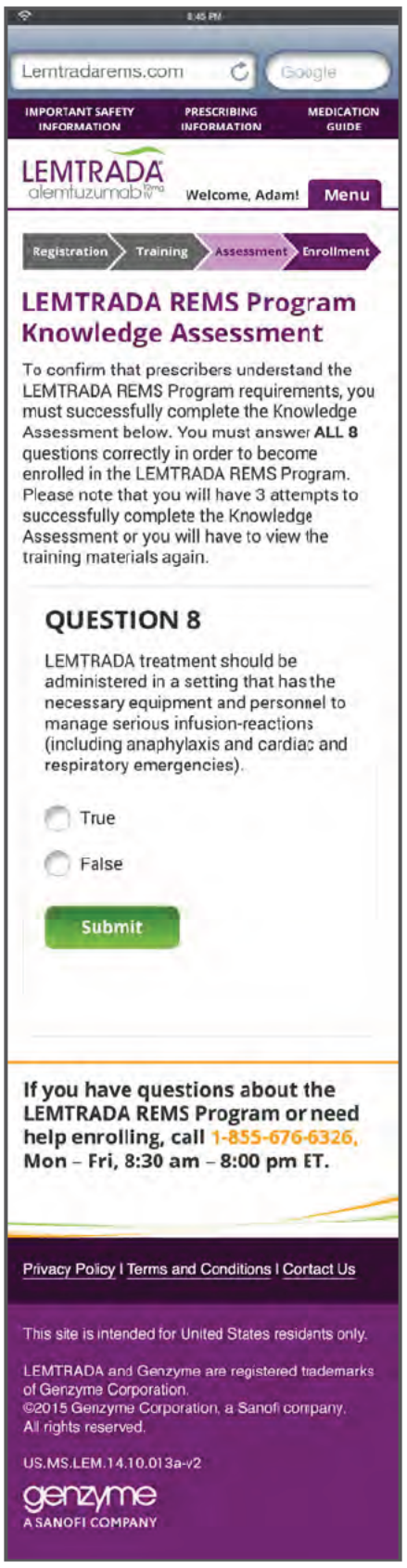
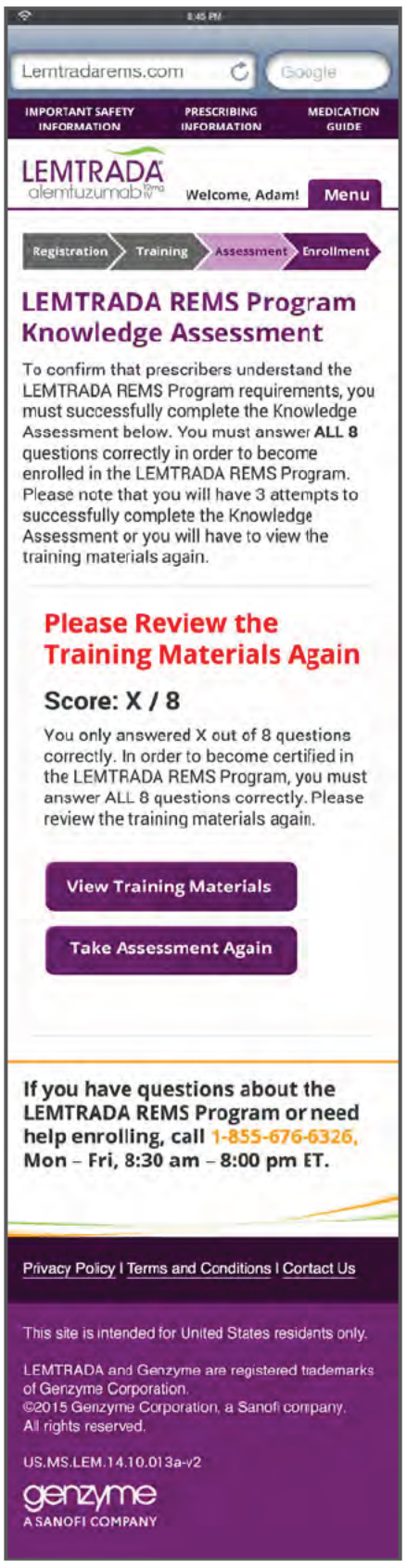


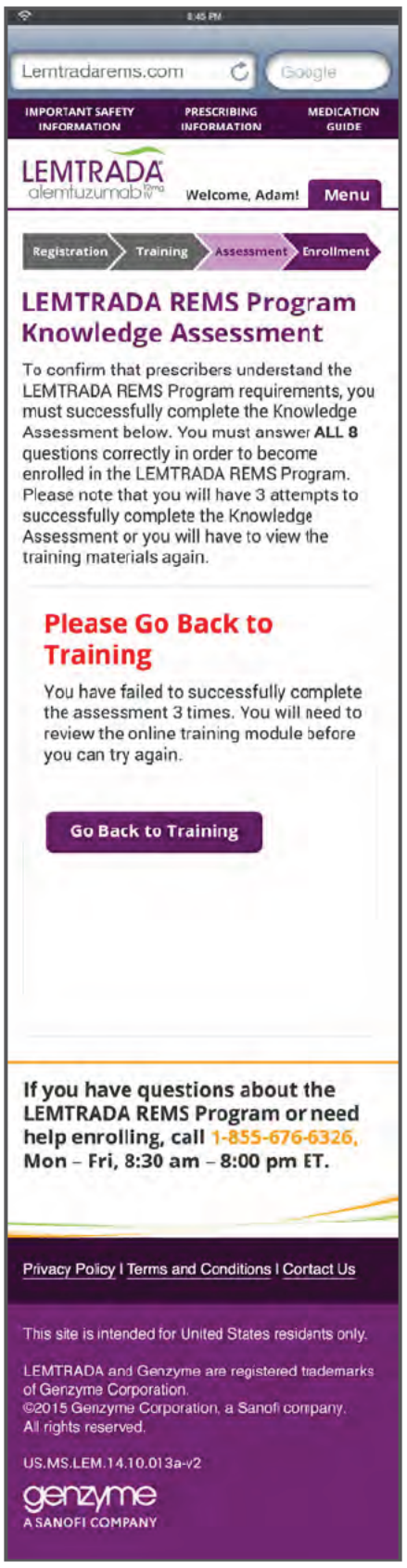
LEMTRADA REMS Mobile - Prescriber Training, Assessment Question 8



LEMTRADA REMS Mobile - Prescriber Training, Failed Assessment



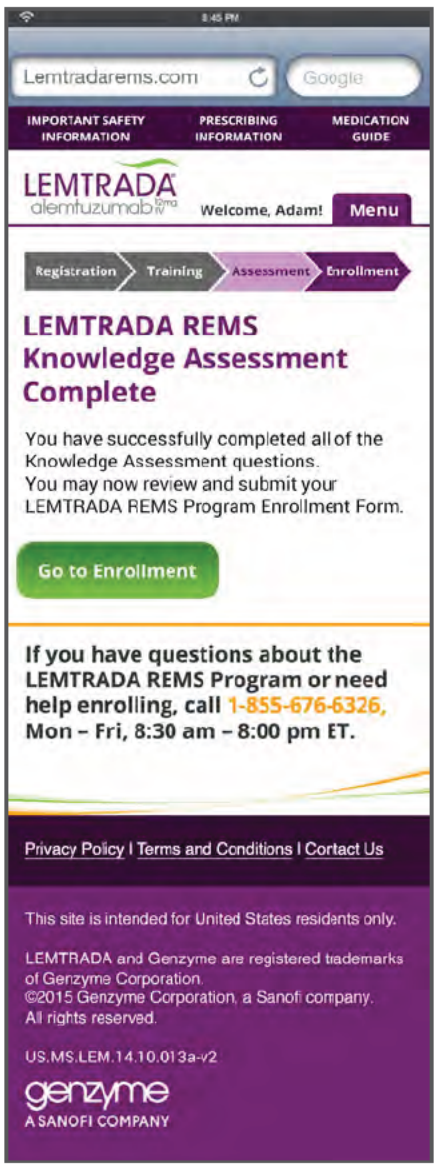
LEMTRADA REMS Mobile - Prescriber Training, Failed Assessment 3 Times



LEMTRADA REMS Mobile - Prescriber Training, Failed Assessment 6 Times



LEMTRADA REMS Mobile - Prescriber Training, Assessment Complete



LEMTRADA REMS Mobile - Prescriber Enrollment

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IMPORTANT SAFETY INFORMATION | PRESCRIBING INFORMATION | MEDICATION GUIDE

LEMTRADA alemtuzumab Welcome, Adam! Menu

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LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

LEMTRADA is available only through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. Please review the following information and submit to Genzyme using the button below. Complete any missing information and correct any errors prior to submission.

*Required

PRESCRIBER INFORMATION

First Name*: Adam

Last Name*: Smith

Degree*: Medical Doctor

Name of Institution or Healthcare Facility*: Massachusetts Institute

Street Address*: 72-04 Maple Lane

City*: Boston

State*: Massachusetts

ZIP Code*: 012314

Office Phone Number*: 555 555 5555

Fax Number*: 555 555 5555

Mobile Phone Number: 555 555 5555

Email Address*: asmith@abc123.com

National Provider Identification (NPI) Number*: 0123456789

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

PRESCRIBER AGREEMENT

By completing this form, I attest that:

- I understand that LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- I understand that LEMTRADA is only available through the LEMTRADA REMS Program and that I must comply with the program requirements in order to prescribe LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Prescribers*, including a review of the LEMTRADA Prescribing Information, and successfully completed the LEMTRADA REMS Knowledge Assessment.
- I understand that by completing the training program and signing this LEMTRADA REMS Prescriber Enrollment Form, I will be enrolled in the LEMTRADA REMS Program and can prescribe LEMTRADA.
- I understand that I am responsible for reviewing *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with each patient, and counseling each patient on an ongoing basis about the serious risks associated with the use of LEMTRADA and how to mitigate these risks through periodic monitoring.
- I understand that I must enroll all patients being treated with LEMTRADA into the LEMTRADA REMS Program prior to initiating the patient on treatment with LEMTRADA. I am responsible for completing a LEMTRADA REMS Patient Enrollment Form with the patient (or patient's legal representative), obtaining the patient's (or patient's legal representative's) signature on the form, and submitting the signed form to the LEMTRADA REMS Program. A completed copy should be provided to the patient and another copy should be stored in the patient's records.
- I will provide enrolled patients with a LEMTRADA Patient Safety Information Card and instruct patients to carry this card with them at all times in case of an emergency.
- I understand that I must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription. I understand that I am responsible for completing baseline lab monitoring within 30 days prior to infusion of LEMTRADA.
- I understand that I must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form indicating completion of each patient's baseline labs within 30 days prior to the patient's infusion date.
- I understand the risks of autoimmune conditions and malignancies associated with the use of LEMTRADA, and the need for periodic monitoring in order to identify and mitigate these risks:
  - Complete blood counts with differential obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Serum creatinine levels obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Urinalysis with urine cell counts obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Thyroid function tests, such as thyroid stimulating hormone (TSH) level obtained within 30 days prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion.
  - Baseline and yearly skin examinations.
- I will report any adverse events of autoimmune conditions, infusion reactions, or malignancies to Genzyme.
- I will complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

I understand that the LEMTRADA REMS Program will publish my name, business address and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-855-676-6326.

☐ Yes ☐ No

☐ I have verified that all details are correct.

By providing my e-signature, I attest that I have completed the educational training about LEMTRADA for prescribers and that I understand the benefits and risks of LEMTRADA. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name*:

NPI Number*:

Password*:

Cancel | Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-5326, Mon – Fri, 8:30 am – 8:00 pm ET.

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LEMTRADA REMS Mobile - Prescriber Enrollment, Degree Selection

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LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

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*Required

PRESCRIBER INFORMATION

First Name*: Adam

Last Name*: Smith

Degree*:
- Select
- Doctor of Osteopathy
- Doctor of Pharmacy
- Medical Doctor
- Nurse Practitioner
- Physician Assistant
- Registered Nurse
- Registered Pharmacist

Massachusetts

ZIP Code*: 012314

Office Phone Number*: 555 555 5555

Fax Number*: 555 555 5555

Mobile Phone Number: 555 555 5555

Email Address*: asmith@abc123.com

National Provider Identification (NPI) Number*: 0123456789

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PRESCRIBER AGREEMENT

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- I will complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

I understand that the LEMTRADA REMS Program will publish my name, business address and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-855-676-6326.

☐ Yes ☐ No

☐ I have verified that all details are correct.

By providing my e-signature, I attest that I have completed the educational training about LEMTRADA for prescribers and that I understand the benefits and risks of LEMTRADA. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name*:

NPI Number*:

Password*:

Cancel | Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-5326, Mon – Fri, 8:30 am – 8:00 pm ET.

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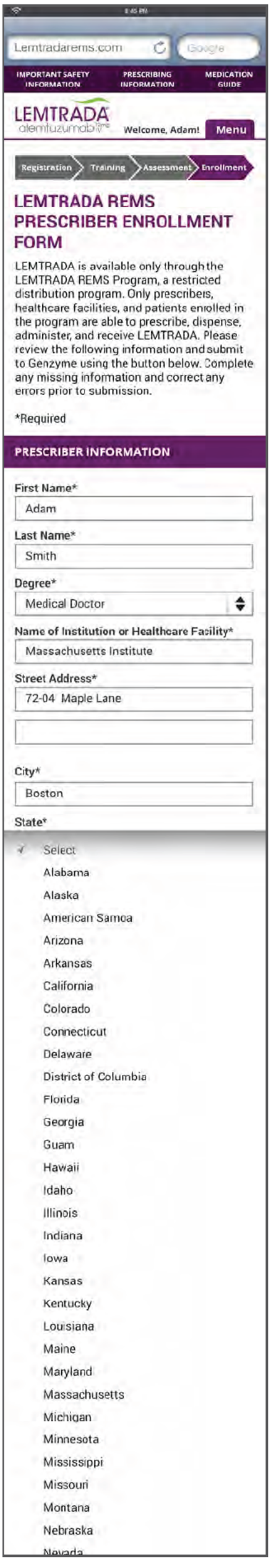

LEMTRADA REMS Mobile - Prescriber Enrollment, Error

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IMPORTANT SAFETY INFORMATION | PRESCRIBING INFORMATION | MEDICATION GUIDE

LEMTRADA alemtuzumab

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LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

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*Required

PRESCRIBER INFORMATION

First Name*
Please enter your first name.
Last Name*
Please enter your last name.
Degree*
Please select degree.
Name of Institution or Healthcare Facility*
Please enter name of institution or healthcare facility.
Street Address*
Please enter your street address.
City*
Please enter city.
State*
Please select a state.
ZIP Code*
Please enter a 5-digit ZIP Code.
Office Phone Number*
Please enter a 10-digit phone number.
Fax Number*
Please enter a 10-digit fax number.
Mobile Phone Number
Email Address*
Please enter a valid email address.
National Provider Identification (NPI) Number*
Please enter a valid NPI number.

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

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I understand that the LEMTRADA REMS Program will publish my name, business address and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-855-676-6326.

Yes No *Please make a selection.*

I have verified that all details are correct.
Please indicate information has been verified.

By providing my e-signature, I attest that I have completed the educational training about LEMTRADA for prescribers and that I understand the benefits and risks of LEMTRADA. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name*
Please enter your full name.
NPI Number*
Please enter a valid NPI number.
Password*
Please enter a valid password.

Cancel Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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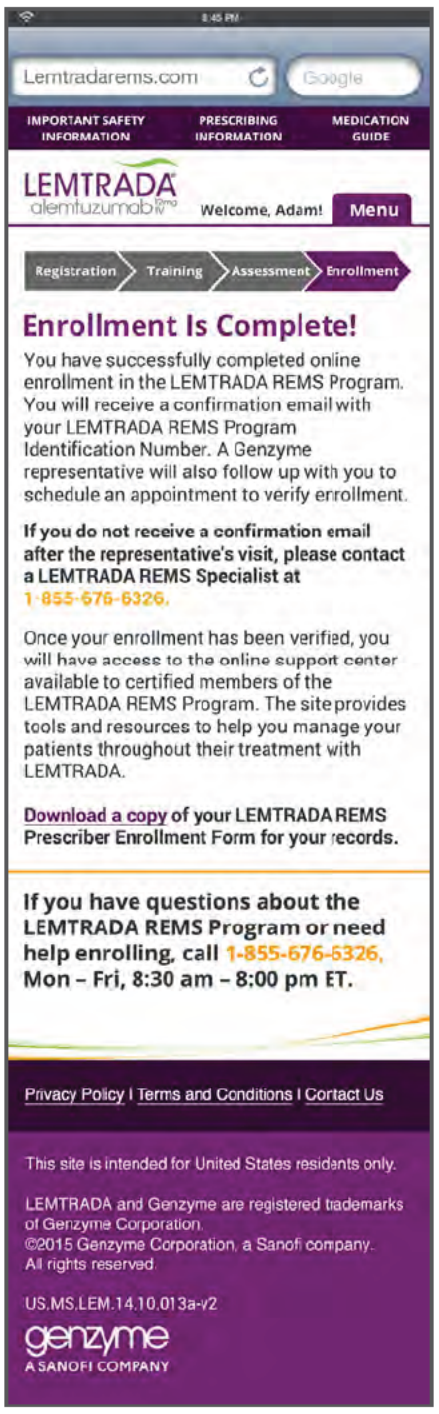
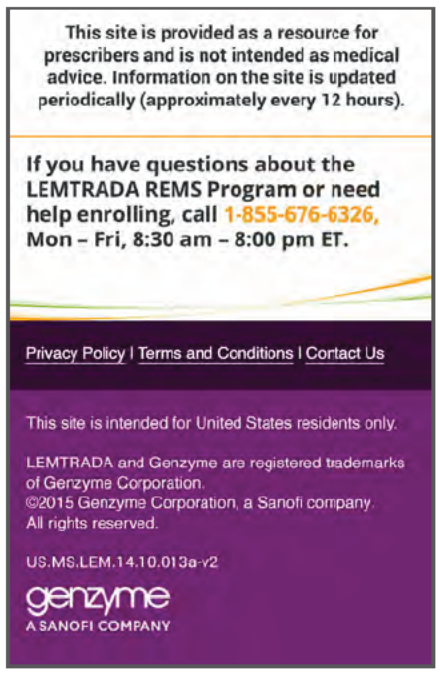
LEMTRADA REMS Mobile - Prescriber Enrollment, Confirmation

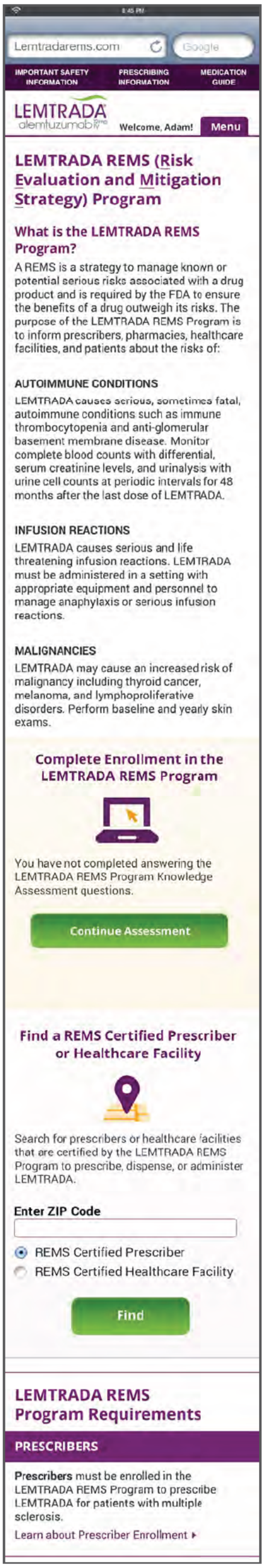


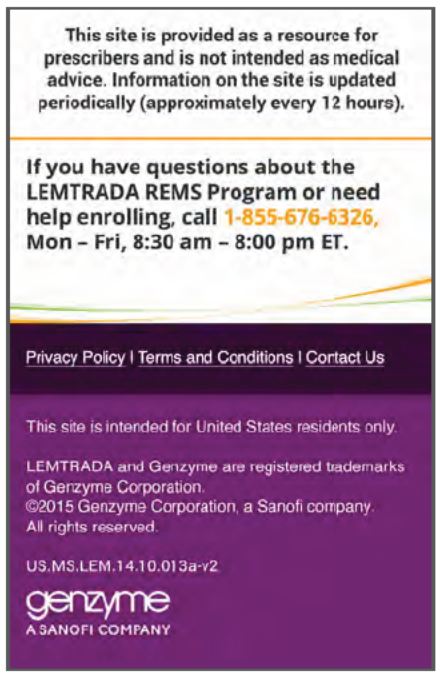
LEMTRADA REMS Mobile - Pre-REMS Certification, Prescriber Training Incomplete





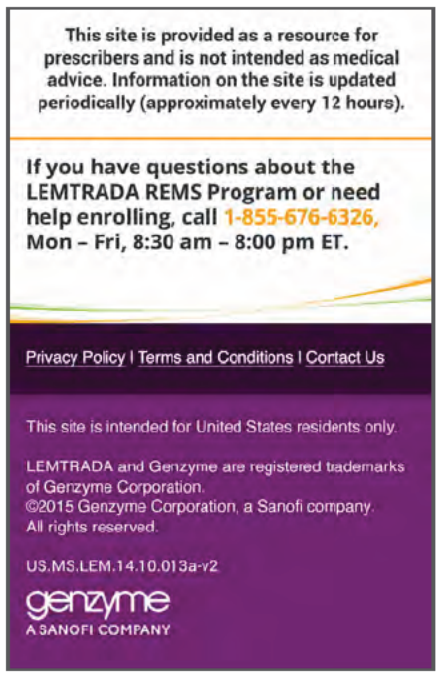
LEMTRADA REMS Mobile - Pre-REMS Certification, Prescriber Assessment Incomplete





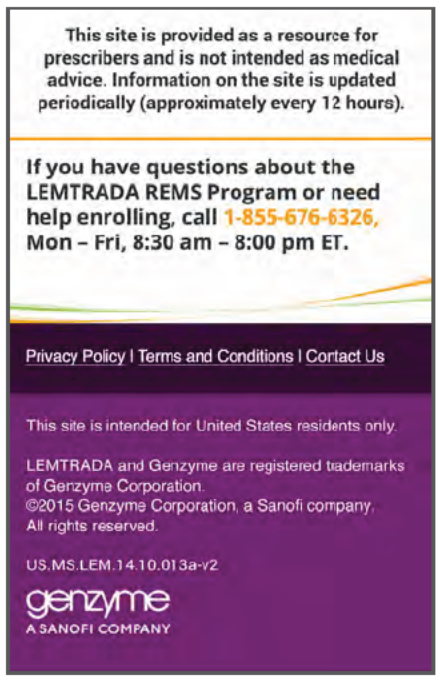
LEMTRADA REMS Mobile - Pre-REMS Certification, Prescriber Training Invalid





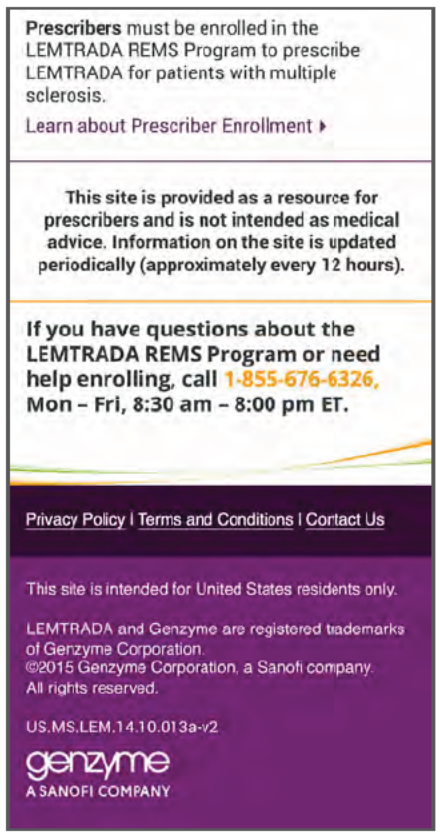
LEMTRADA REMS Mobile - Pre-REMS Certification, Prescriber Enrollment Incomplete





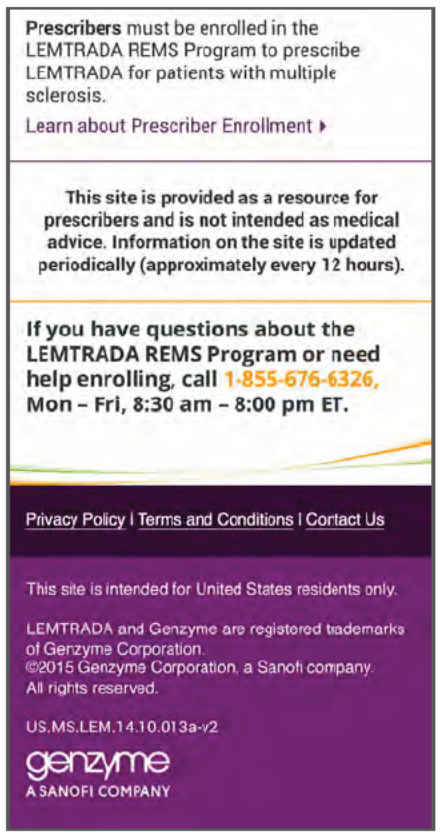
LEMTRADA REMS Mobile - Pre-REMS Certification, Prescriber Enrollment Complete



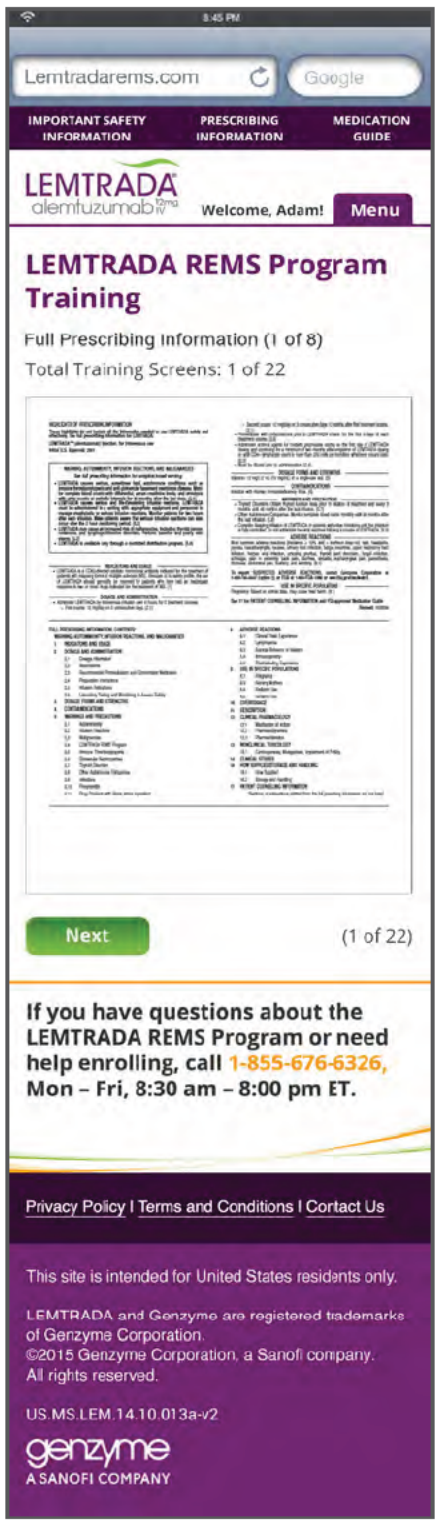


LEMTRADA REMS Mobile - Prescriber Dashboard, Dropdown Navigation



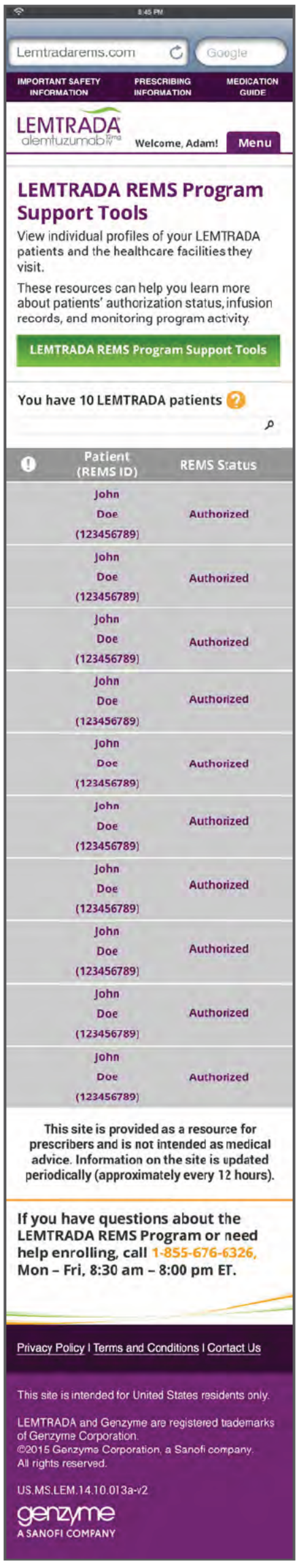


LEMTRADA REMS Mobile - Prescriber Training Materials - Page 1

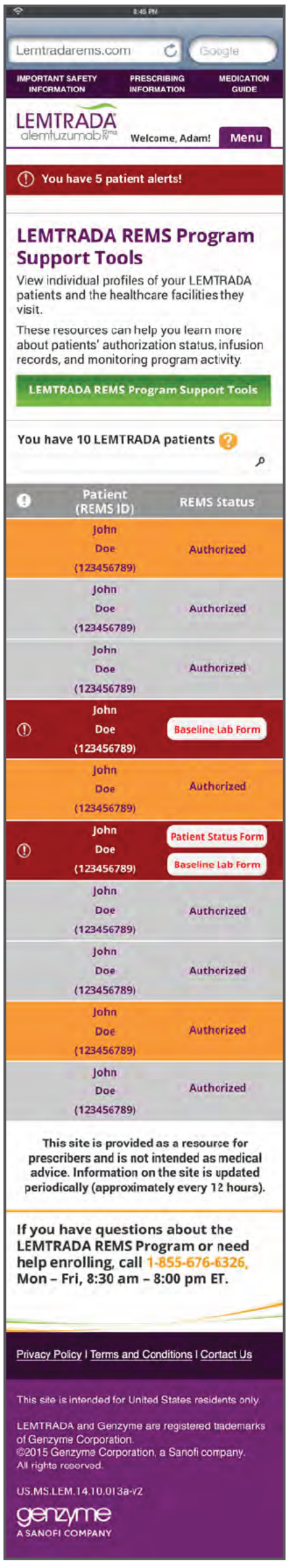


PRESCRIBER DASHBOARD PAGES

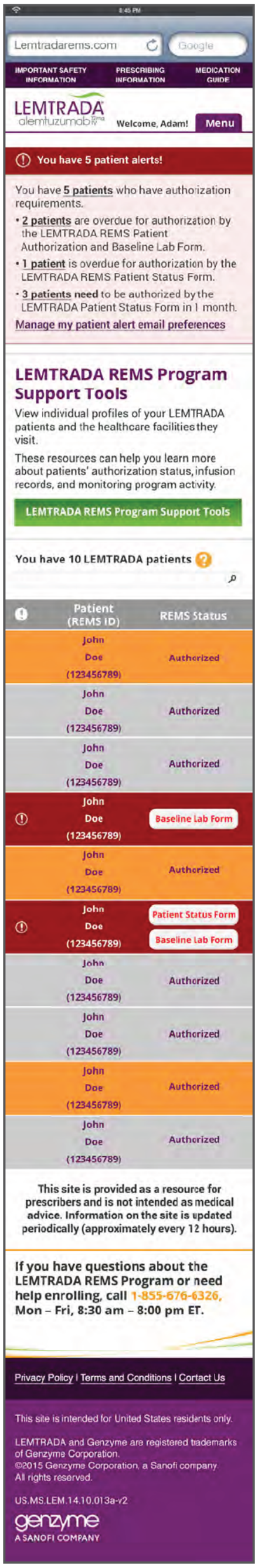
LEMTRADA REMS Mobile - Prescriber Dashboard, My Patients, No Patient Alerts



LEMTRADA REMS Mobile - Prescriber Dashboard, My Patients, Alert



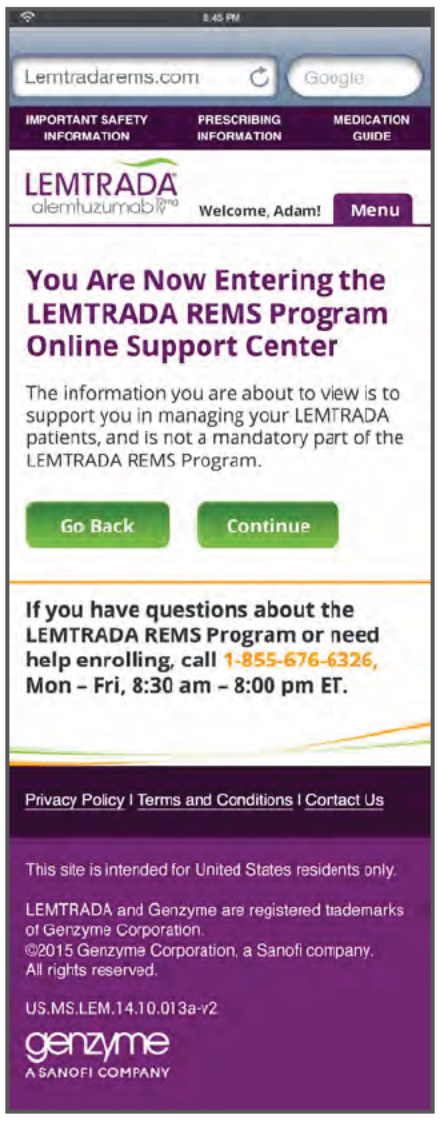
LEMTRADA REMS Mobile - Prescriber Dashboard, My Patients, Alert Expanded



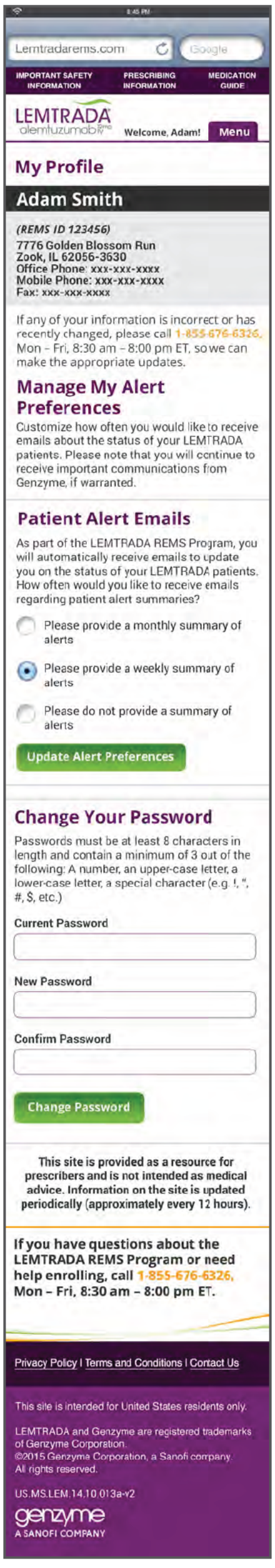
LEMTRADA REMS Mobile - Prescriber Dashboard, My Patients, Tool Tip Expanded



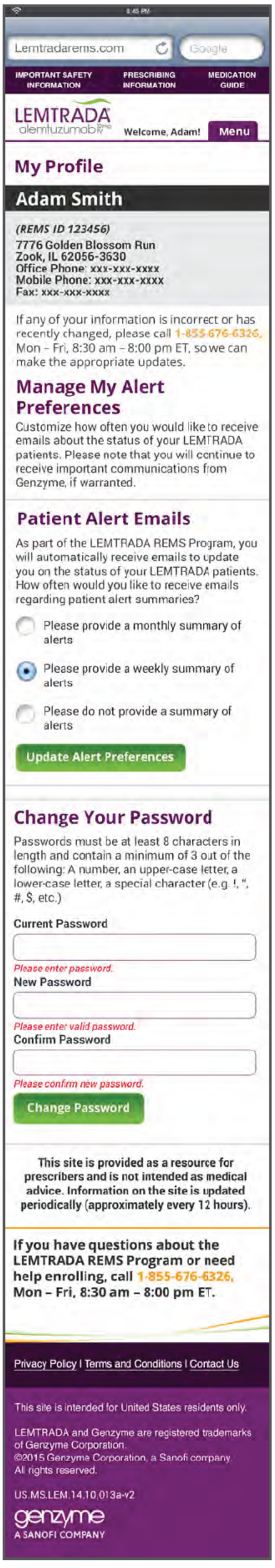
LEMTRADA REMS Mobile - Prescriber Dashboard, My Patients, External Monitoring Interstitial Page



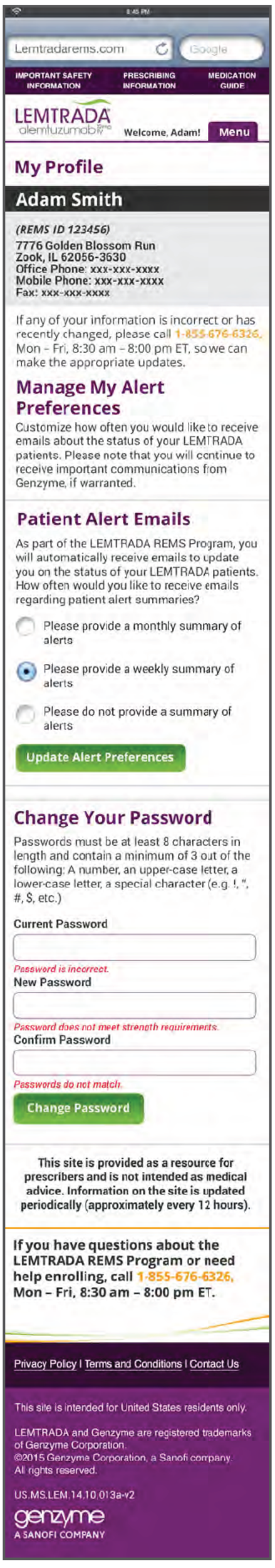
LEMTRADA REMS Mobile - Prescriber Dashboard, My Profile



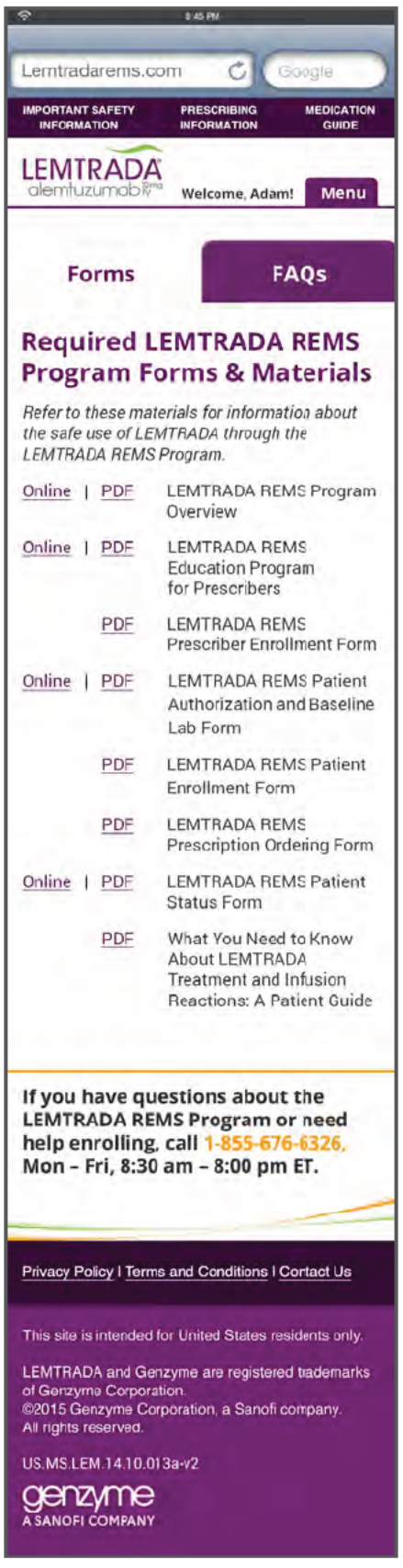
LEMTRADA REMS Mobile - Prescriber Dashboard, My Profile, Error



LEMTRADA REMS Mobile - Prescriber Dashboard, My Profile, Passwords do not match Error



LEMTRADA REMS Mobile - Prescriber Dashboard, Support, Forms



LEMTRADA REMS Mobile - Patient Status Form, Yes Selected

Lemtradarems.com

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IMPORTANT SAFETY INFORMATION | PRESCRIBING INFORMATION | MEDICATION GUIDE

LEMTRADA alemtuzumab | Welcome, Adam! | Menu

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LEMTRADA REMS PATIENT STATUS FORM

This form must be completed every 6 months for each LEMTRADA patient under your care. Please complete this form 6 months after your patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the patient's last infusion. Please complete the form and submit to Genzyme using the button below.

All fields are required.

PRESCRIBER INFORMATION

First Name
Prefilled Doctor's first name

Last Name
Prefilled Doctor's last name

Office Phone Number
Prefilled Doctor's phone

Address Line 1
Prefilled Doctor's address

Address Line 2
Prefilled Doctor's address

City
Prefilled Doctor's city

State | ZIP Code
Prefilled Doctor's state | Prefilled Doctor's ZIP Code

PATIENT INFORMATION

First Name
Prefilled Patient's first name

Last Name
Prefilled Patient's last name

Patient LEMTRADA REMS Program Identification Number
Prefilled Patient's REMS ID

Date of Birth (MM/DD/YYYY)
Prefilled Patient's birthdate

Date of Last LEMTRADA Infusion (MM/DD/YYYY)
Prefilled Patient's last infusion

Is the above-named patient still under your care?

(•) Yes ( ) No

IF YES, please complete the following information

The patient has completed the periodic monitoring within the last 6 months:

( ) Yes ( ) No

Since submitting the last LEMTRADA REMS Patient Status Form, has the patient been diagnosed with any of the following?

Autoimmune conditions

( ) Yes ( ) No

Infusion reactions

( ) Yes ( ) No

Malignancies

( ) Yes ( ) No

This adverse event has already been reported to Genzyme (specify date of report):

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

In signing this form, I acknowledge that I have reviewed *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with this patient and counseled the patient about the serious risks associated with the use of LEMTRADA, and how to mitigate these risks through periodic monitoring.

By providing my e-signature, I attest that I have filled out the Patient Status Form to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name

National Provider Identification (NPI) Number

Password

Cancel | Submit

Previous Page

This site is provided as a resource for prescribers and is not intended as medical advice. Information on the site is updated periodically (approximately every 12 hours).

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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US.MS.LEM.14.10.013a-v2

genzyme
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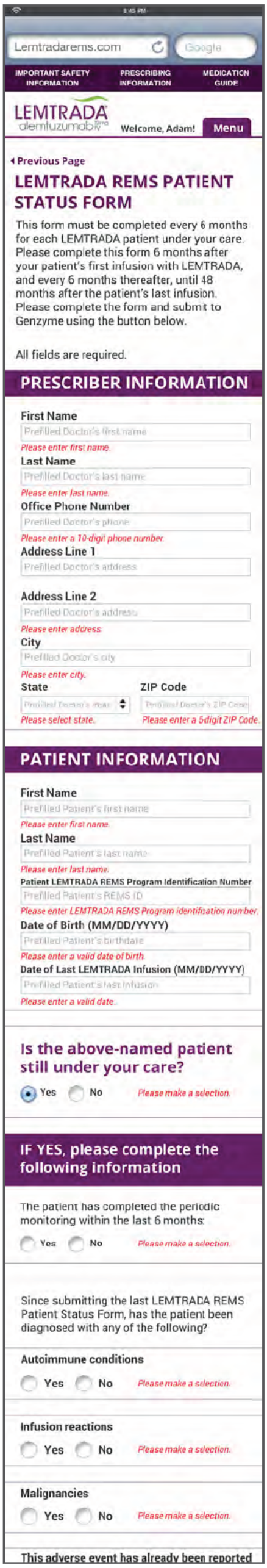
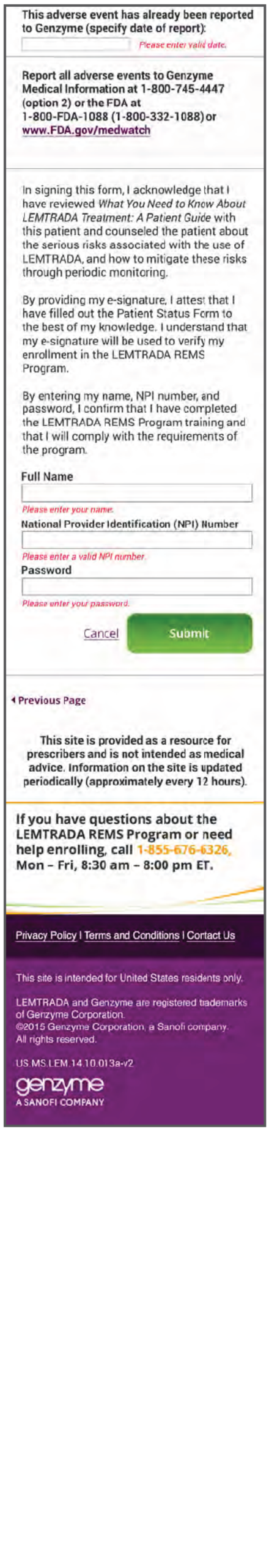
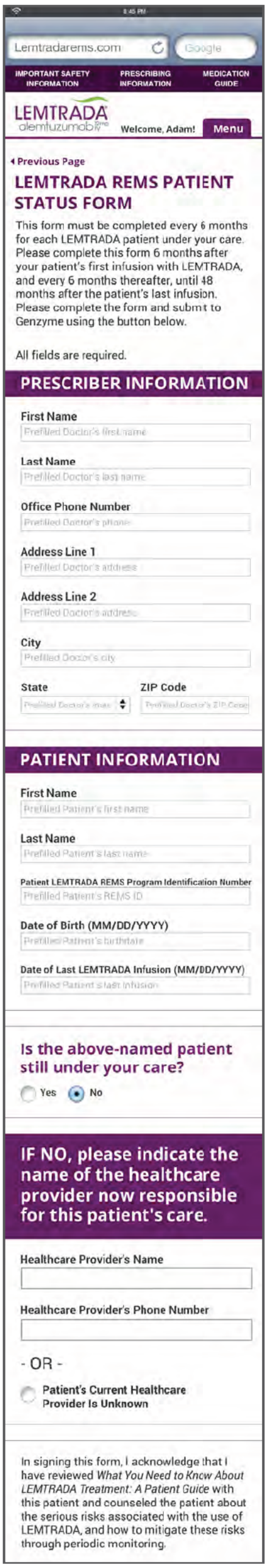
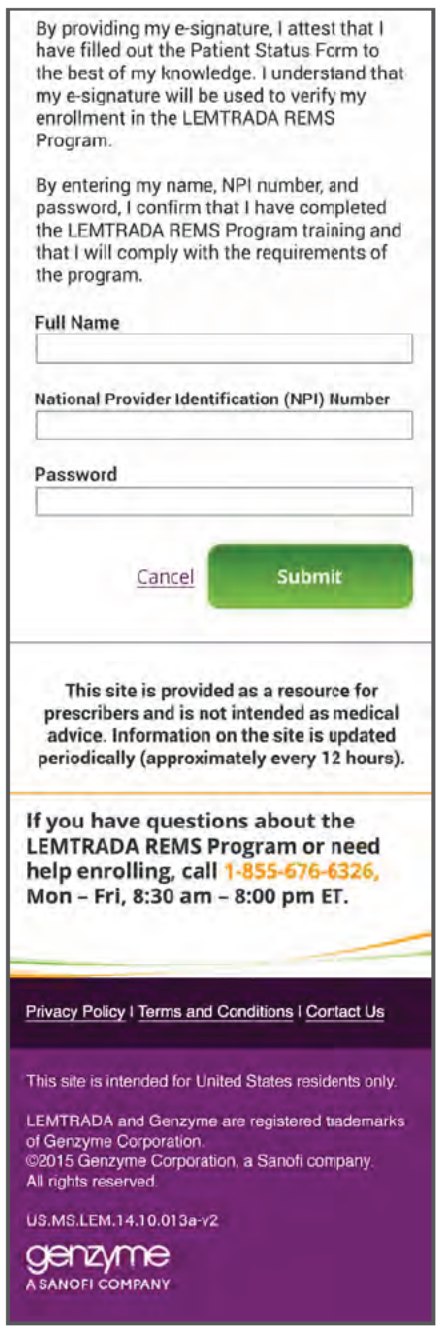
LEMTRADA REMS Mobile - Patient Status Form, Yes Selected, Error



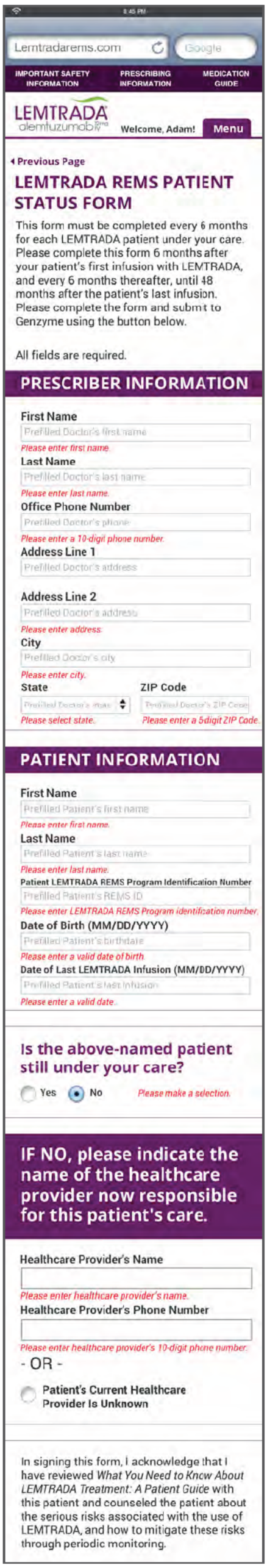


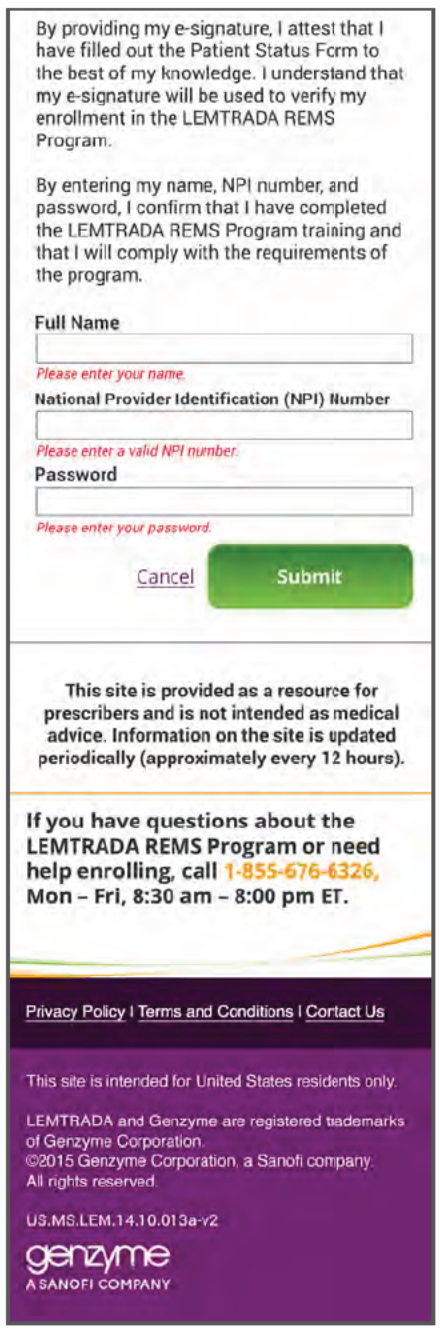
LEMTRADA REMS Mobile - Patient Status Form, No Selected



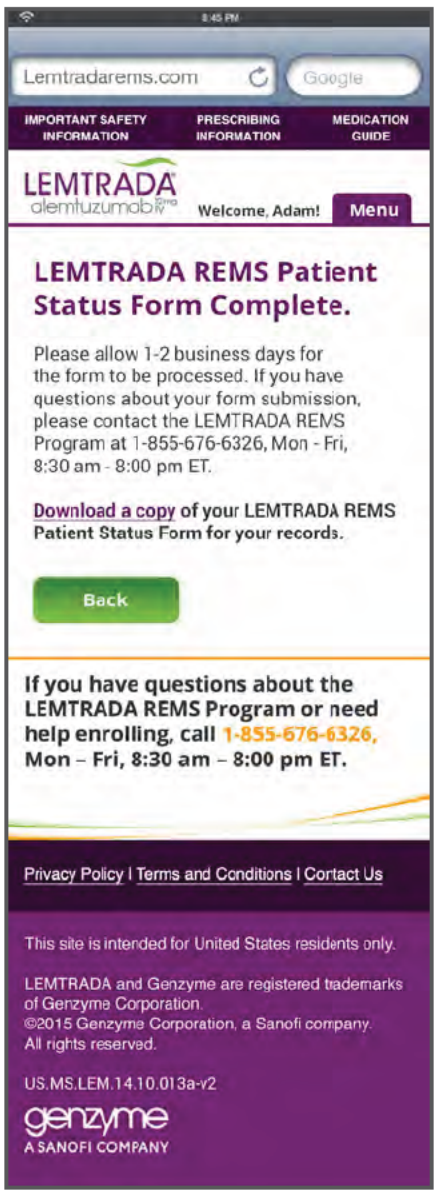


LEMTRADA REMS Mobile - Patient Status Form, No Selected, Error

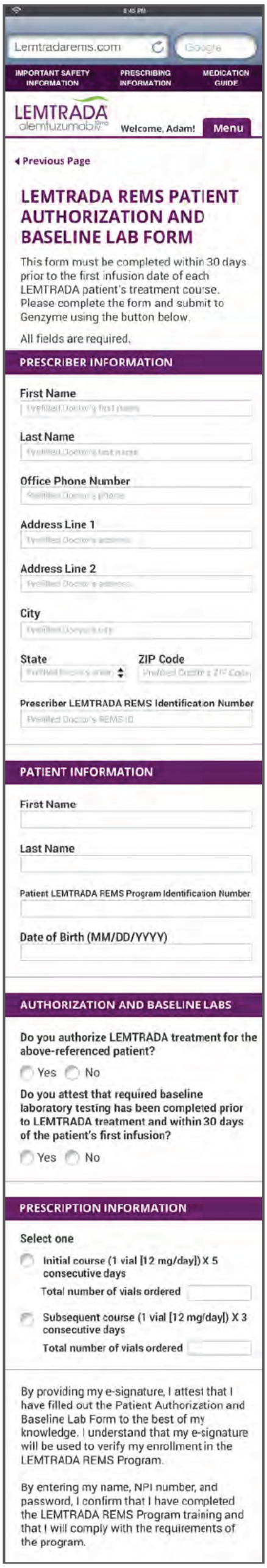


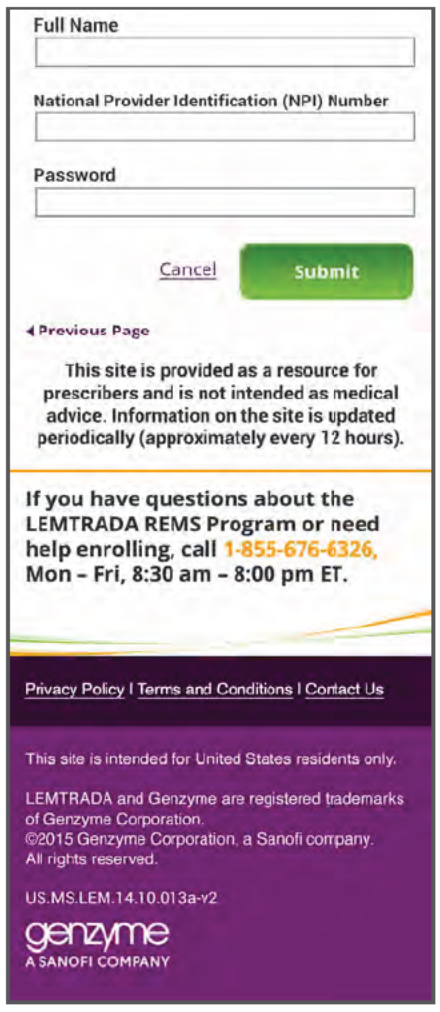


LEMTRADA REMS Mobile - Patient Status Form, Confirmation

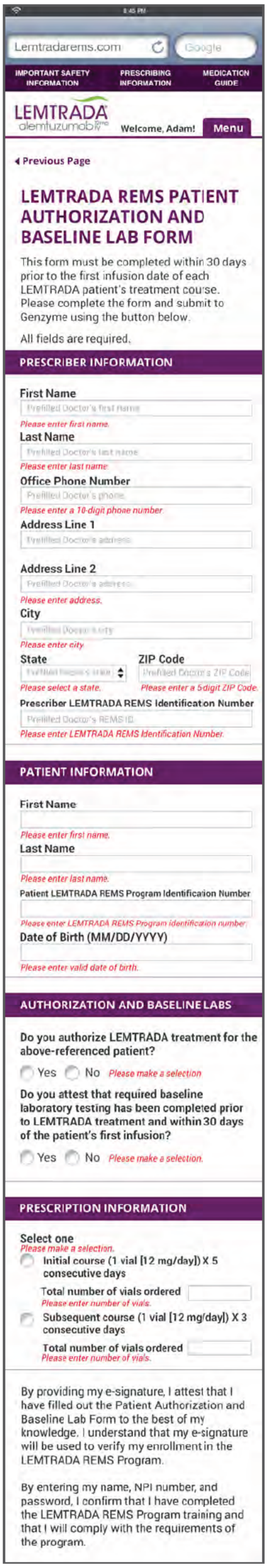


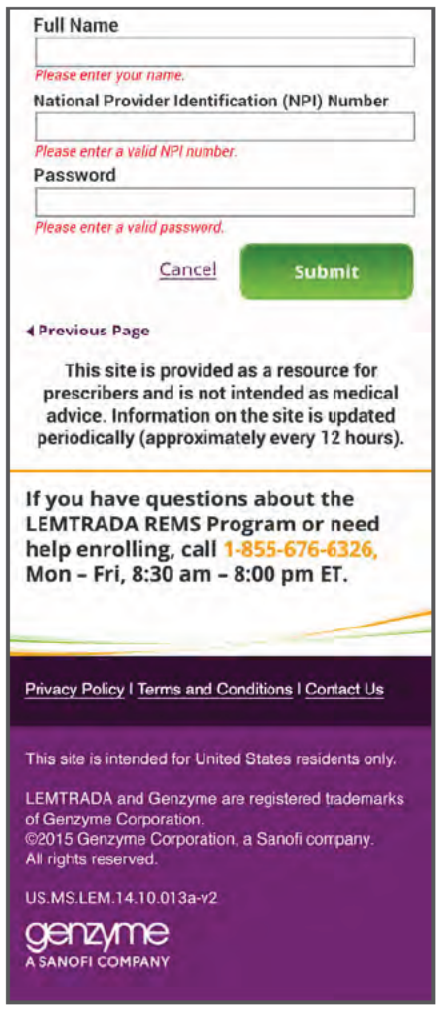
LEMTRADA REMS Mobile - Patient Status Form, Patient Authorization and Baseline Lab Form



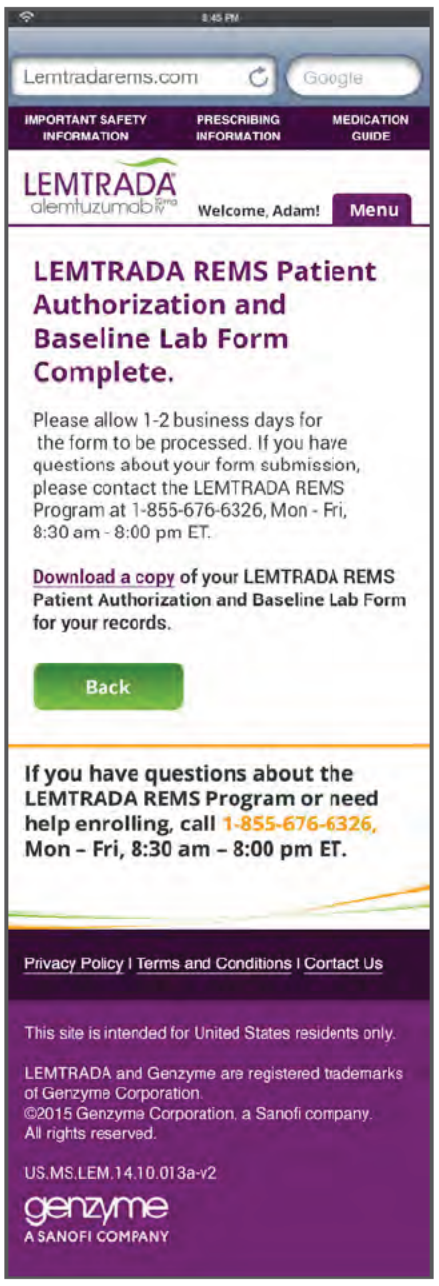


LEMTRADA REMS Mobile - Patient Status Form, Patient Authorization and Baseline Lab Form, Error

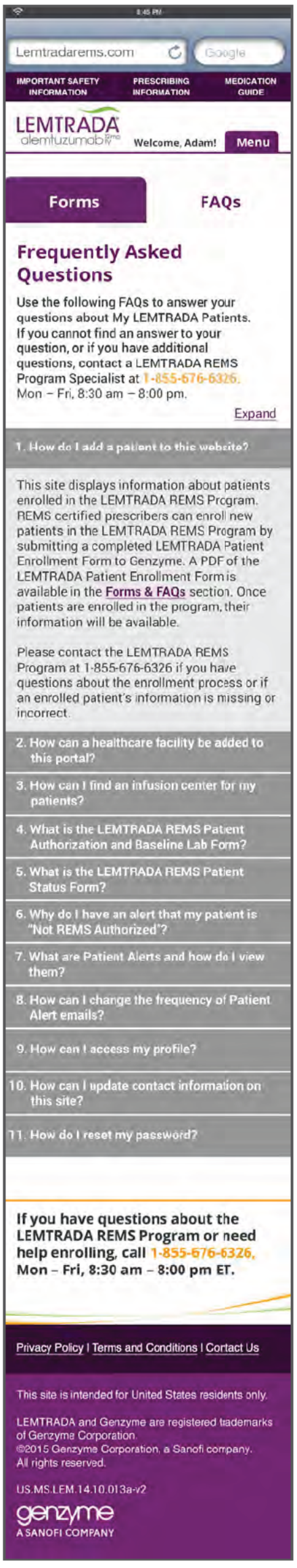




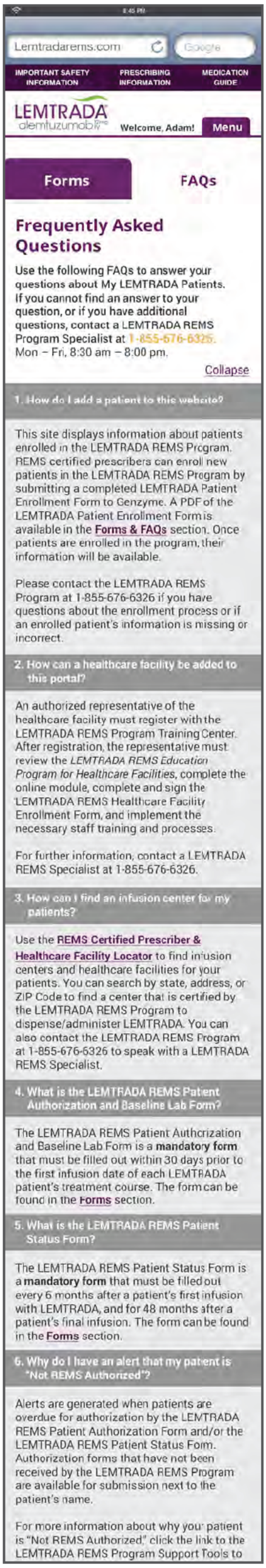
LEMTRADA REMS Mobile - Patient Status Form, Patient Authorization and Baseline Lab Form, Confirmation



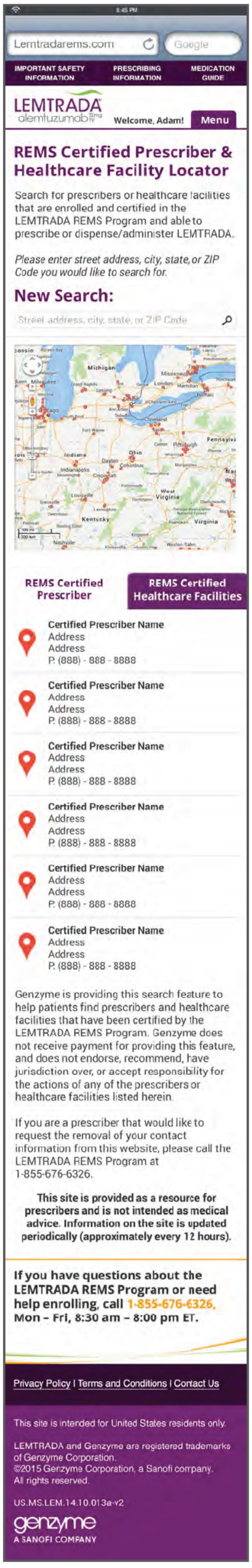
LEMTRADA REMS Mobile - Prescriber Dashboard, Support, FAQs



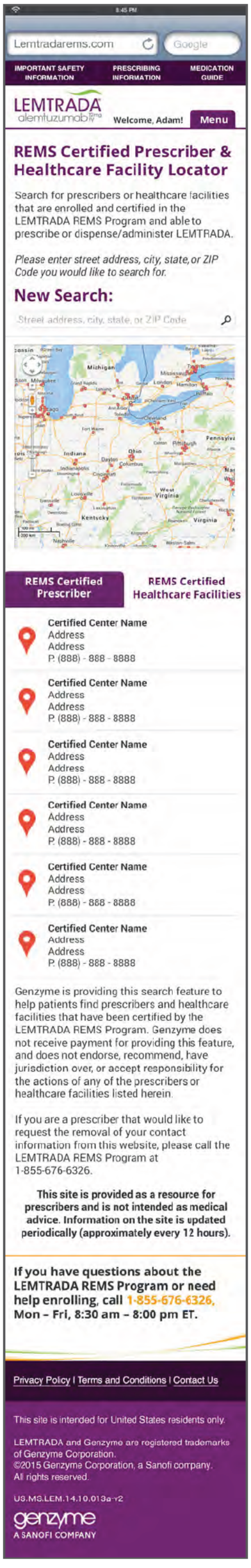
LEMTRADA REMS Mobile - Prescriber Dashboard, Support, FAQs Expanded



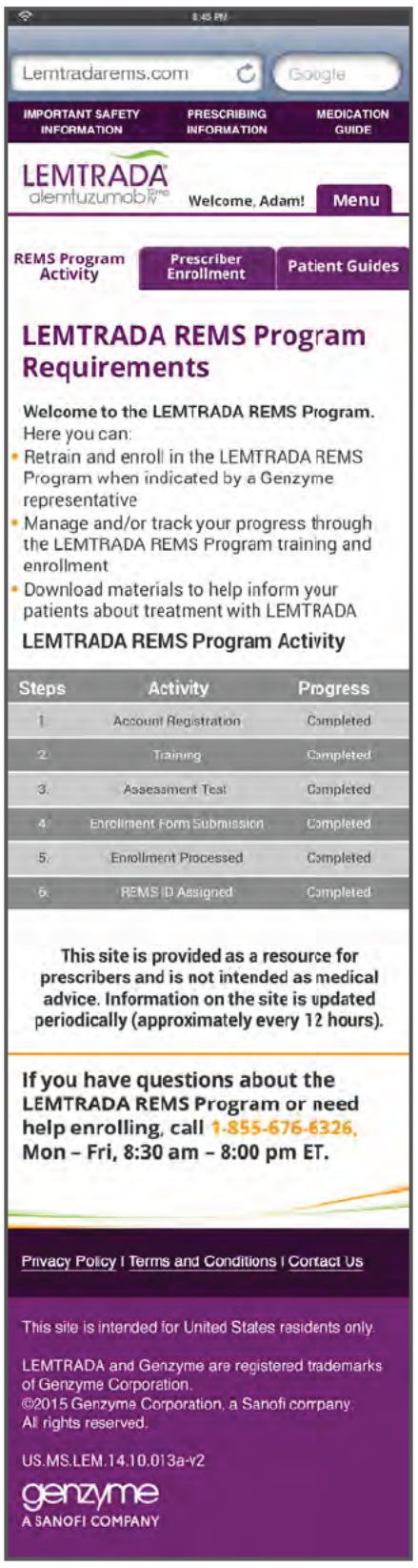
LEMTRADA REMS Mobile - Prescriber Dashboard, REMS Certified Prescriber and Healthcare Facility Locator



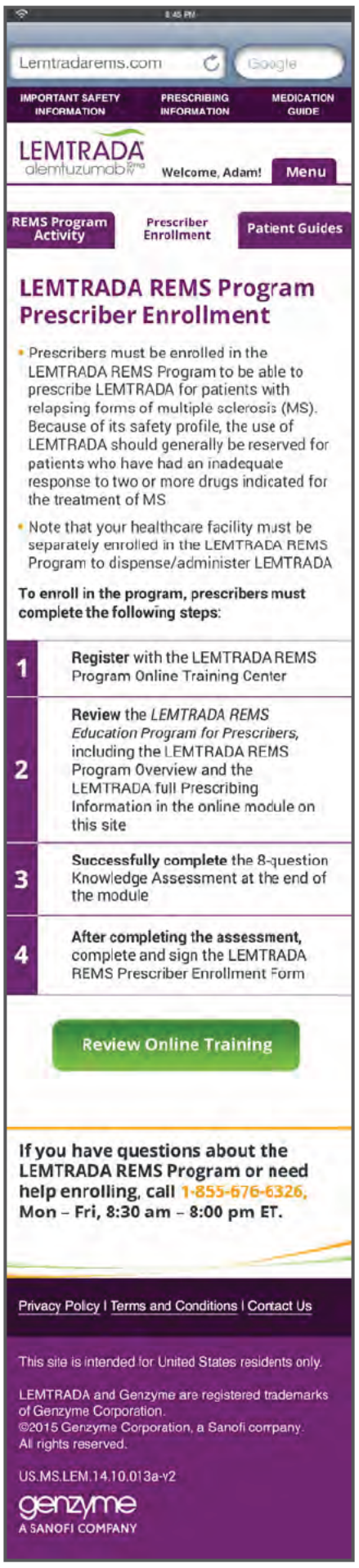
LEMTRADA REMS Mobile - Prescriber Dashboard, REMS Certified Prescriber and Healthcare Facility Locator



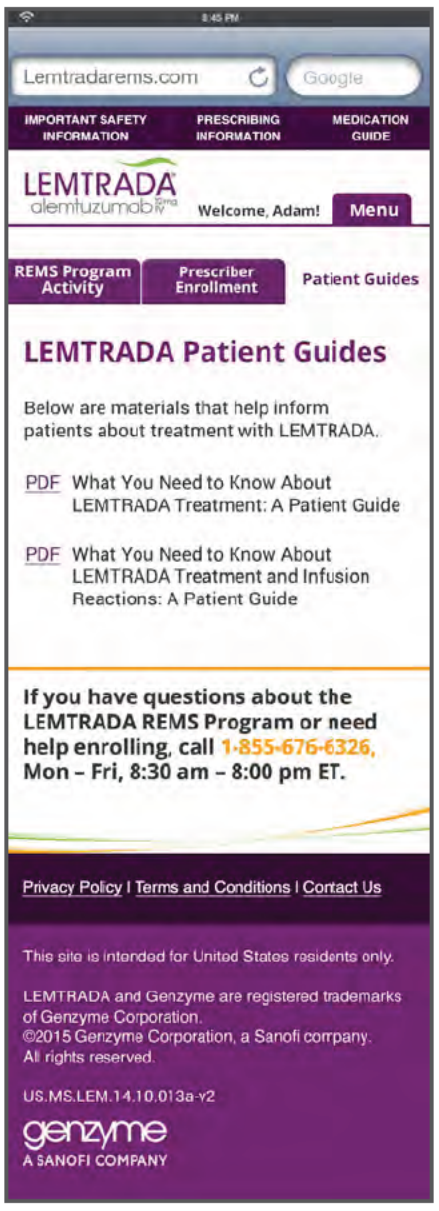
LEMTRADA REMS Mobile - Prescriber Dashboard, About REMS, REMS Program Activity



LEMTRADA REMS Mobile - Prescriber Dashboard, About REMS, HCP Enrollment



LEMTRADA REMS Mobile - Prescriber Dashboard, About REMS, Patient Guides

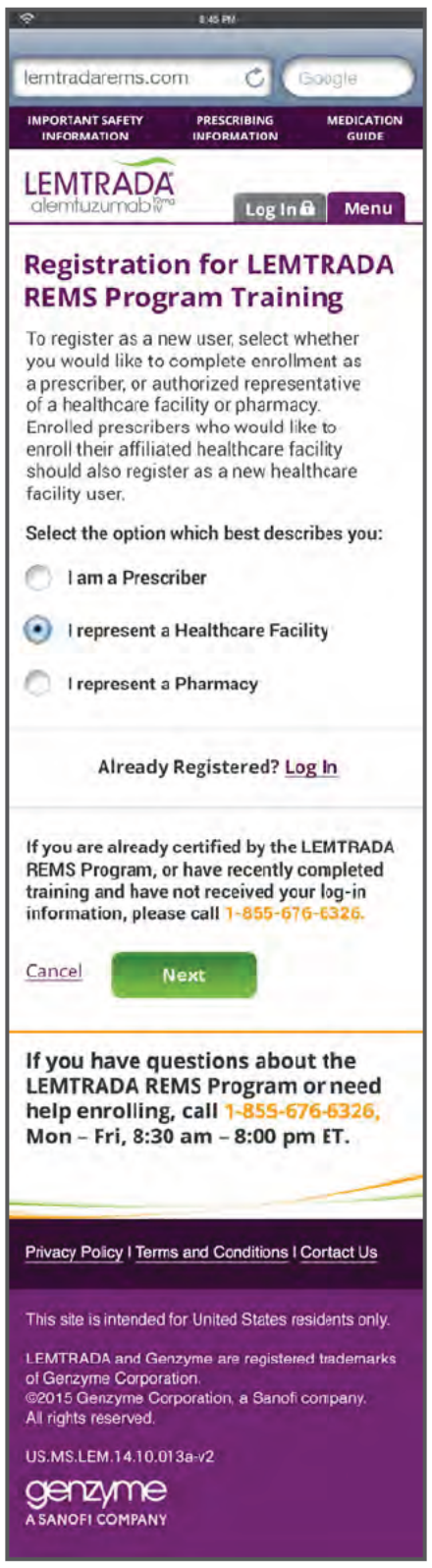


LEMTRADA REMS MOBILE

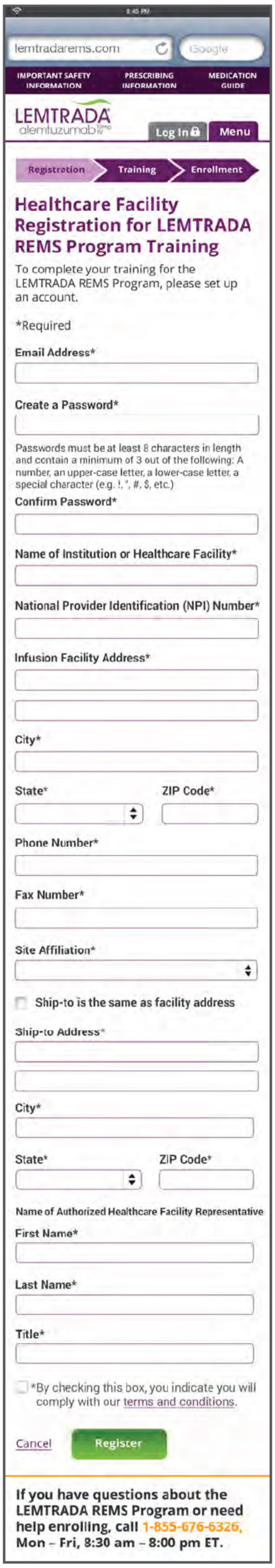
REMS Certified Healthcare Facility Pages Only

HEALTHCARE FACILITY TRAINING PAGES

LEMTRADA REMS Mobile - HCF Registration Home Selection

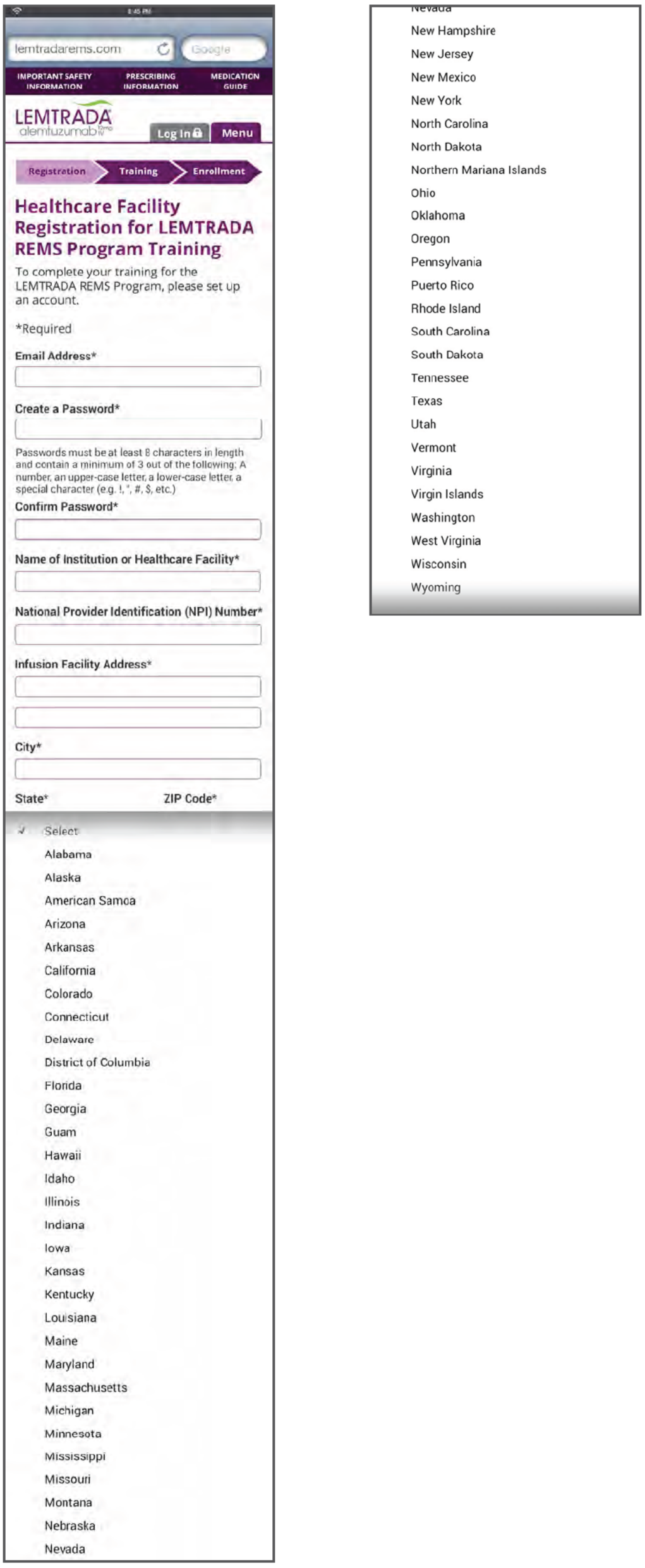


LEMTRADA REMS Mobile - HCF Registration





LEMTRADA REMS Mobile - HCF Registration, State Selection



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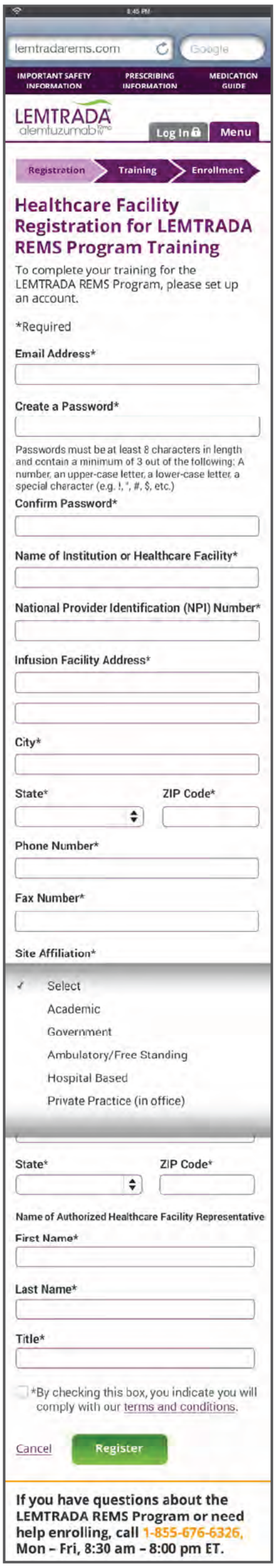
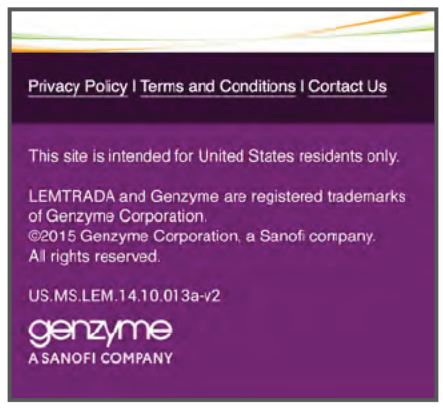
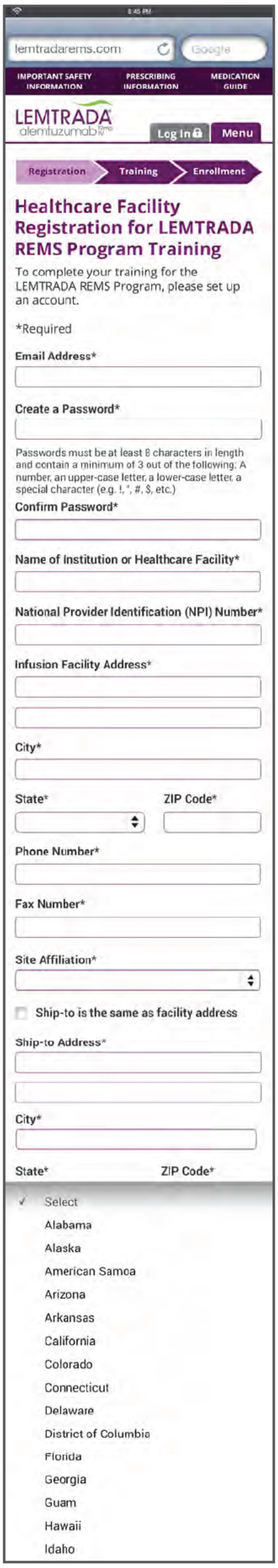
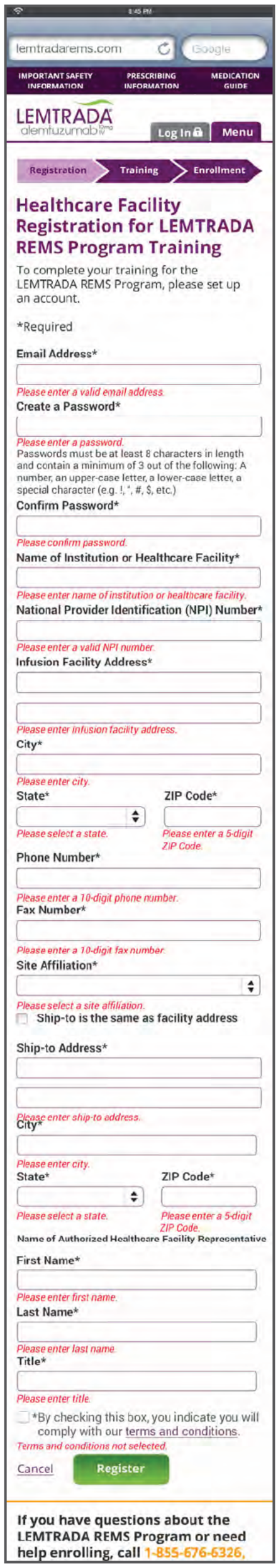


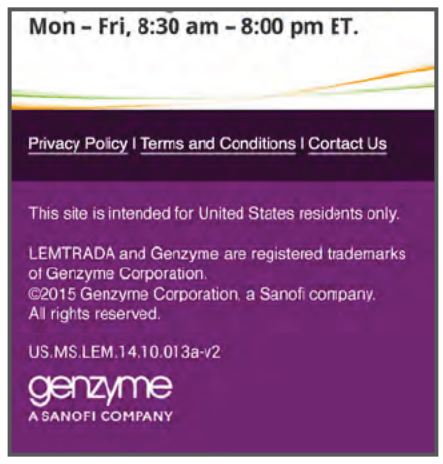


LEMTRADA REMS Mobile - HCF Registration, State Selection 2

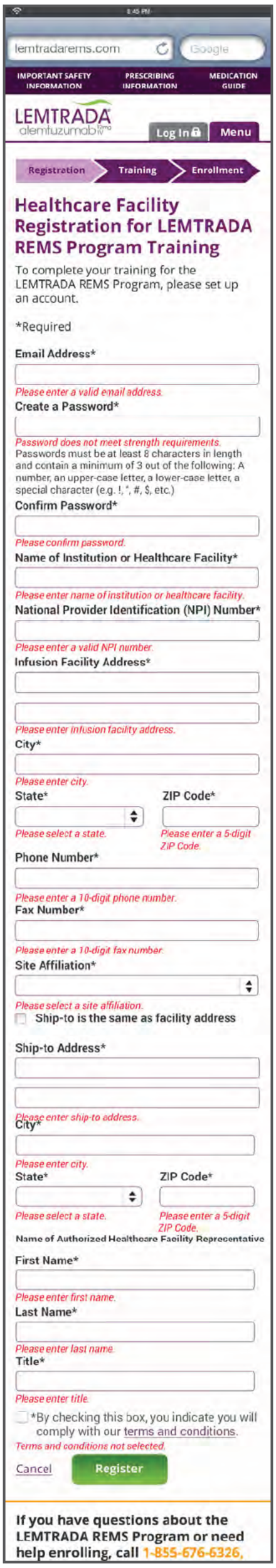


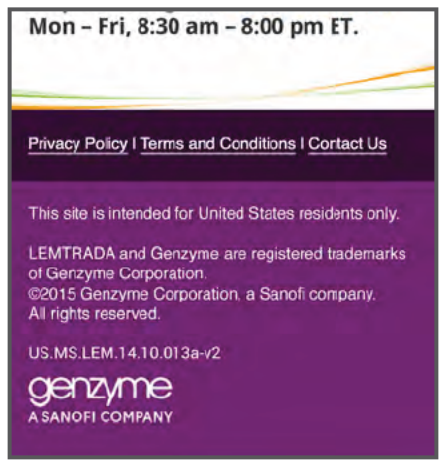
LEMTRADA REMS Mobile - HCF Registration, Error





LEMTRADA REMS Mobile - HCF Registration, Password Strength Error

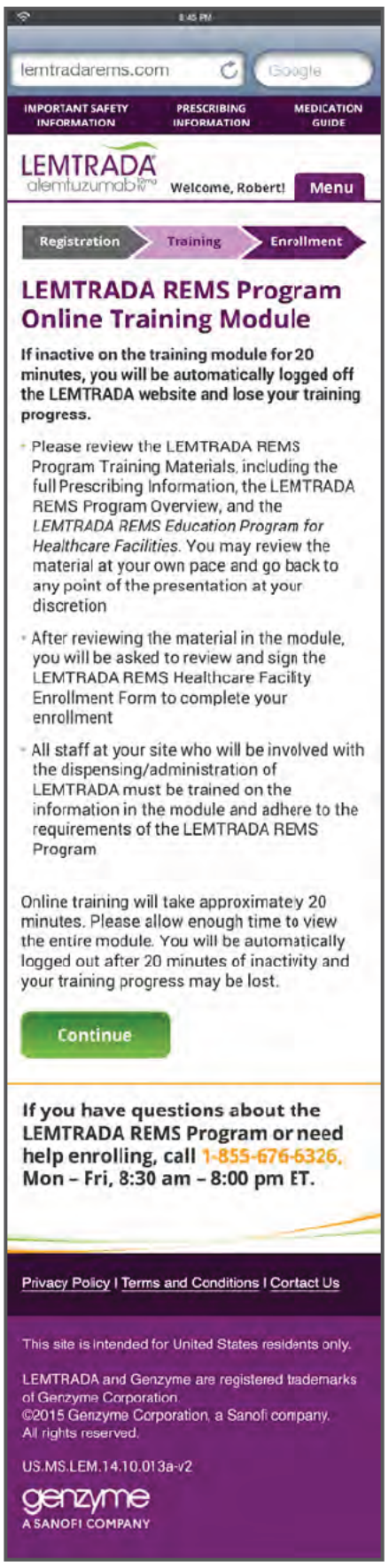




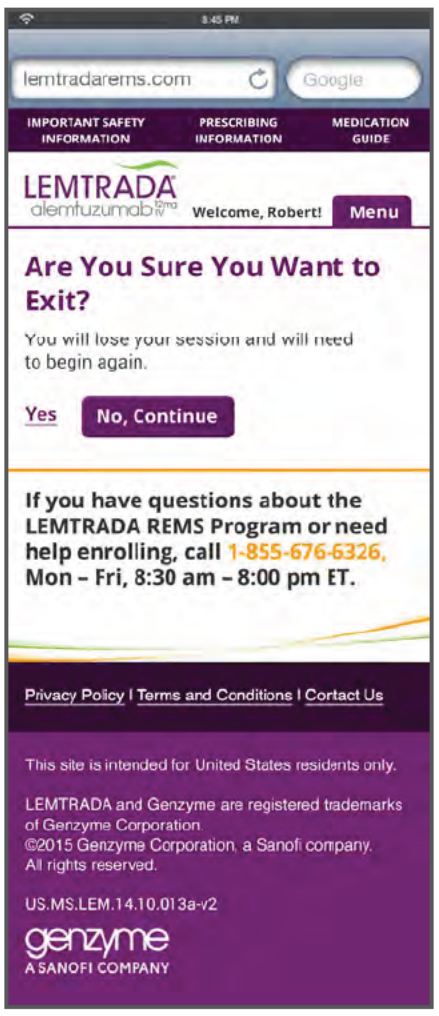
LEMTRADA REMS Mobile - HCF Registration, Confirmation



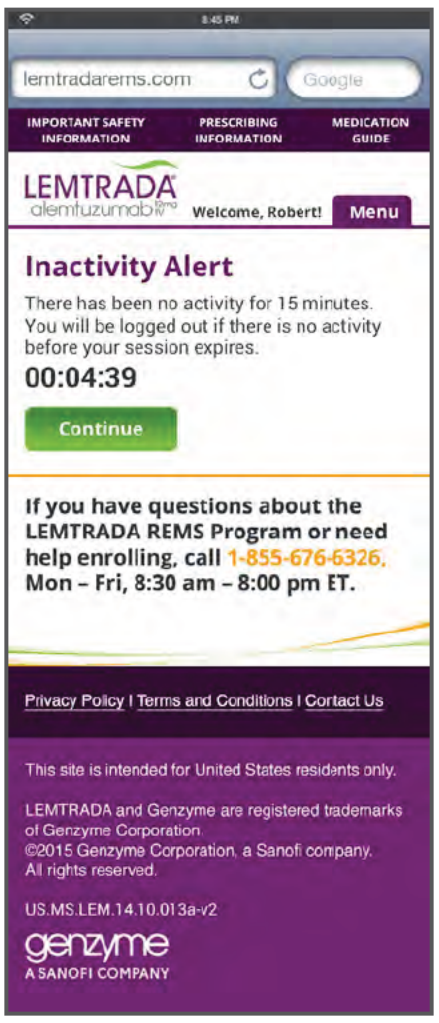
LEMTRADA REMS Mobile - HCF Training Module



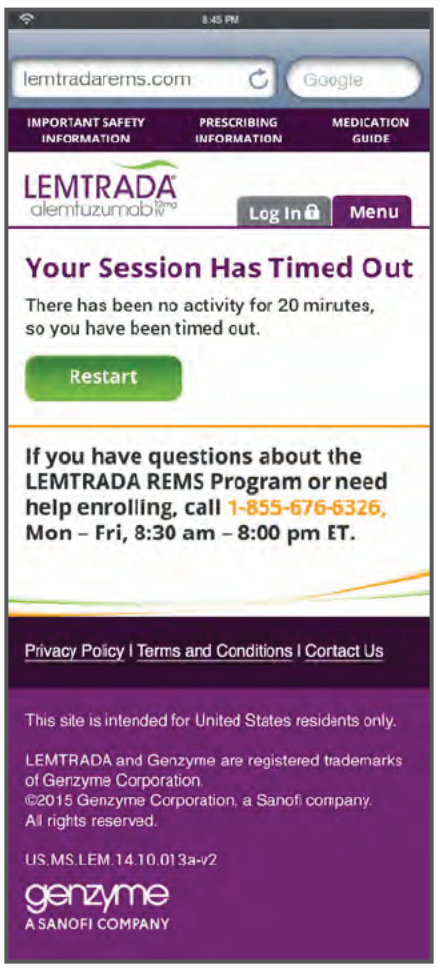
LEMTRADA REMS Mobile - HCF Training Module, Exit



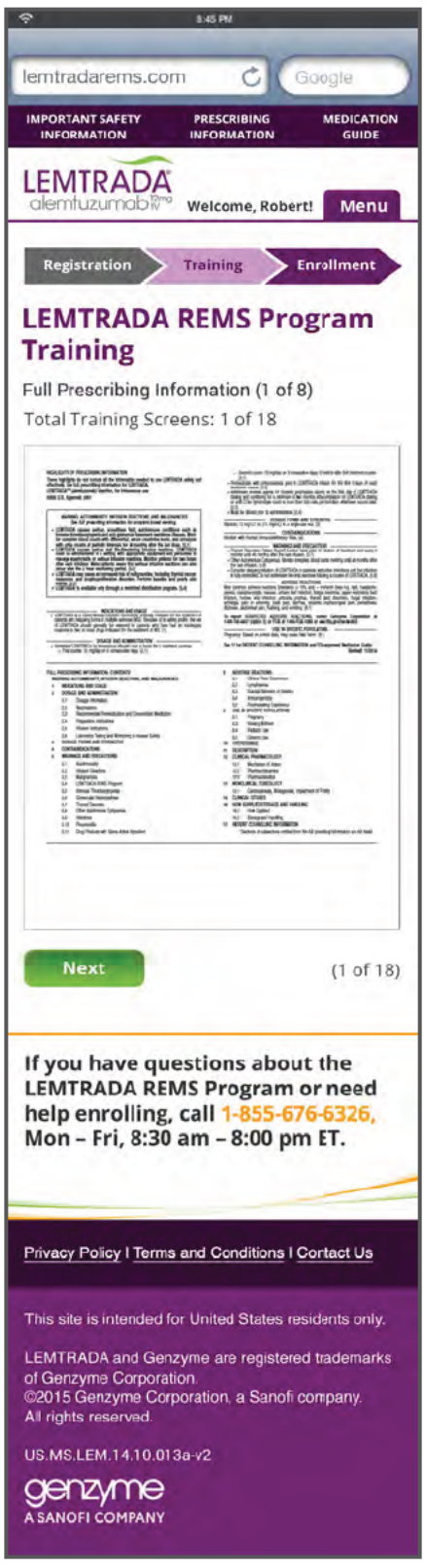
LEMTRADA REMS Mobile - HCF Training Module, Timer



LEMTRADA REMS Mobile - HCF Training, Timed Out



LEMTRADA REMS Mobile - HCF Training, PI Page 1



LEMTRADA REMS Mobile - HCF Training, PI Page 2



LEMTRADA REMS Mobile - HCF Training, PI Page 3



LEMTRADA REMS Mobile - HCF Training, PI Page 4



LEMTRADA REMS Mobile - HCF Training, PI Page 5



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LEMTRADA REMS Mobile - HCF Training, PI Page 7



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LEMTRADA REMS Mobile - HCF Training, Program Overview Page 1



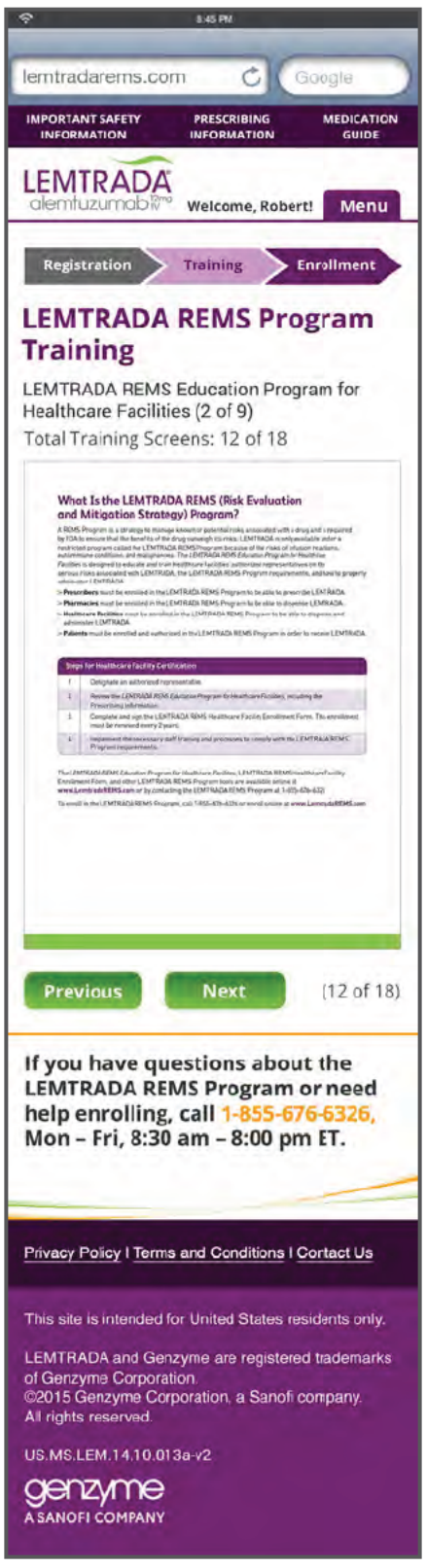
LEMTRADA REMS Mobile - HCF Training, Program Overview Page 2



LEMTRADA REMS Mobile - HCF Training, Training Page 1



LEMTRADA REMS Mobile - HCF Training, Training Page 2



LEMTRADA REMS Mobile - HCF Training, Training Page 3



LEMTRADA REMS Mobile - HCF Training, Training Page 4



LEMTRADA REMS Mobile - HCF Training, Training Page 5



LEMTRADA REMS Mobile - HCF Training, Training Page 6



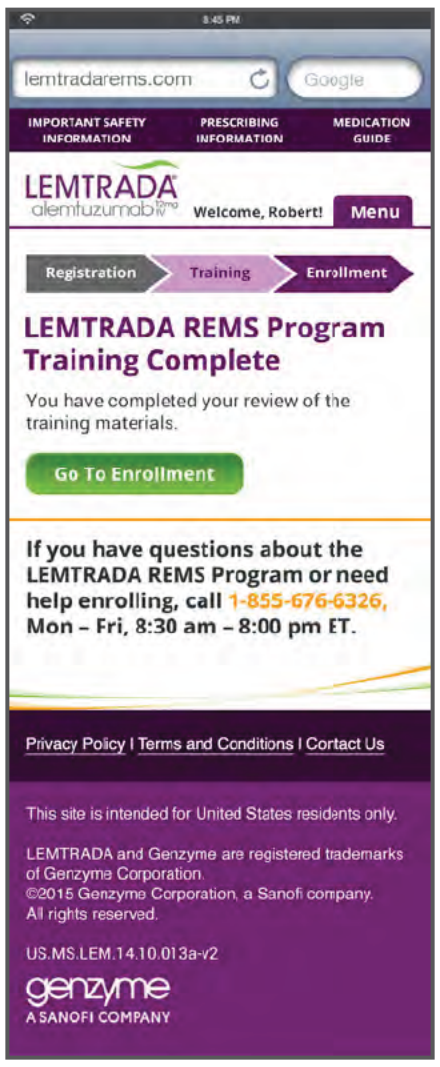
LEMTRADA REMS Mobile - HCF Training, Training Page 7



LEMTRADA REMS Mobile - HCF Training, Training Page 8

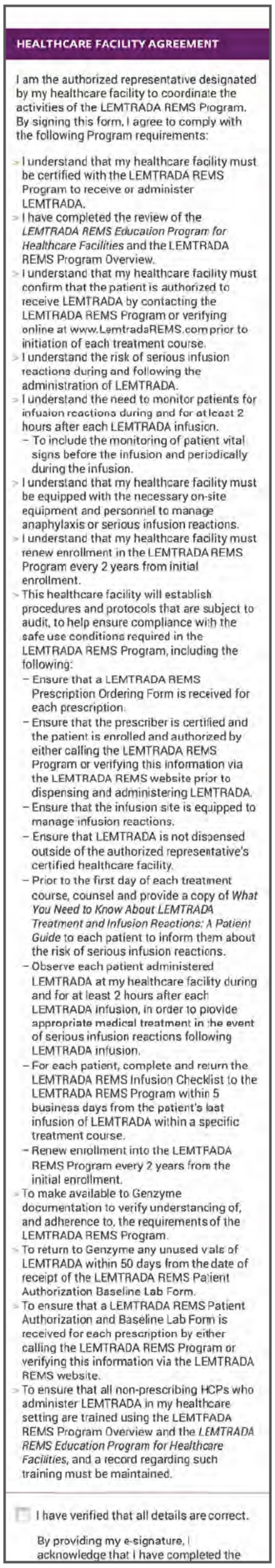


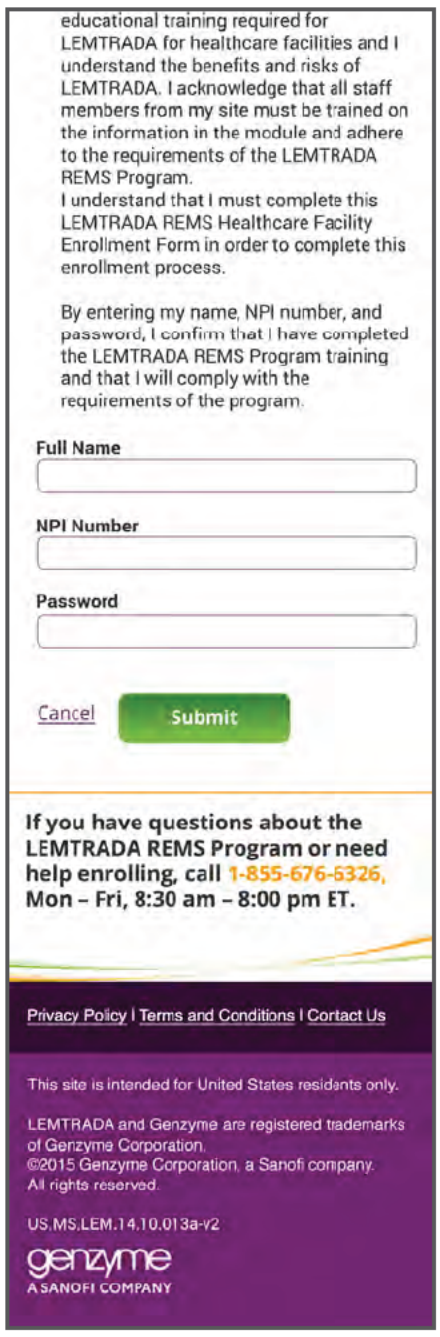
LEMTRADA REMS Mobile - HCF Training, Training Confirmation



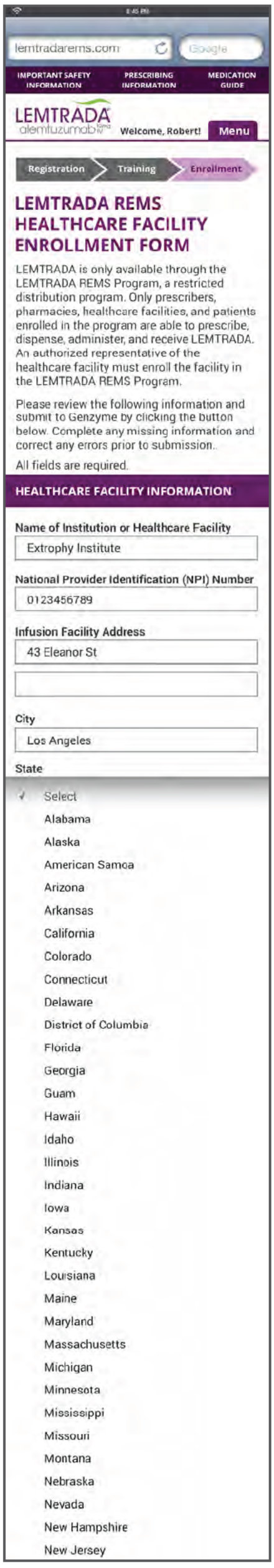
LEMTRADA REMS Mobile - HCF Enrollment





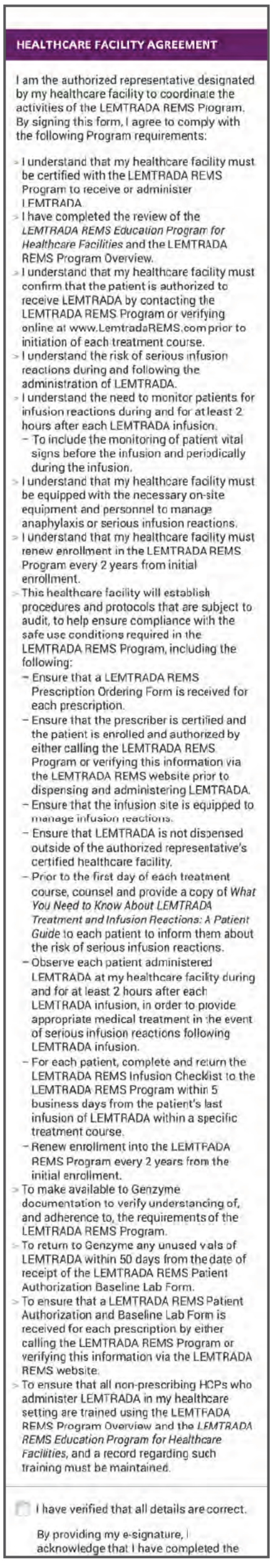


LEMTRADA REMS Mobile - HCF Enrollment, State Selection



LEMTRADA REMS Mobile - HCF Enrollment, Site Affiliation Selection



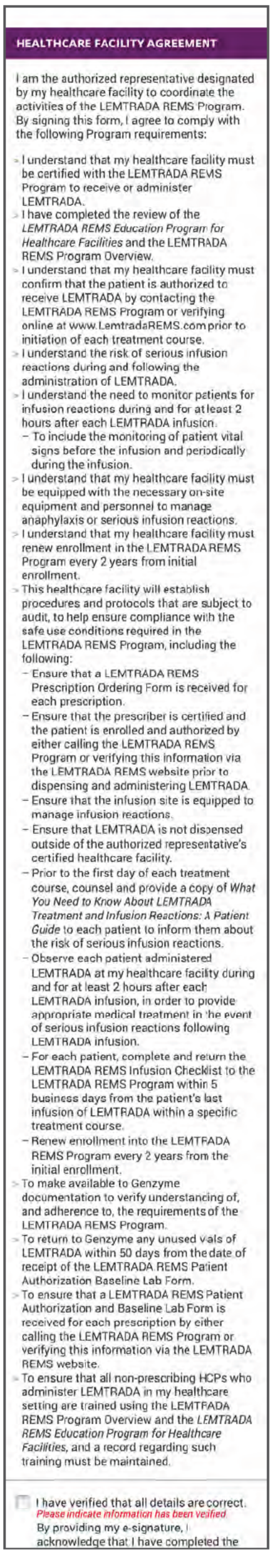


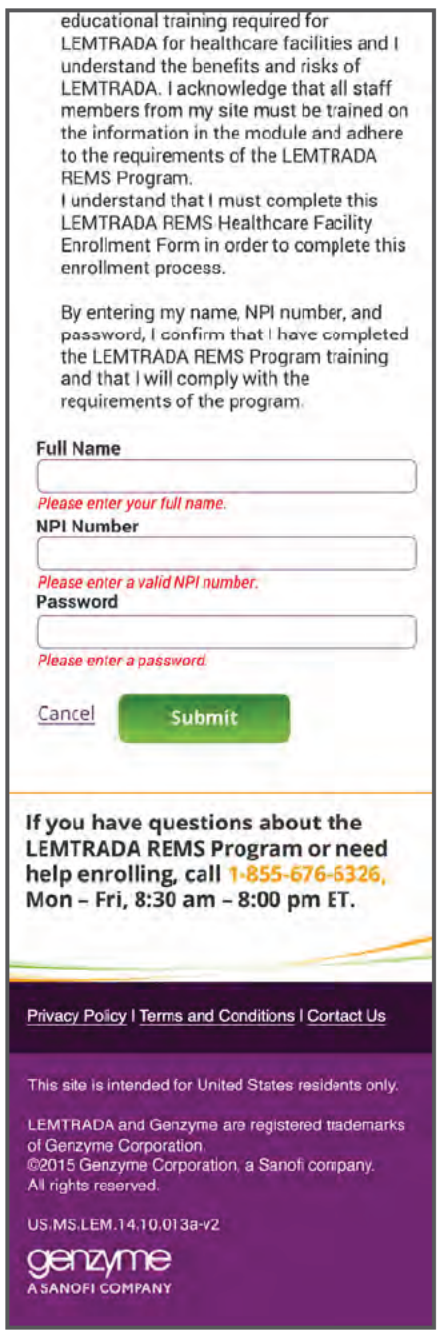
LEMTRADA REMS Mobile - HCF Enrollment, Ship-to State Selection



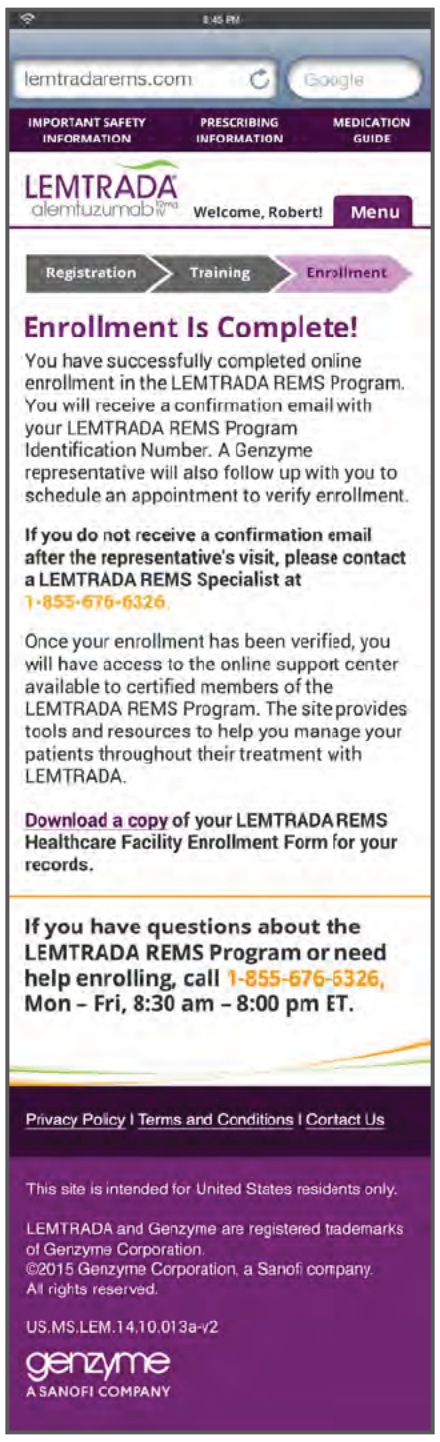
LEMTRADA REMS Mobile - HCF Enrollment, Error





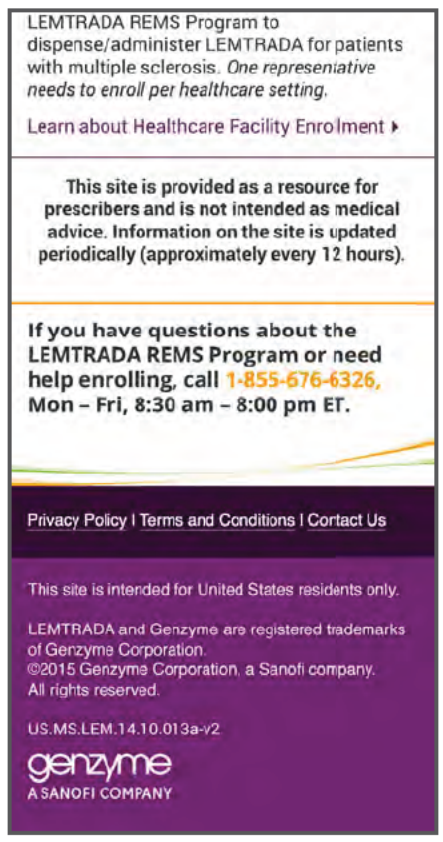


LEMTRADA REMS Mobile - HCF Enrollment Confirmation



LEMTRADA REMS Mobile - HCF, Pre-REMS Cert, Training Incomplete





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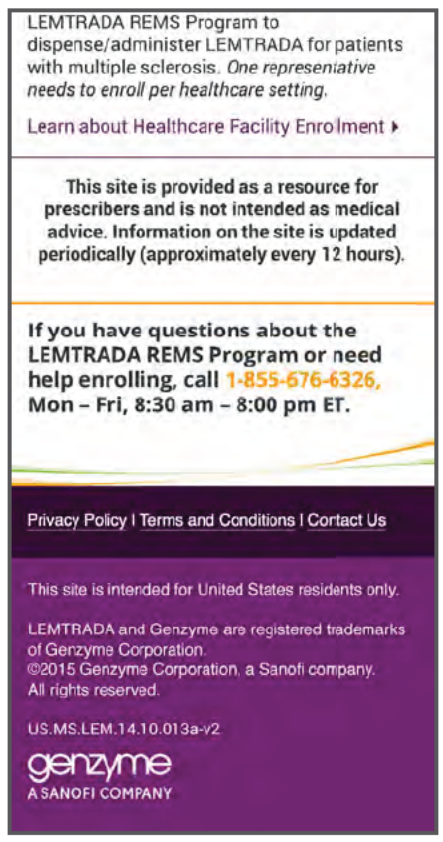
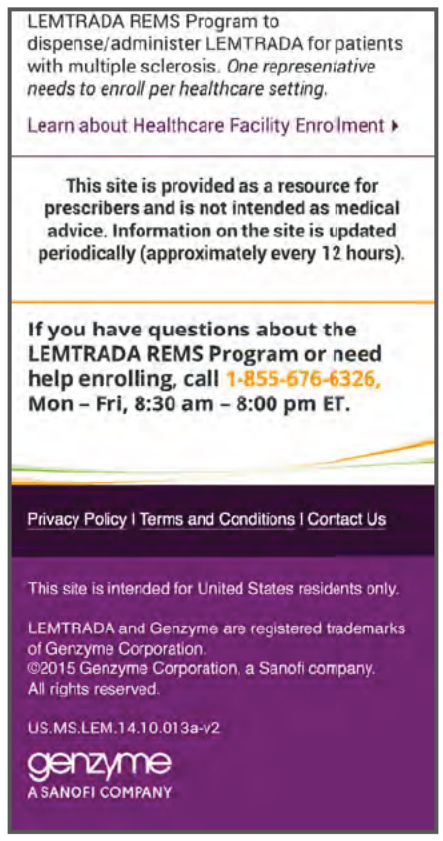


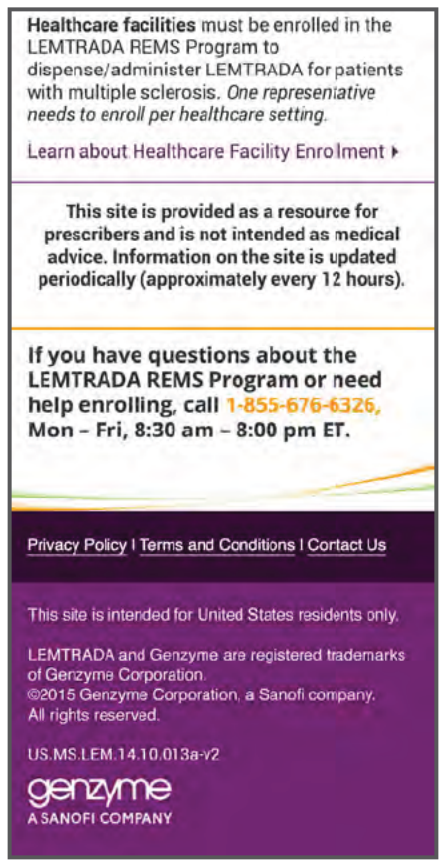
LEMTRADA REMS Mobile - HCF, Pre-REMS Cert, Enrollment Incomplete





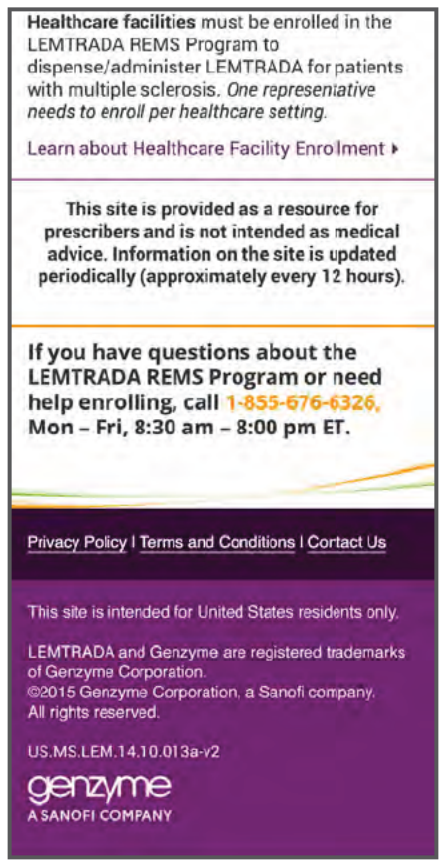
LEMTRADA REMS Mobile - HCF, Pre-REMS Cert, Enrollment Complete



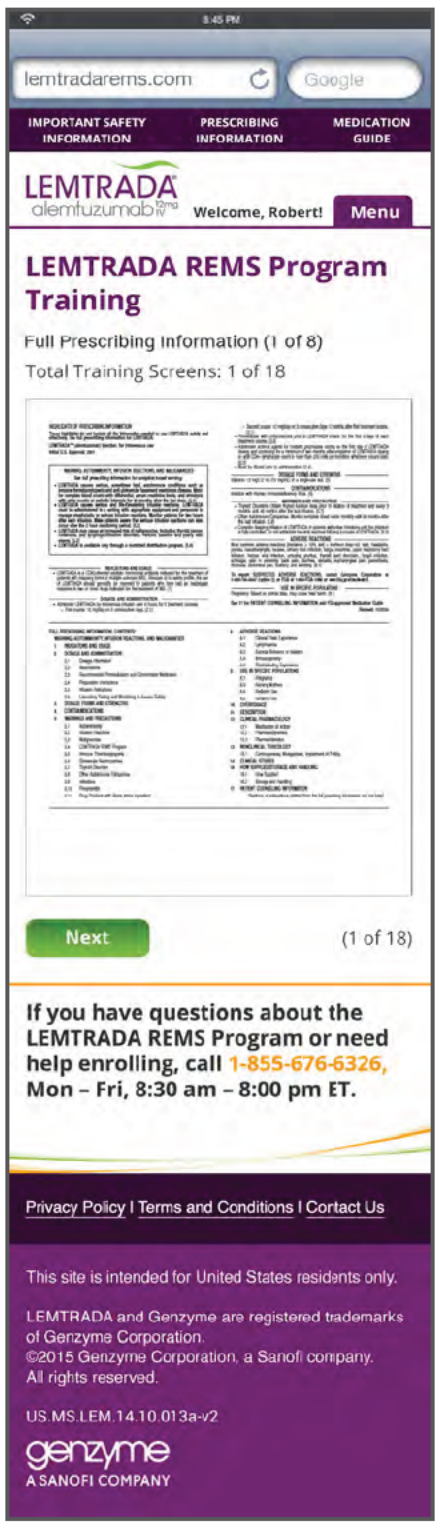


LEMTRADA REMS Mobile - HCF, Dropdown Navigation



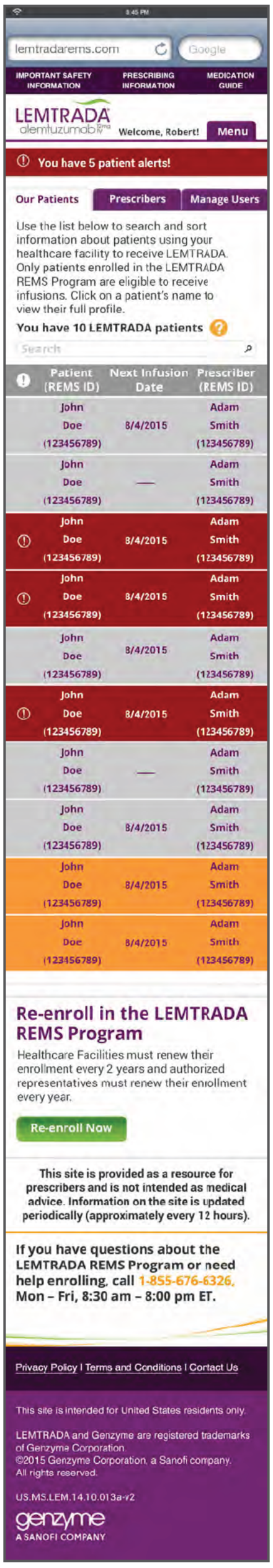


LEMTRADA REMS Mobile - HCF Training Materials - Page 1

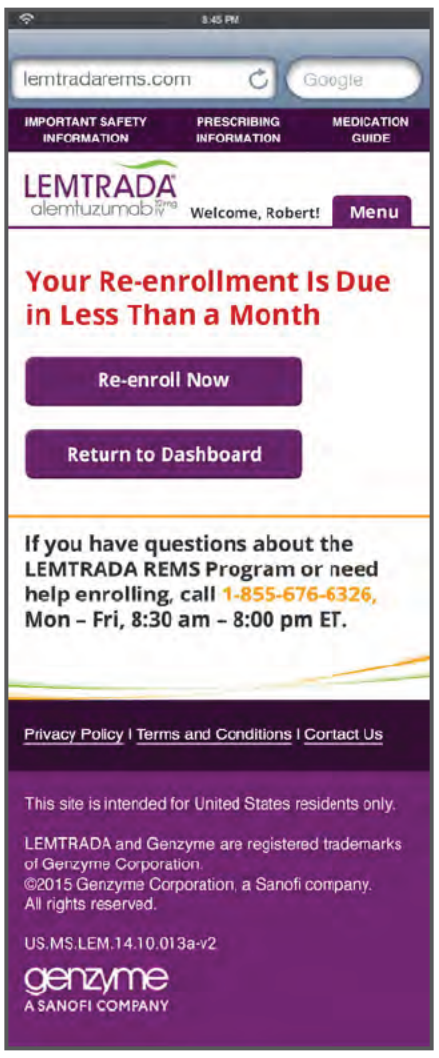


REMS CERTIFIED HEALTHCARE FACILITY DASHBOARD PAGES

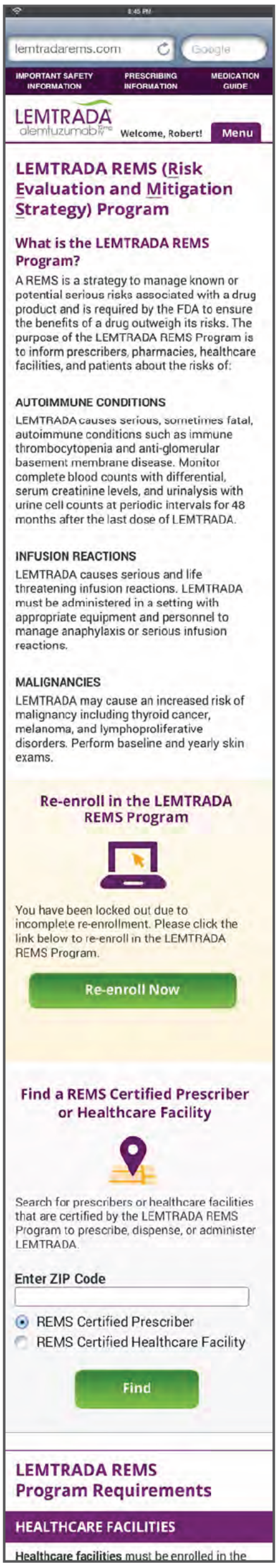
LEMTRADA REMS Mobile - HCF Dashboard - Patient List, Alert On

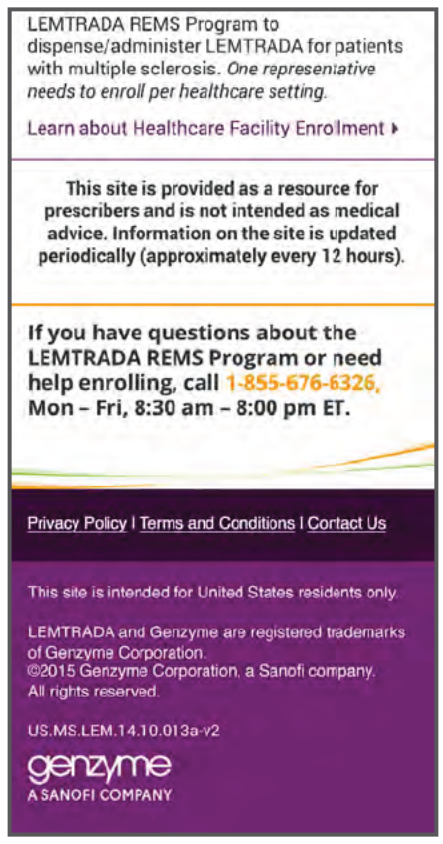


LEMTRADA REMS Mobile - HCF Dashboard - Patient List, Alert On, Re-enrollment Message

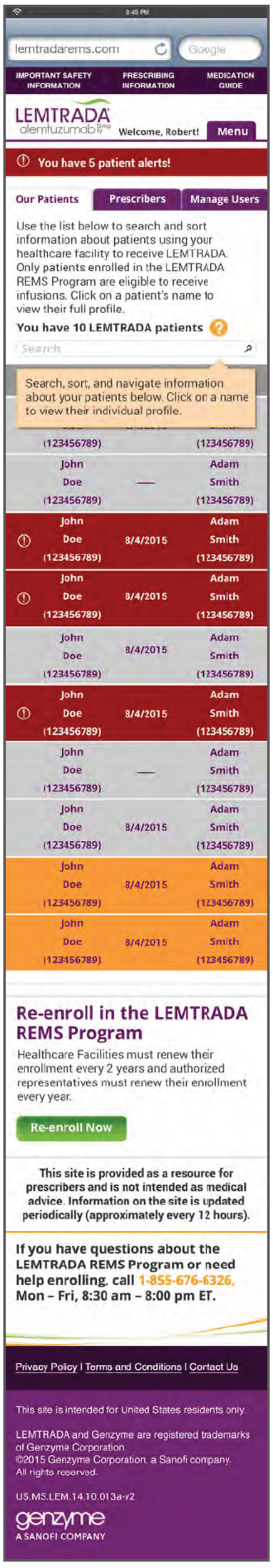


LEMTRADA REMS Mobile - HCF Dashboard - Re-enrollment Lockout

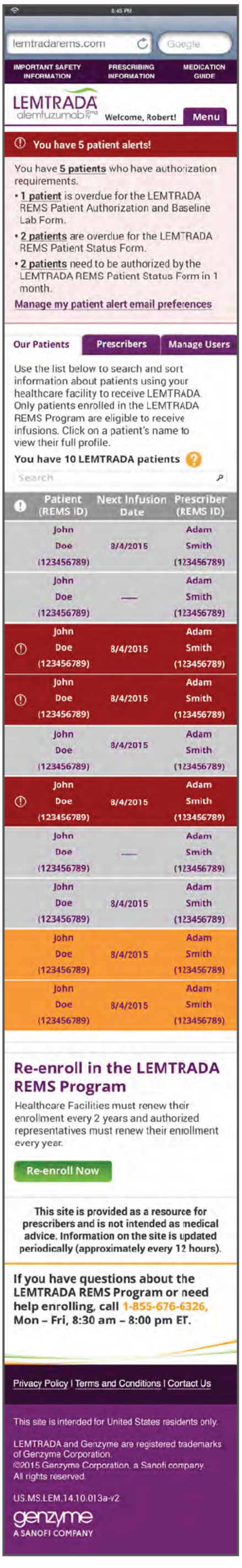




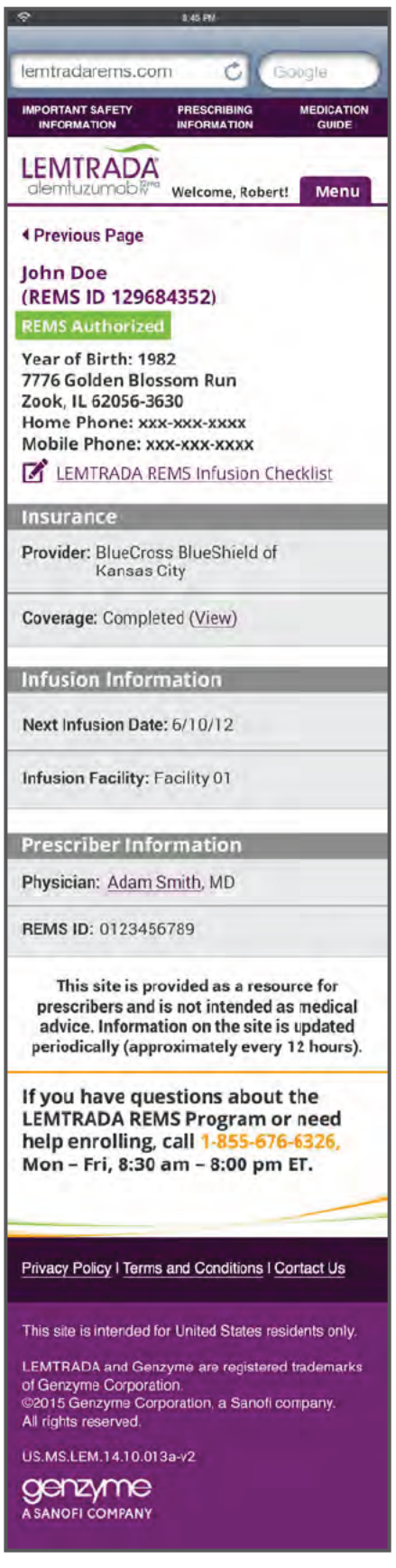
LEMTRADA REMS Mobile - HCF Dashboard - Patient List, Tool Tip Expanded



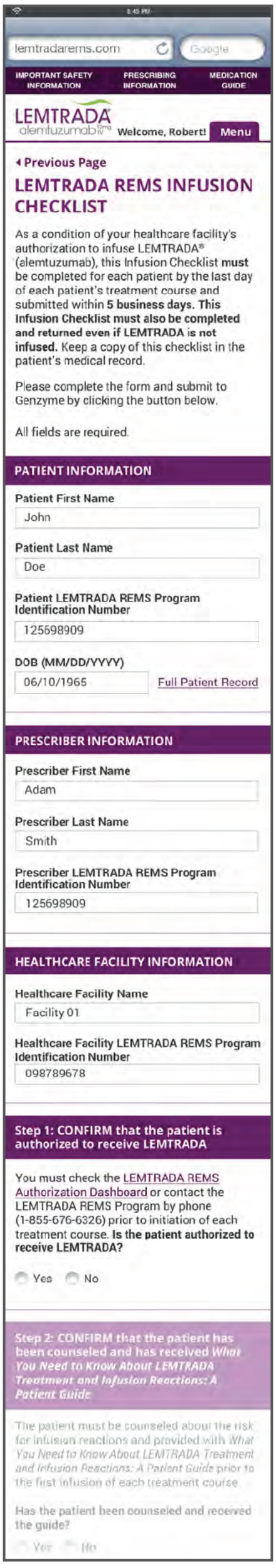
LEMTRADA REMS Mobile - HCF Dashboard - Patient List, Alert Expanded



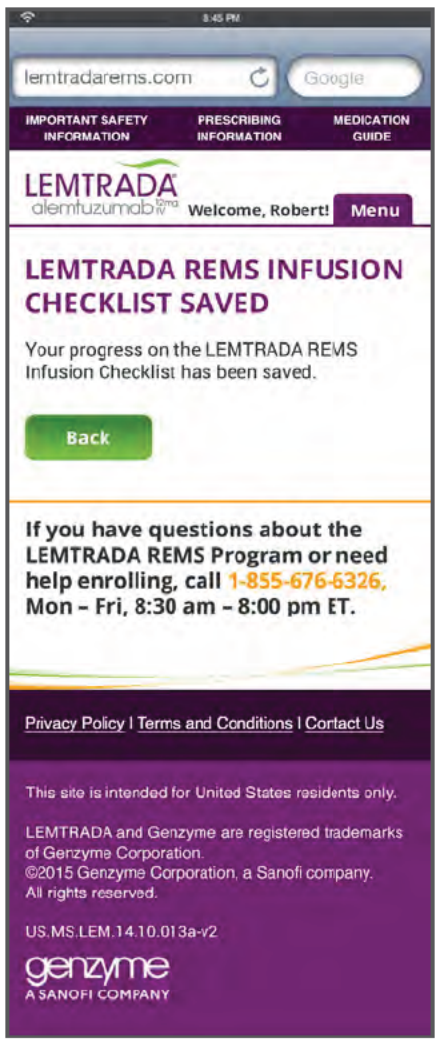
LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, Authorized, Before 1st Infusion



LEMTRADA REMS Mobile - Infusion Checklist Form - Default Save



LEMTRADA REMS Mobile - Infusion Checklist Form - Checklist Saved



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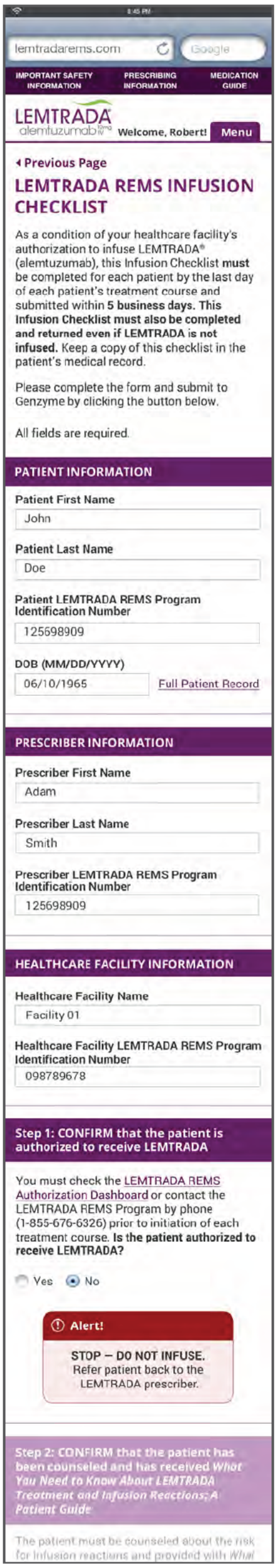

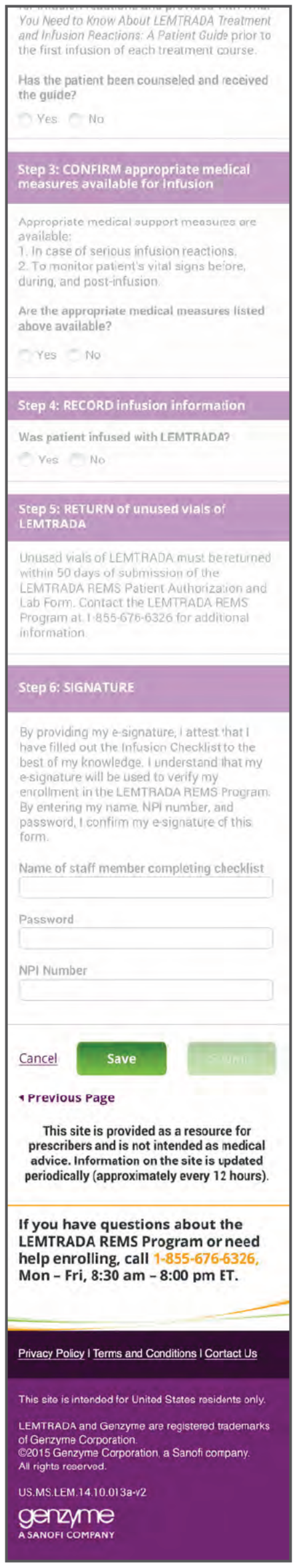

LEMTRADA REMS Mobile - Infusion Checklist Form - Error Save

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LEMTRADA alemtuzumab Welcome, Robert! Menu

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LEMTRADA REMS INFUSION CHECKLIST

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and submitted within **5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

Please complete the form and submit to Genzyme by clicking the button below.

All fields are required.

PATIENT INFORMATION

Patient First Name

Please enter patient's first name.

Patient Last Name

Please enter patient's last name.

Patient LEMTRADA REMS Program Identification Number

Please enter patient's LEMTRADA REMS Program Identification Number.

DOB (MM/DD/YYYY)

Full Patient Record

Please enter patient's valid date of birth.

PRESCRIBER INFORMATION

Prescriber First Name

Please enter prescriber's first name.

Prescriber Last Name

Please enter prescriber's last name.

Prescriber LEMTRADA REMS Program Identification Number

Please enter prescriber's LEMTRADA REMS Program Identification Number.

HEALTHCARE FACILITY INFORMATION

Healthcare Facility Name

Please enter healthcare facility name.

Healthcare Facility LEMTRADA REMS Program Identification Number

Please enter Healthcare Facility LEMTRADA REMS Program Identification Number.

Step 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must check the LEMTRADA REMS Authorization Dashboard or contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course. **Is the patient authorized to receive LEMTRADA?**

Yes No

Alert!

STOP – DO NOT INFUSE. Refer patient back to the LEMTRADA prescriber.

Step 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A*

Patient Guide

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course.

Has the patient been counseled and received the guide?

Yes No

Alert!

STOP – Provide the patient guide. Proceed to the next question after the patient has received the guide and has been counseled.

Step 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:
1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available?

Yes No

Alert!

STOP – DO NOT INFUSE until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information.

Step 4: RECORD infusion information

Was patient infused with LEMTRADA?

Yes No

Alert!

Proceed to Step 5.

Step 5: RETURN of unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Step 6: SIGNATURE

By providing my e-signature, I attest that I have filled out the Infusion Checklist to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program. By entering my name, NPI number, and password, I confirm my e-signature of this form.

Name of staff member completing checklist

Password

NPI Number

Cancel Save

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This site is provided as a resource for prescribers and is not intended as medical advice. Information on the site is updated periodically (approximately every 12 hours).

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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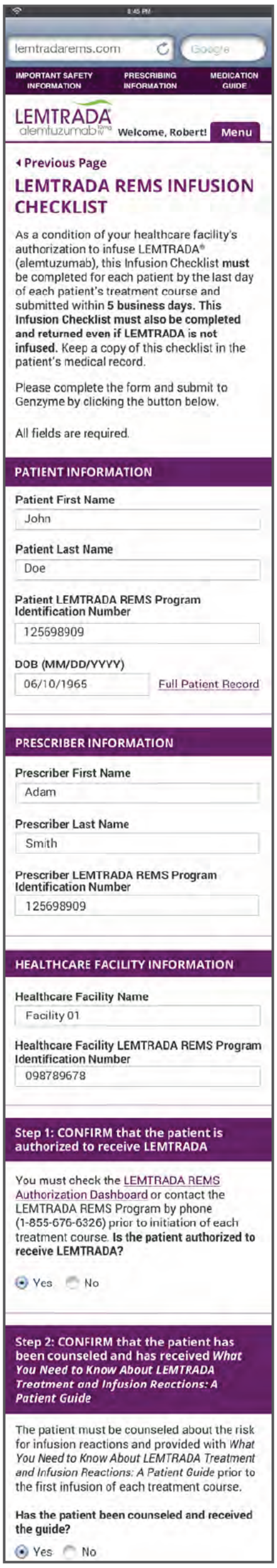
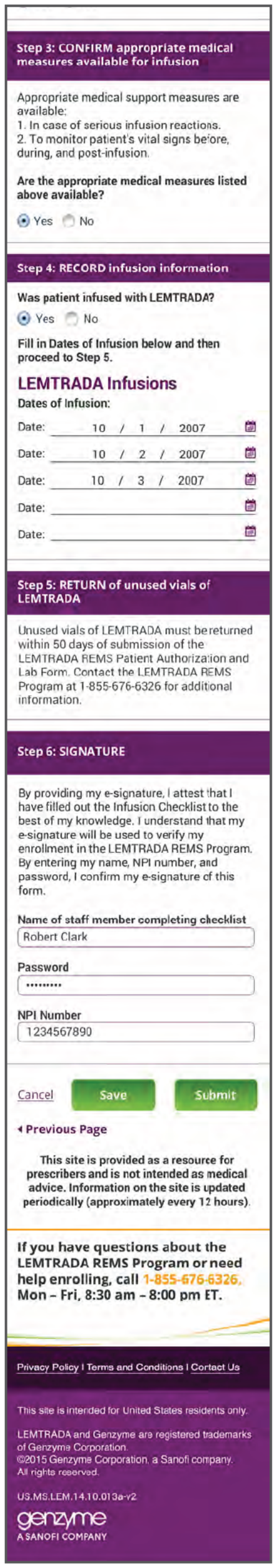
LEMTRADA REMS Mobile - Infusion Checklist Form - "Yes" Selected Save





LEMTRADA REMS Mobile - Infusion Checklist Form - "Yes" Selected, Infusion Dates Added Save

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LEMTRADA REMS INFUSION CHECKLIST

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and submitted within **5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

Please complete the form and submit to Genzyme by clicking the button below.

All fields are required.

PATIENT INFORMATION

Patient First Name
John

Patient Last Name
Doe

Patient LEMTRADA REMS Program Identification Number
125698909

DOB (MM/DD/YYYY)
06/10/1965 Full Patient Record

PRESCRIBER INFORMATION

Prescriber First Name
Adam

Prescriber Last Name
Smith

Prescriber LEMTRADA REMS Program Identification Number
125698909

HEALTHCARE FACILITY INFORMATION

Healthcare Facility Name
Facility 01

Healthcare Facility LEMTRADA REMS Program Identification Number
098789678

Step 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must check the LEMTRADA REMS Authorization Dashboard or contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course. **Is the patient authorized to receive LEMTRADA?**

(•) Yes ( ) No

Step 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course.

Has the patient been counseled and received the guide?

(•) Yes ( ) No

Step 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:
1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available?

(•) Yes ( ) No

Step 4: RECORD infusion information

Was patient infused with LEMTRADA?

(•) Yes ( ) No

Fill in Dates of Infusion below and then proceed to Step 5.

LEMTRADA Infusions

Dates of Infusion:

Date: 10 / 1 / 2007
Date: 10 / 2 / 2007
Date: 10 / 3 / 2007
Date: 10 / 4 / 2007
Date: 10 / 5 / 2007

Step 5: RETURN of unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Step 6: SIGNATURE

By providing my e-signature, I attest that I have filled out the Infusion Checklist to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program. By entering my name, NPI number, and password, I confirm my e-signature of this form.

Name of staff member completing checklist
Robert Clark

Password
••••••••

NPI Number
1234567890

Cancel | Save | Submit

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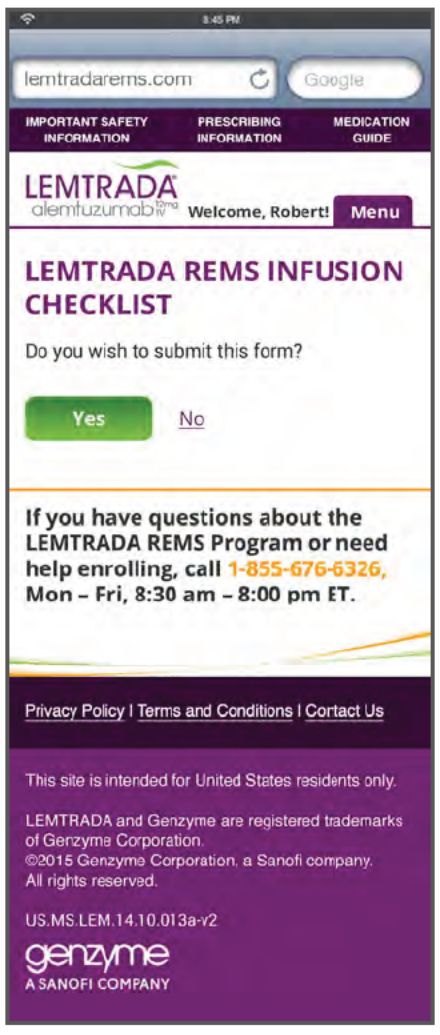
LEMTRADA REMS Mobile - Infusion Checklist Form - Submit Confirmation



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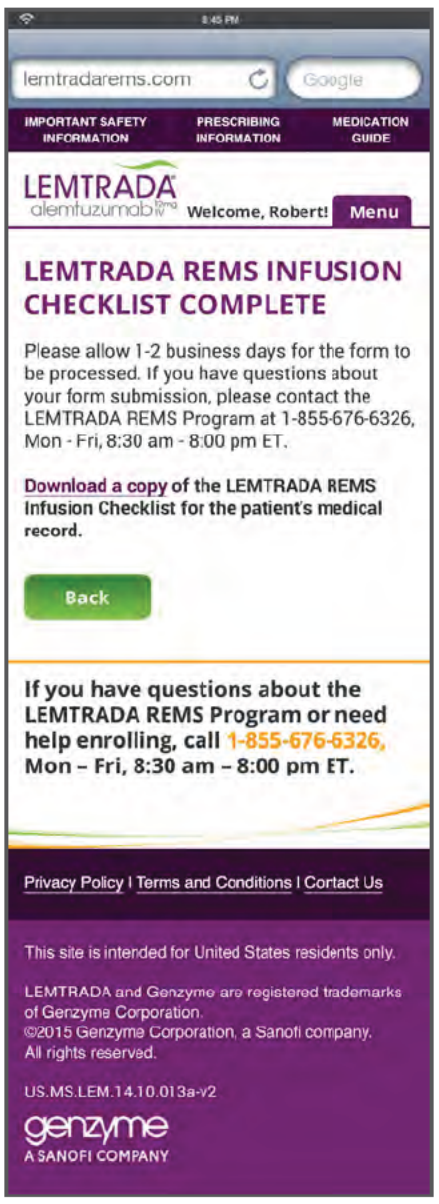


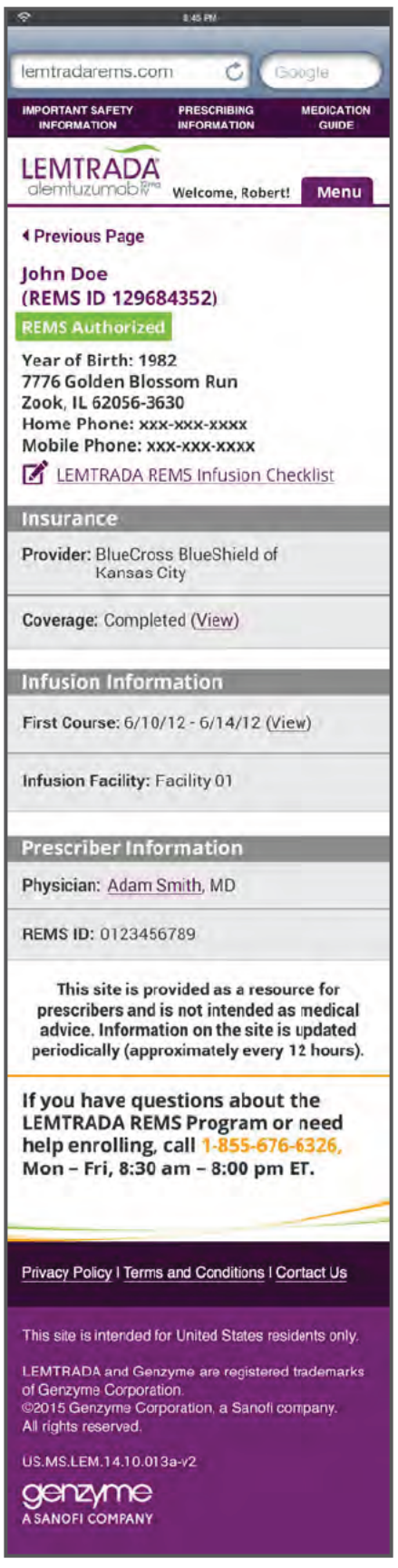
LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, Checklist Saved



LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, 1st Infusion Checklist Completed



LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, After 1st Infusion



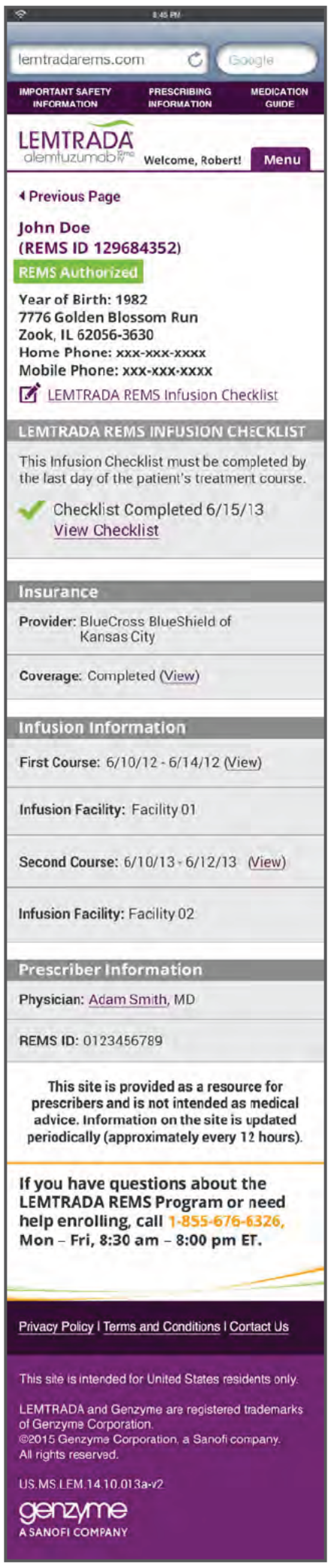
LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, Alert Expanded



LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, 2 Alerts Expanded



LEMTRADA REMS Mobile - HCF Dashboard - Single Patient Detail, 2nd Infusion Checklist Completed



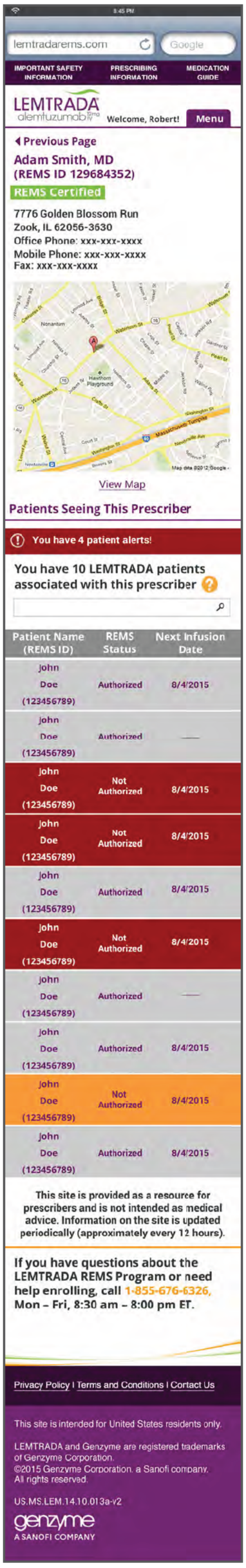
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers



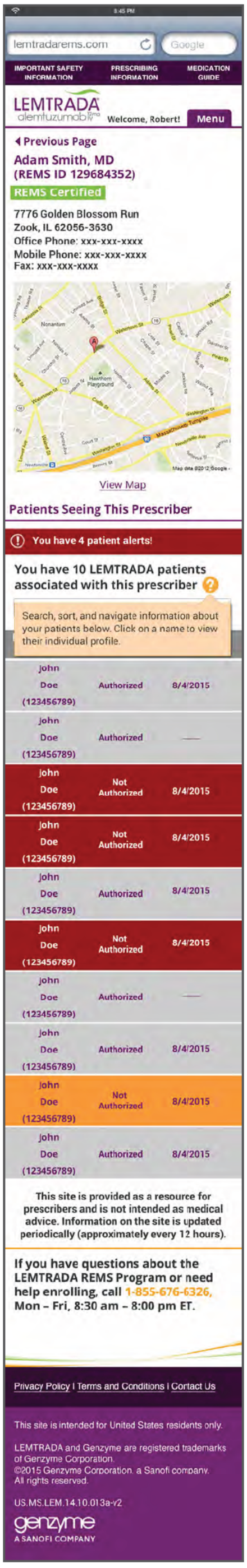
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers, Tool Tip Expanded



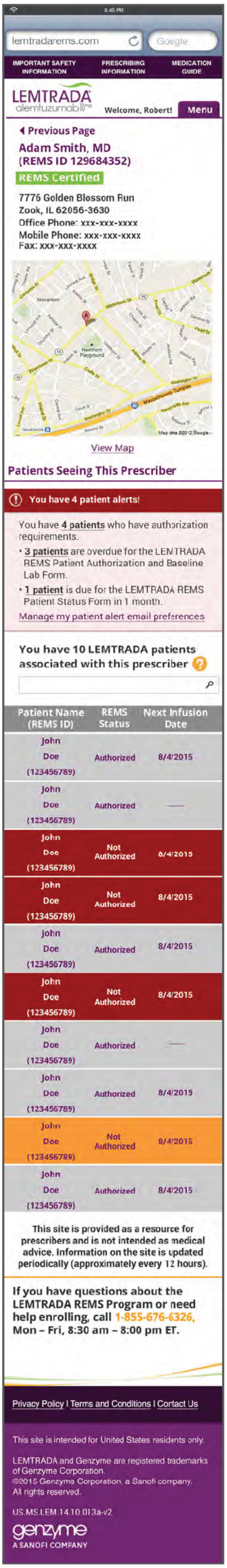
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers, Single Prescriber Detail, Certified



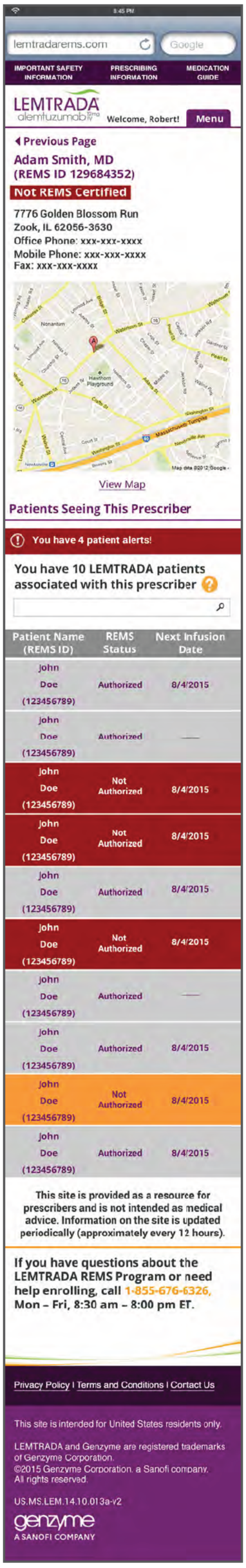
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers, Single Prescriber Detail, Tool Tip Expanded



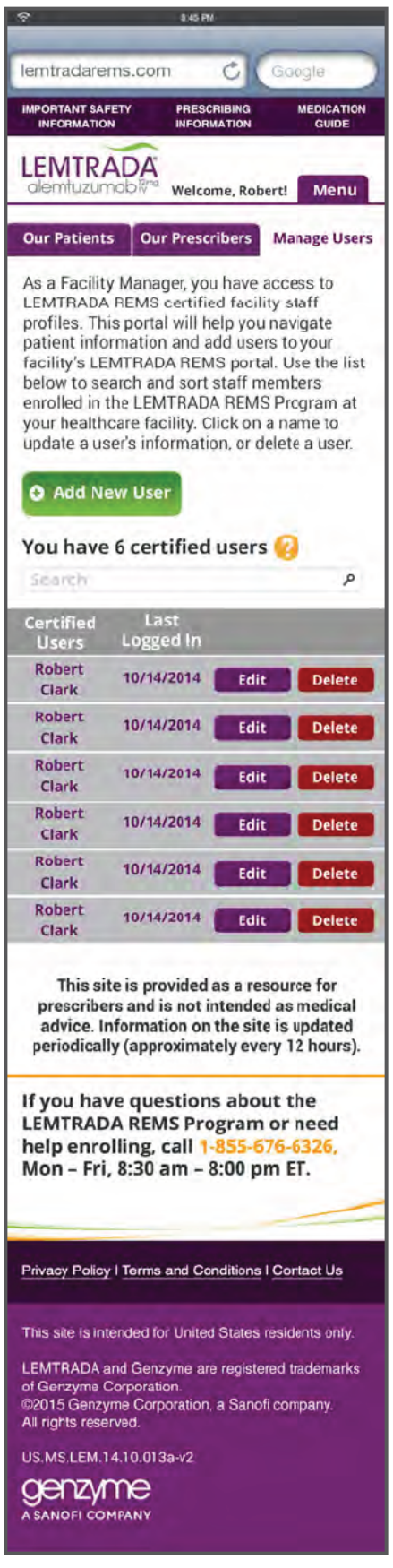
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers, Single Prescriber Detail, Alert Expanded



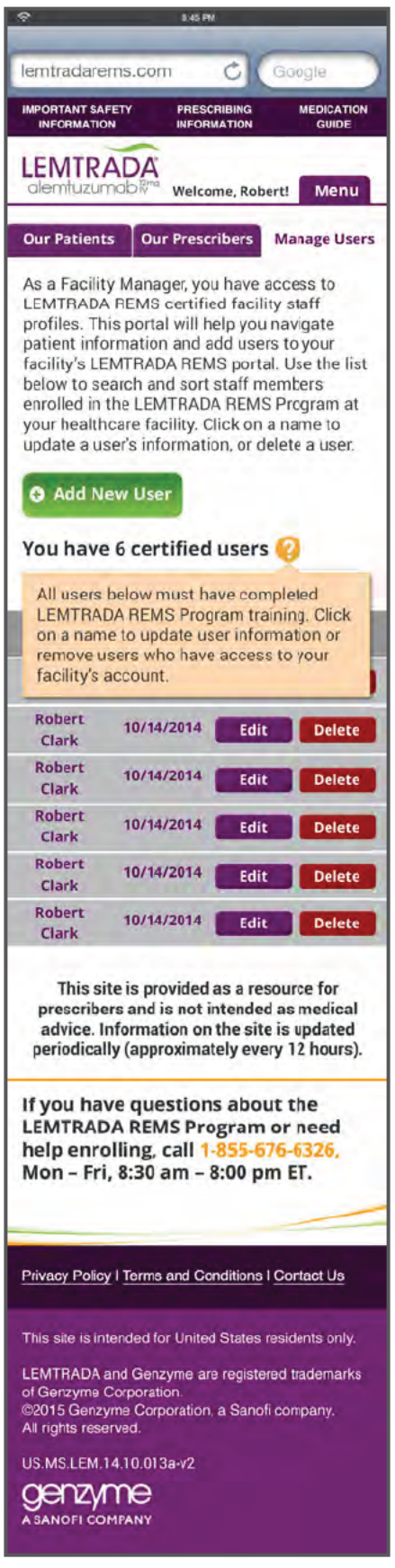
LEMTRADA REMS Mobile - HCF Dashboard - Prescribers, Single Prescriber Detail, Not Certified



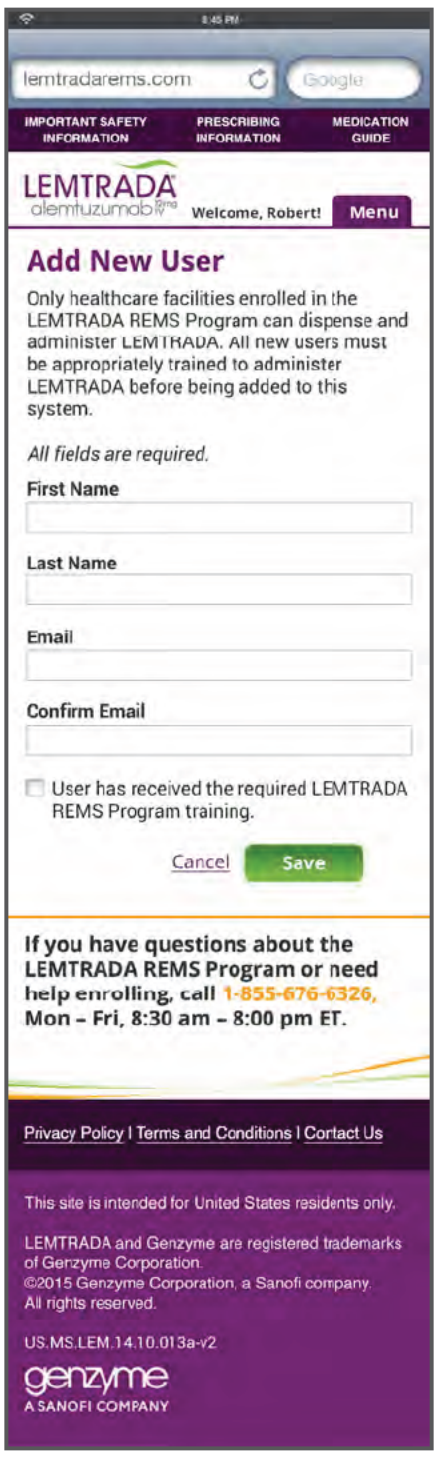
LEMTRADA REMS Mobile - HCF Dashboard - Manage Users



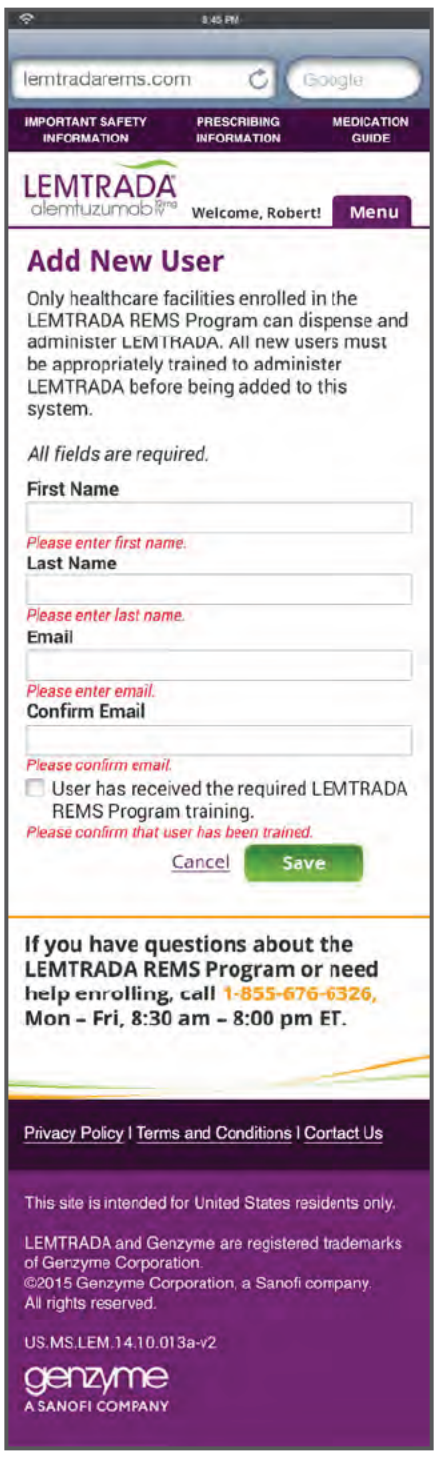
LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Tool Tip Expanded



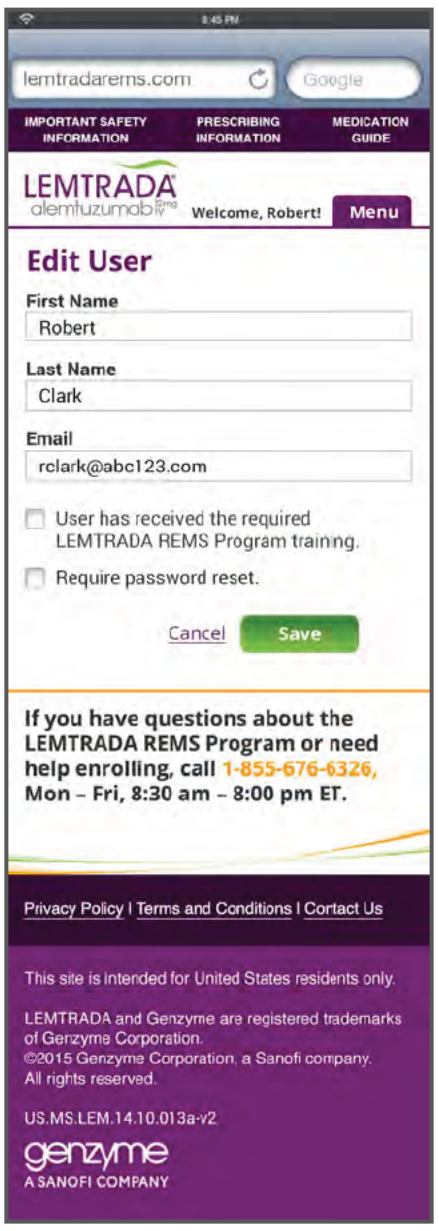
LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Add New User



LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Add New User, Error



LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Edit User



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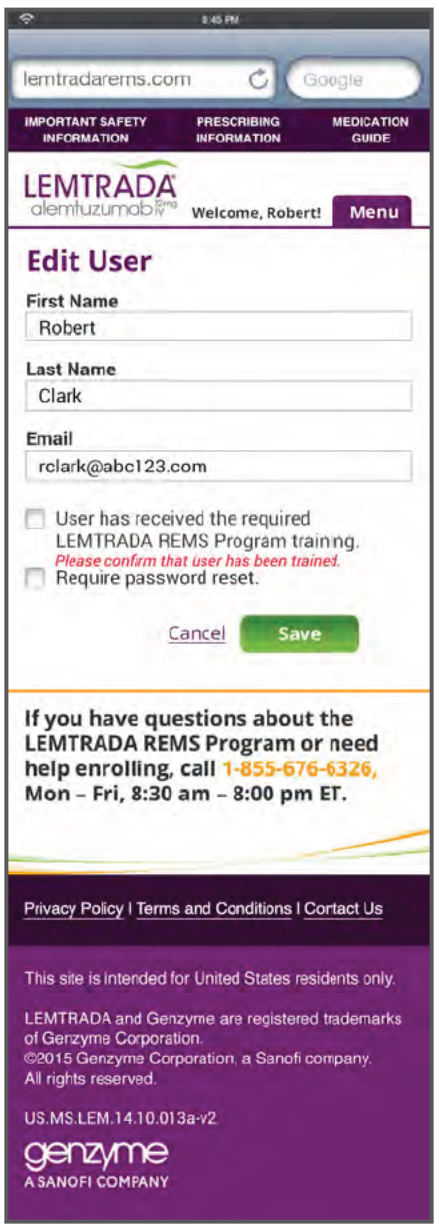
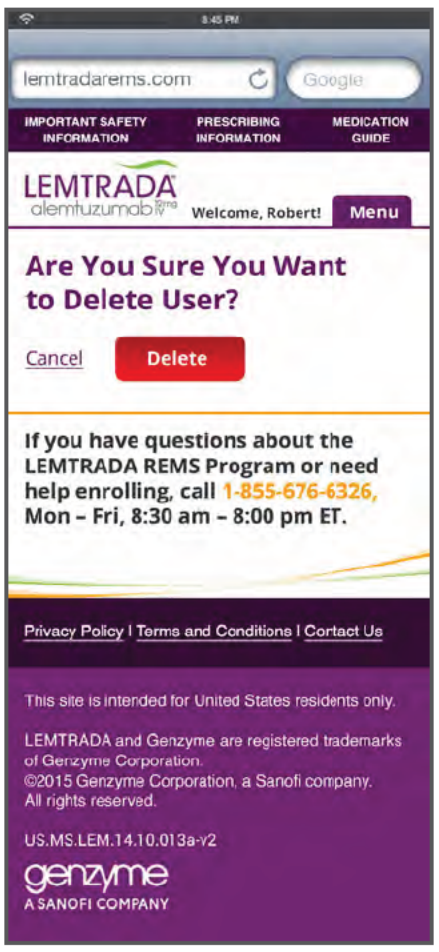
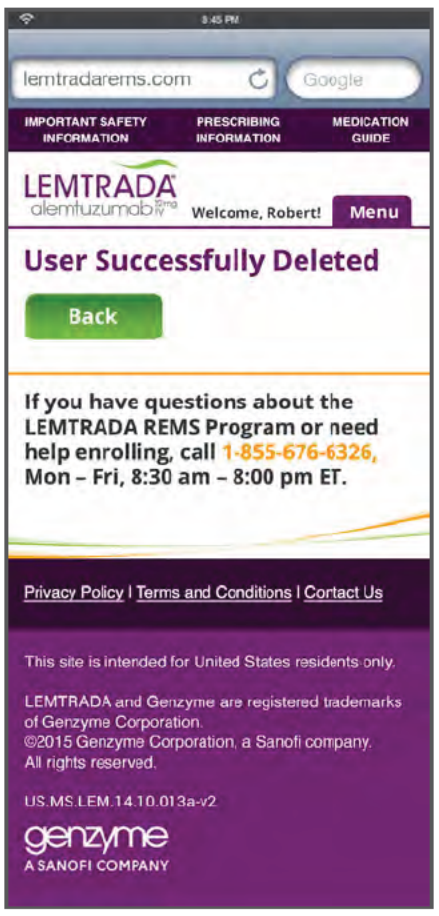


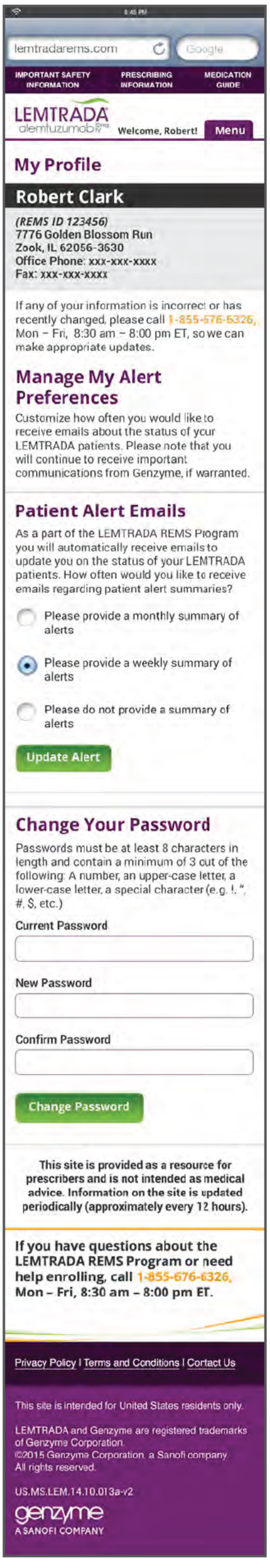
LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Delete User



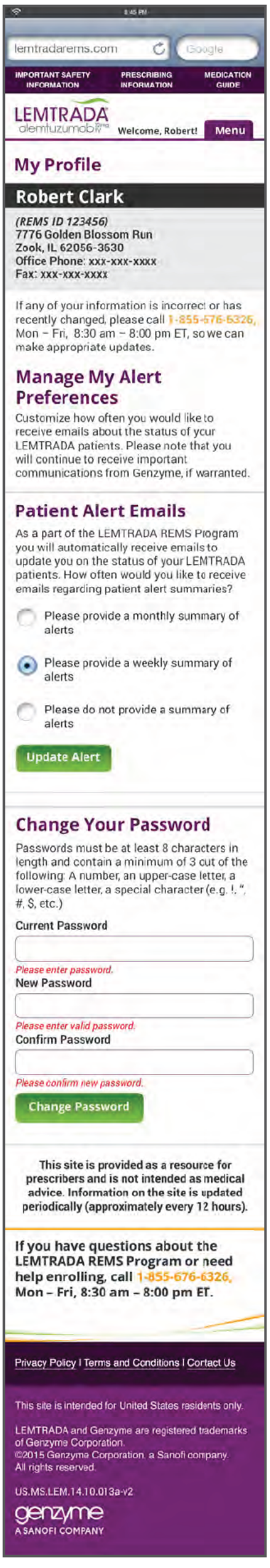
LEMTRADA REMS Mobile - HCF Dashboard - Manage Users, Delete User, Confirmation



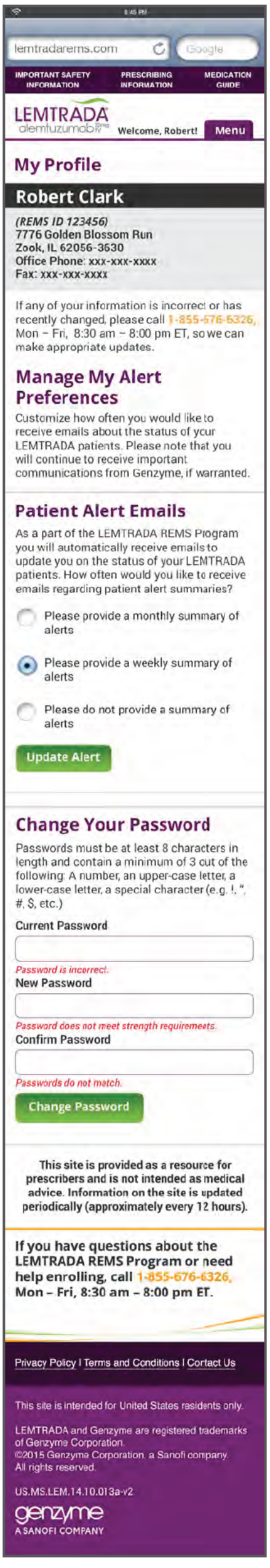
LEMTRADA REMS Mobile - HCF Dashboard - My Profile



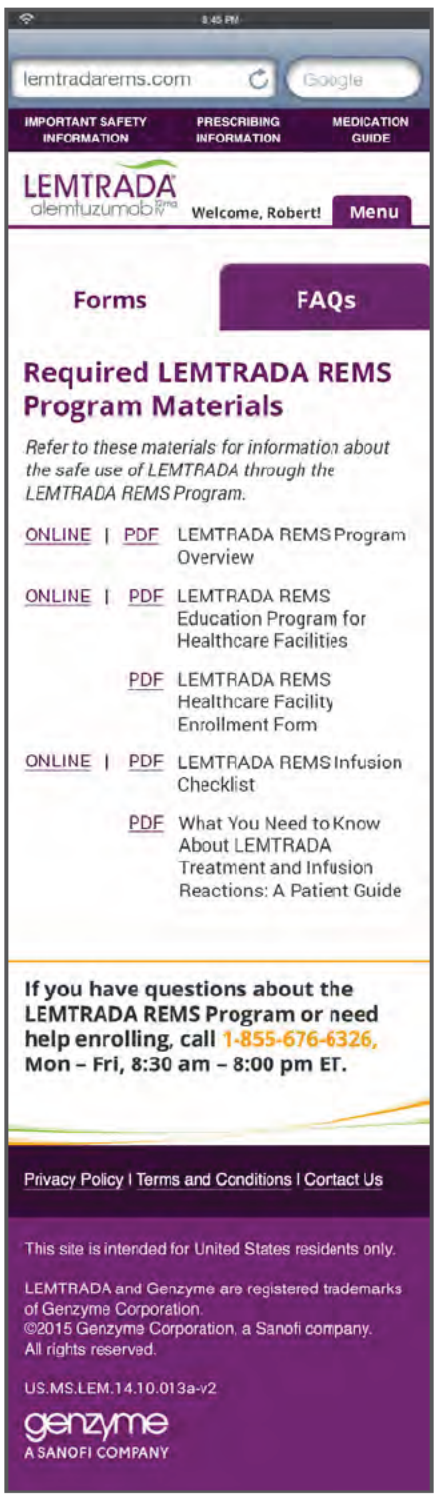
LEMTRADA REMS Mobile - HCF Dashboard - My Profile, Error



LEMTRADA REMS Mobile - HCF Dashboard - My Profile, Password Strength Error



LEMTRADA REMS Mobile - HCF Dashboard - Support, Forms



LEMTRADA REMS Mobile - Infusion Checklist Form - Default

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IMPORTANT SAFETY INFORMATION | PRESCRIBING INFORMATION | MEDICATION GUIDE

LEMTRADA alemtuzumab 12mg/1.2mL IV

Welcome, Robert! Menu

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LEMTRADA REMS INFUSION CHECKLIST

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and submitted within **5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

Please complete the form and submit to Genzyme by clicking the button below.

All fields are required.

PATIENT INFORMATION

Patient First Name
John

Patient Last Name
Doe

Patient LEMTRADA REMS Program Identification Number
125698909

DOB (MM/DD/YYYY)
06/10/1965 Full Patient Record

PRESCRIBER INFORMATION

Prescriber First Name
Adam

Prescriber Last Name
Smith

Prescriber LEMTRADA REMS Program Identification Number
125698909

HEALTHCARE FACILITY INFORMATION

Healthcare Facility Name
Facility 01

Healthcare Facility LEMTRADA REMS Program Identification Number
098789678

Step 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must check the LEMTRADA REMS Authorization Dashboard or contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course. **Is the patient authorized to receive LEMTRADA?**

Yes No

Step 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course.

Has the patient been counseled and received the guide?

Yes No

Step 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:
1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available?

Yes No

Step 4: RECORD infusion information

Was patient infused with LEMTRADA?

Yes No

Step 5: RETURN of unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Step 6: SIGNATURE

By providing my e-signature, I attest that I have filled out the Infusion Checklist to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program. By entering my name, NPI number, and password, I confirm my e-signature of this form.

Name of staff member completing checklist

Password

NPI Number

Cancel Submit

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This site is provided as a resource for prescribers and is not intended as medical advice. Information on the site is updated periodically (approximately every 12 hours).

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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US.MS.LEM.14.10.013a-v2

genzyme
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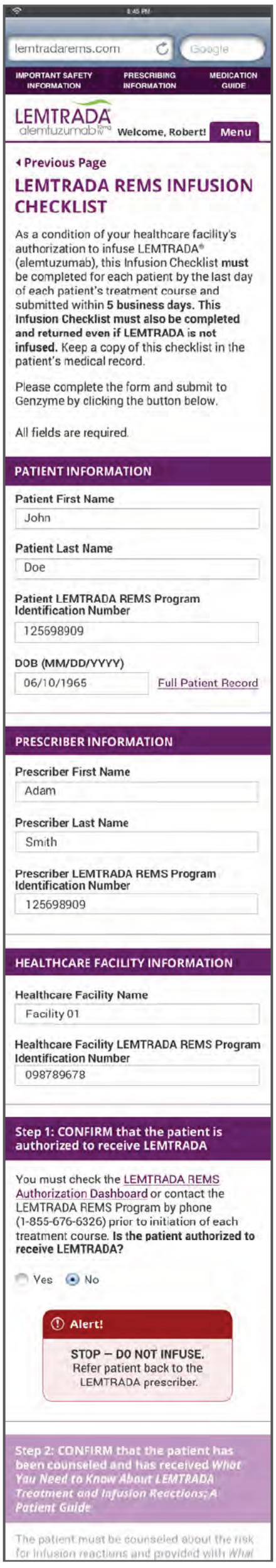
LEMTRADA REMS Mobile - Infusion Checklist Form - "No" Selected



LEMTRADA REMS Mobile - Infusion Checklist Form - Error

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LEMTRADA alemtuzumab | Welcome, Robert! | Menu

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LEMTRADA REMS INFUSION CHECKLIST

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Please complete the form and submit to Genzyme by clicking the button below.

All fields are required.

PATIENT INFORMATION

Patient First Name

Please enter patient's first name.

Patient Last Name

Please enter patient's last name.

Patient LEMTRADA REMS Program Identification Number

Please enter patient's LEMTRADA REMS Program Identification Number.

DOB (MM/DD/YYYY)

Full Patient Record

Please enter patient's valid date of birth.

PRESCRIBER INFORMATION

Prescriber First Name

Please enter prescriber's first name.

Prescriber Last Name

Please enter prescriber's last name.

Prescriber LEMTRADA REMS Program Identification Number

Please enter prescriber's LEMTRADA REMS Program Identification Number.

HEALTHCARE FACILITY INFORMATION

Healthcare Facility Name

Please enter healthcare facility name.

Healthcare Facility LEMTRADA REMS Program Identification Number

Please enter Healthcare Facility LEMTRADA REMS Program Identification Number.

Step 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must check the LEMTRADA REMS Authorization Dashboard or contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course. **Is the patient authorized to receive LEMTRADA?**

Yes No

Alert!

STOP – DO NOT INFUSE. Refer patient back to the LEMTRADA prescriber.

Step 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course.

Has the patient been counseled and received the guide?

Yes No

Alert!

STOP – Provide the patient guide. Proceed to the next question after the patient has received the guide and has been counseled.

Step 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:
1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available?

Yes No

Alert!

STOP – DO NOT INFUSE until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information.

Step 4: RECORD infusion information

Was patient infused with LEMTRADA?

Yes No

Alert!

Proceed to Step 5.

Step 5: RETURN of unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Step 6: SIGNATURE

By providing my e-signature, I attest that I have filled out the Infusion Checklist to the best of my knowledge. I understand that my e-signature will be used to verify my enrollment in the LEMTRADA REMS Program. By entering my name, NPI number, and password, I confirm my e-signature of this form.

Name of staff member completing checklist

Please enter name of staff member completing checklist.

Password

Please enter password.

NPI Number

Please enter a valid NPI number.

Cancel

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Patient Guide

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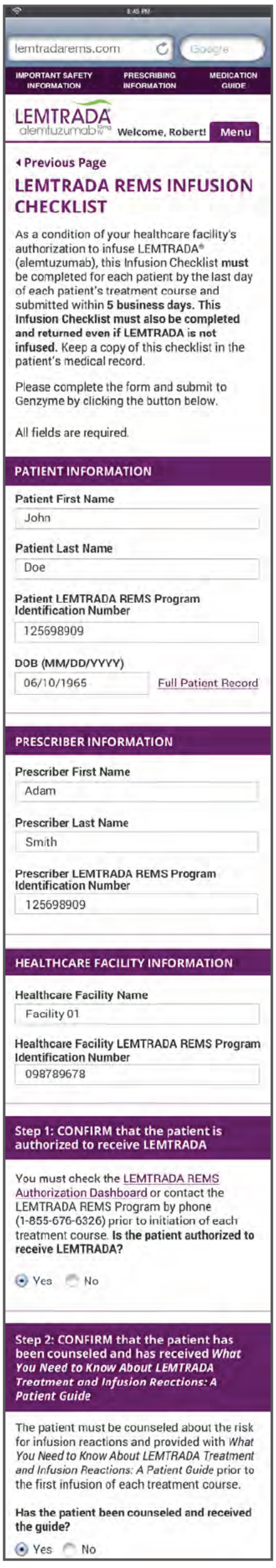
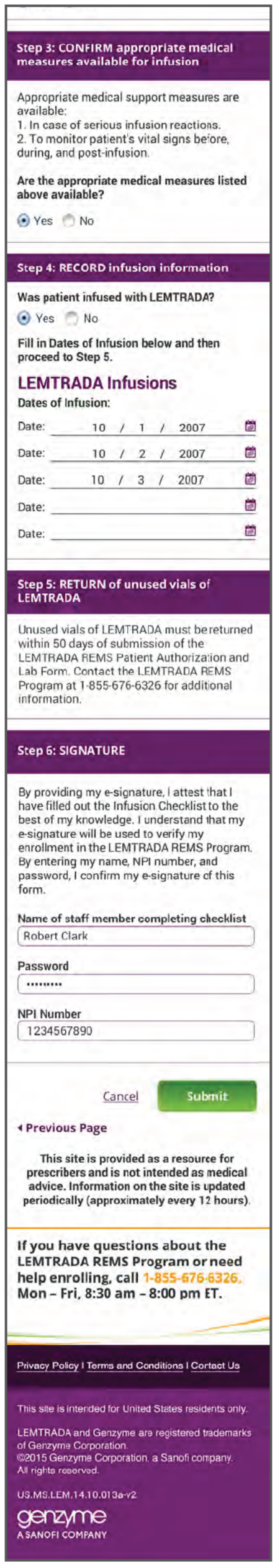
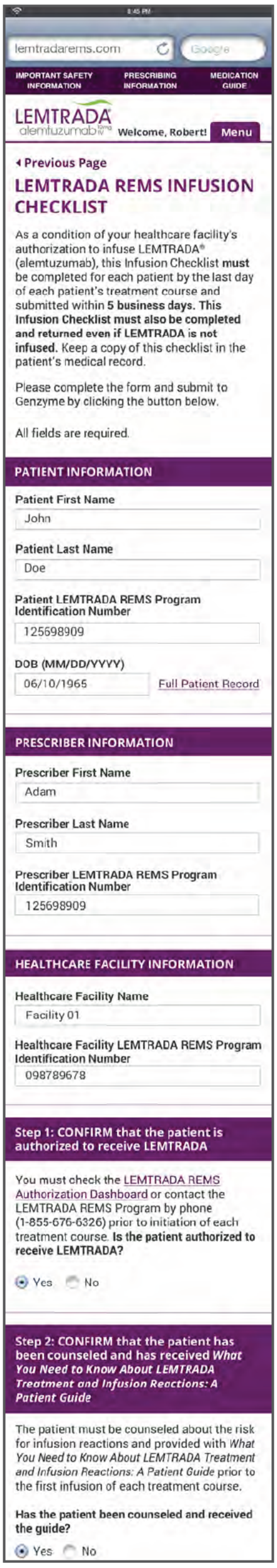
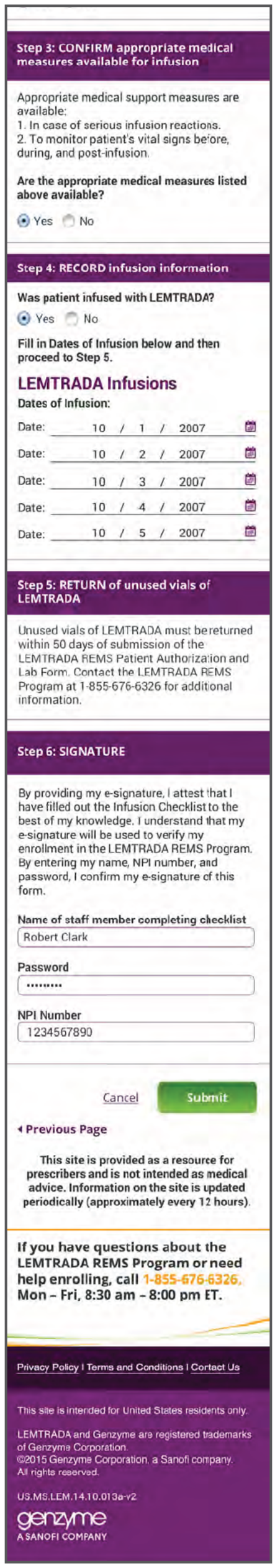
LEMTRADA REMS Mobile - Infusion Checklist Form - "Yes" Selected



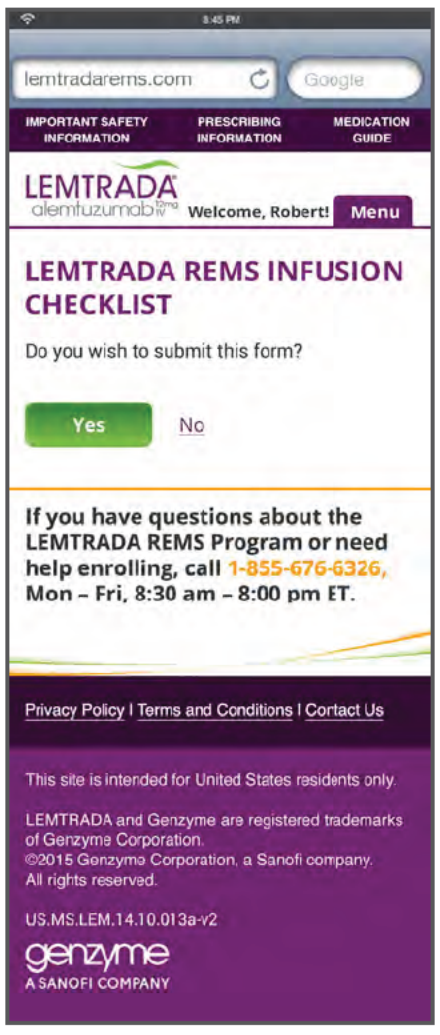


LEMTRADA REMS Mobile - Infusion Checklist Form - "Yes" Selected, Infusion Dates Added

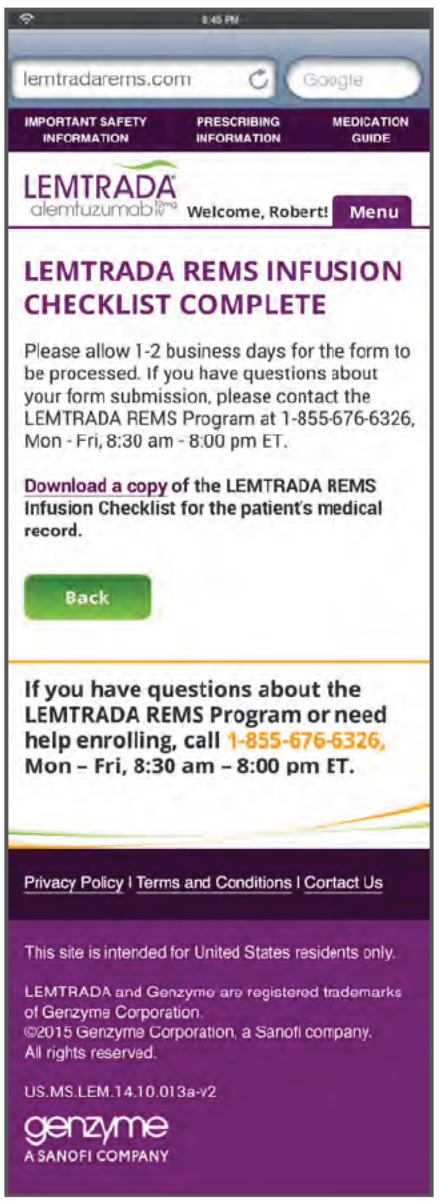




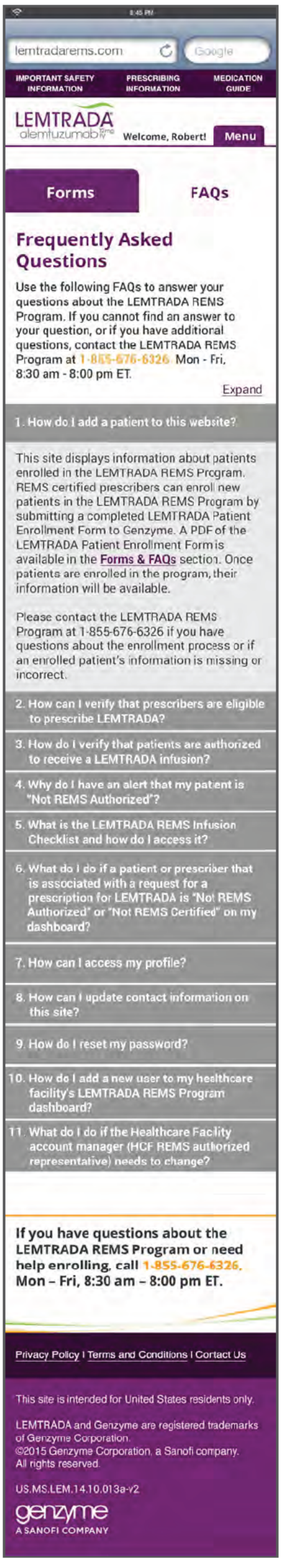
LEMTRADA REMS Mobile - Infusion Checklist Form - Submit Confirmation



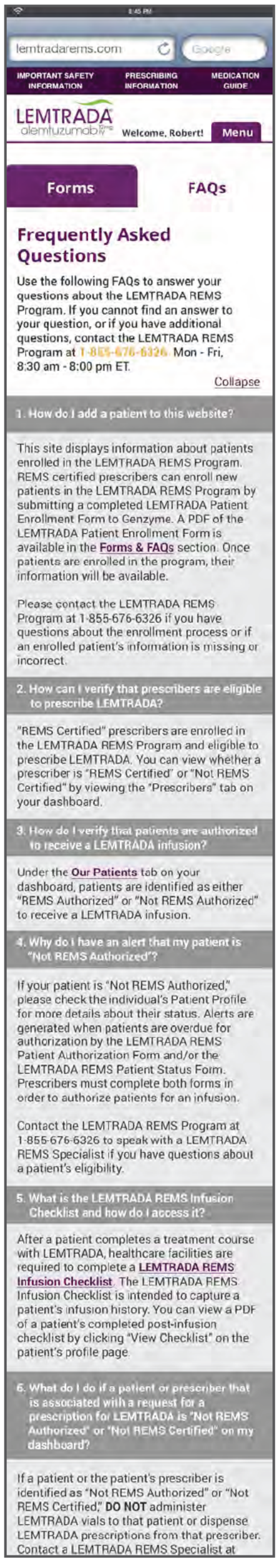
LEMTRADA REMS Mobile - Infusion Checklist Form - Confirmation

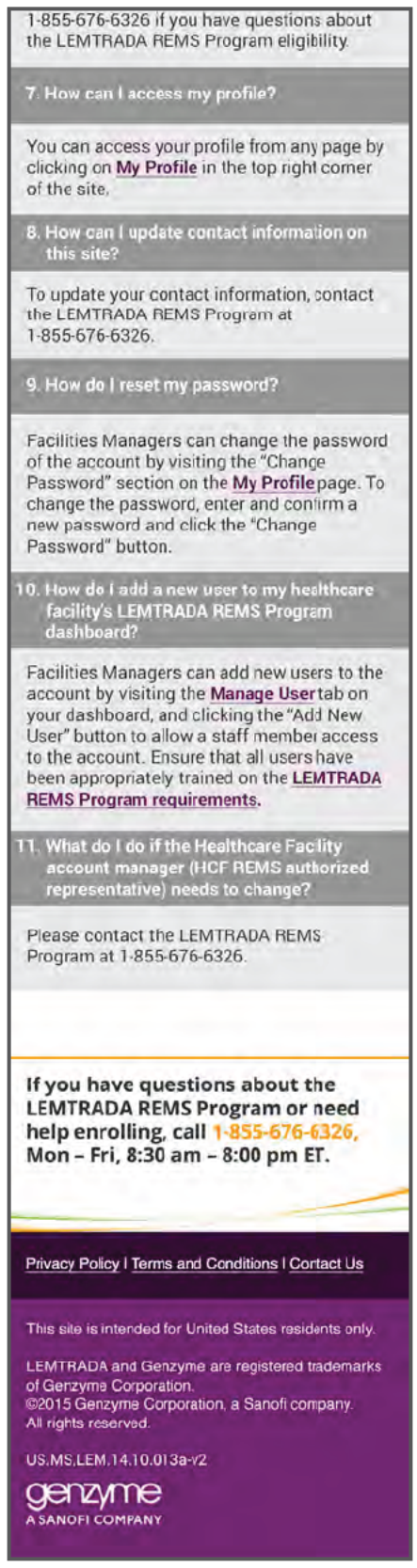


LEMTRADA REMS Mobile - HCF Dashboard - Support, FAQs

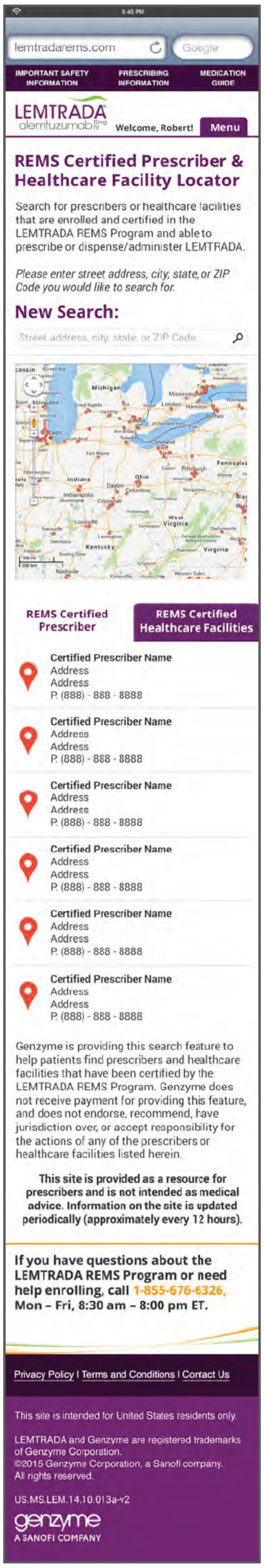


LEMTRADA REMS Mobile - HCF Dashboard - Support, FAQs Expanded





LEMTRADA REMS Mobile - HCF Dashboard - REMS Certified Prescriber & Healthcare Facility Locator



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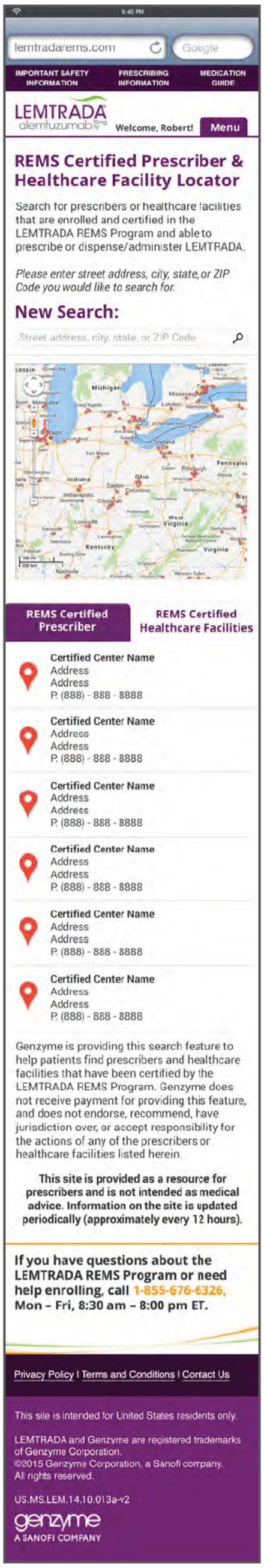
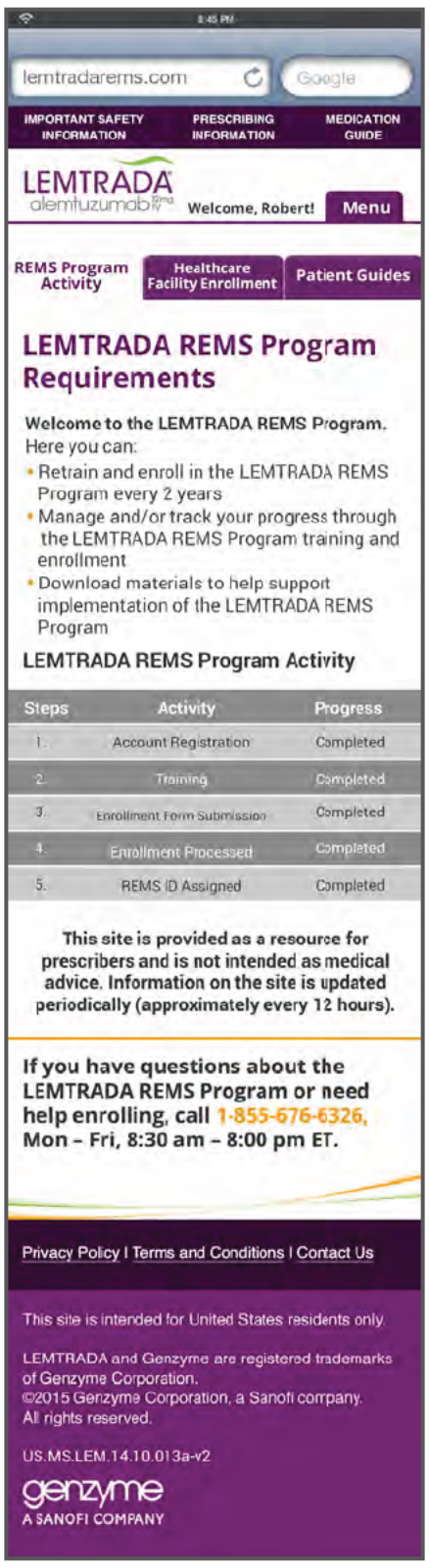
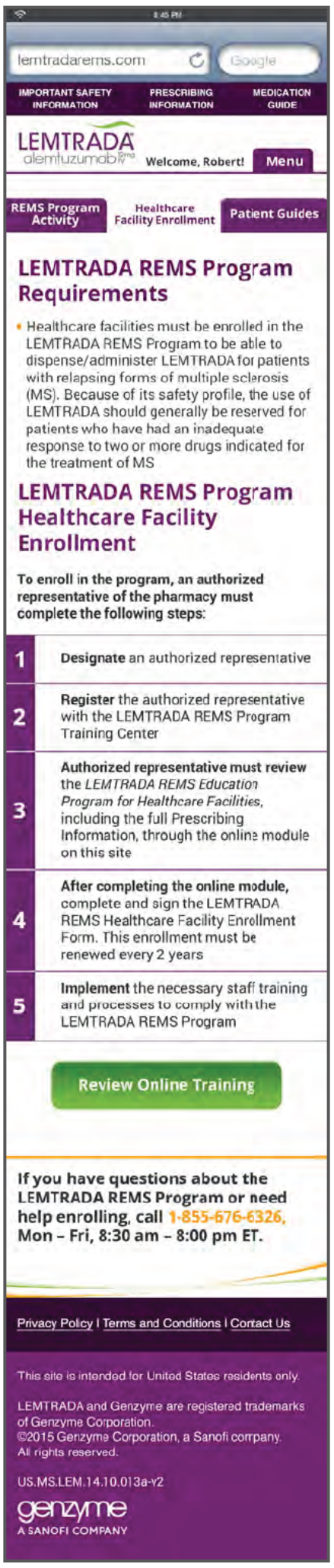


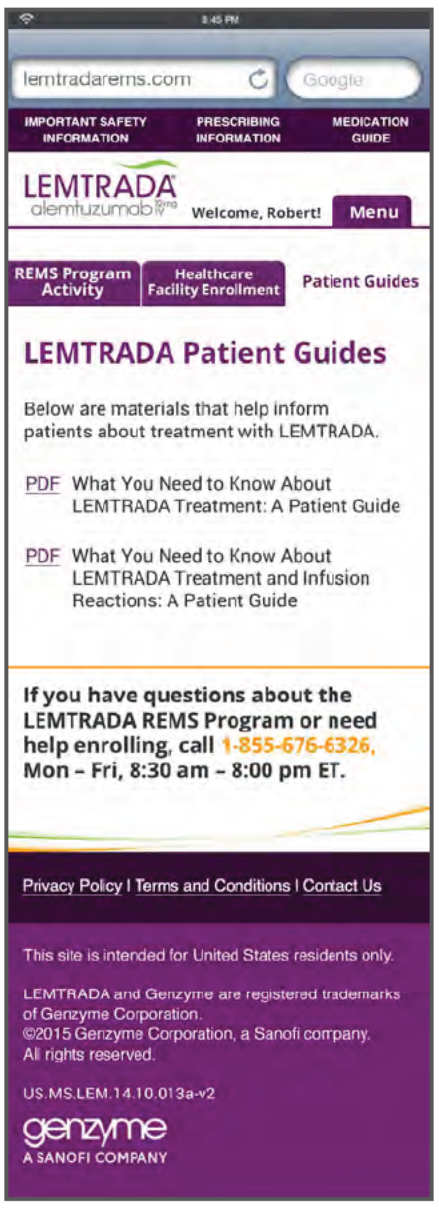
LEMTRADA REMS Mobile - HCF Dashboard - About REMS, REMS Program Activity



LEMTRADA REMS Mobile - HCF Dashboard - About REMS, HCF Enrollment



LEMTRADA REMS Mobile - HCF Dashboard - About REMS, Patient Guides



DASHBOARD PAGES FOR HCF USERS WHO ARE NON-MANAGERS

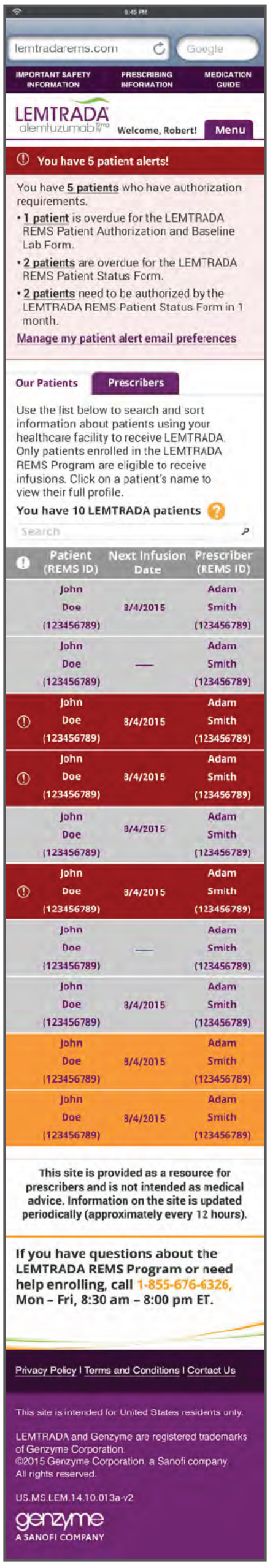
LEMTRADA REMS Mobile - HCF NON-MANAGER Dashboard - Patient List, Alert On



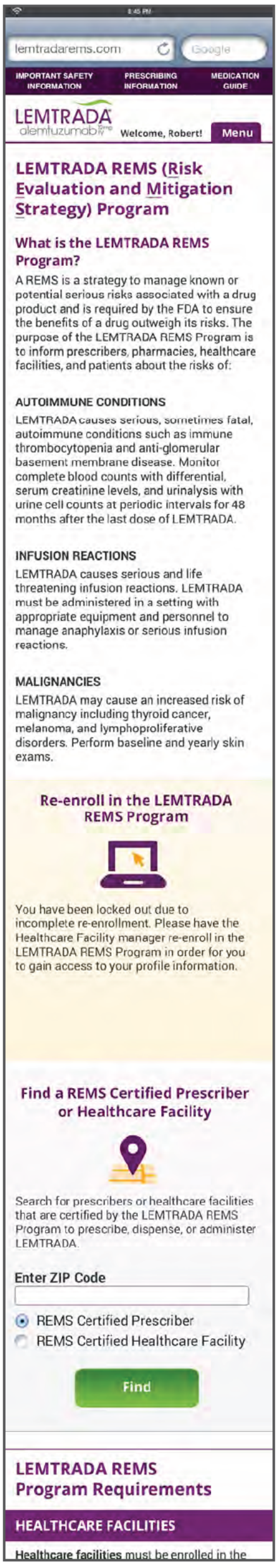
LEMTRADA REMS Mobile - HCF NON-MANAGER Dashboard - Patient List, Tool Tip Expanded

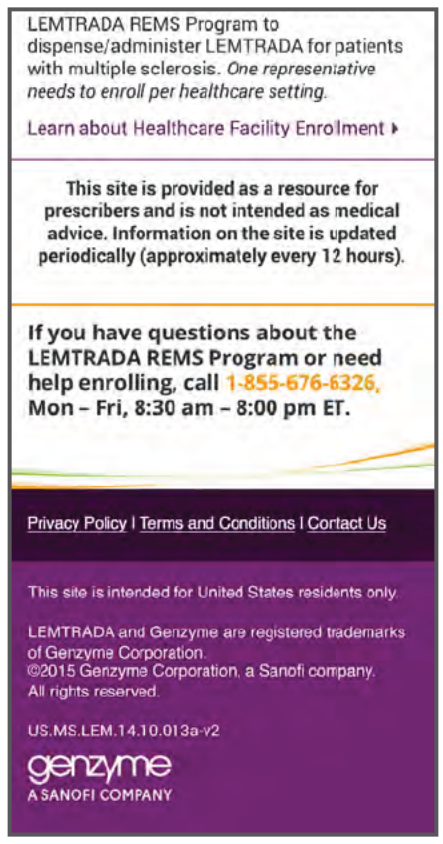


LEMTRADA REMS Mobile - HCF NON-MANAGER Dashboard - Patient List, Alert Expanded



LEMTRADA REMS Mobile - HCF User Dashboard - Re-enrollment Lockout





LEMTRADA REMS Mobile - HCF NON-MANAGER Dashboard - Prescribers



LEMTRADA REMS Mobile - HCF NON-MANAGER Dashboard - Prescribers, Tool Tip Expanded



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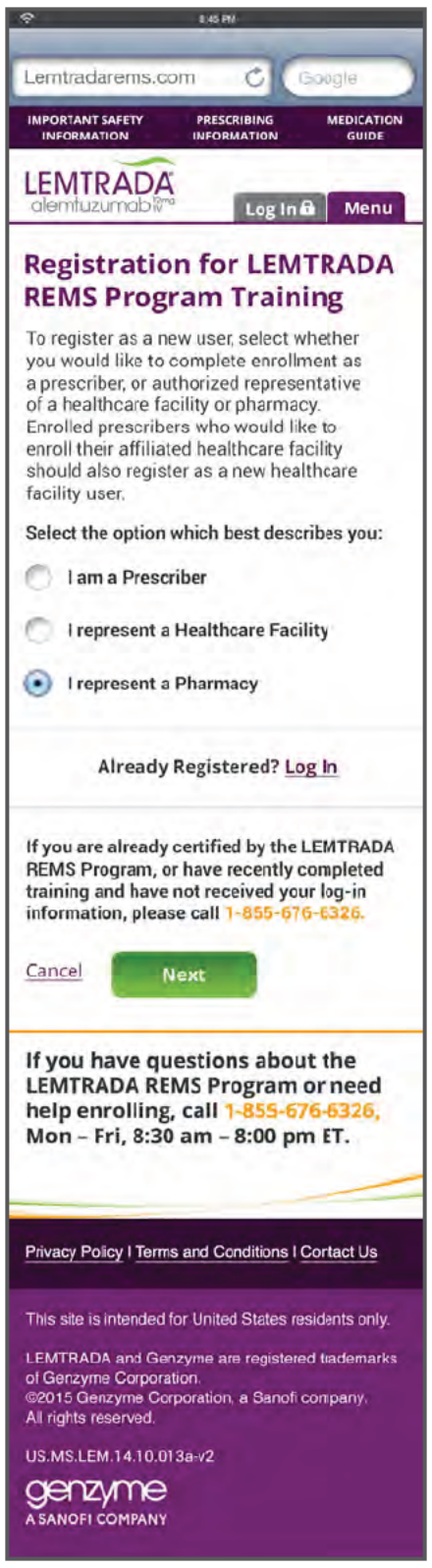
Pharmacy Pages Only

PHARMACY TRAINING PAGES

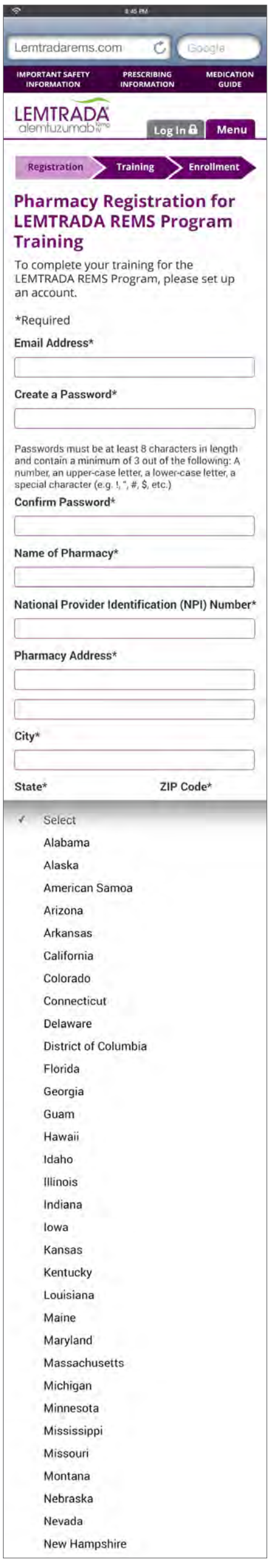
LEMTRADA REMS Mobile - Pharmacy Mobile Dashboard



LEMTRADA REMS Mobile - Pharmacy Registration



LEMTRADA REMS Mobile - Pharmacy Registration, State Selection



LEMTRADA REMS Mobile - Pharmacy Registration, Error



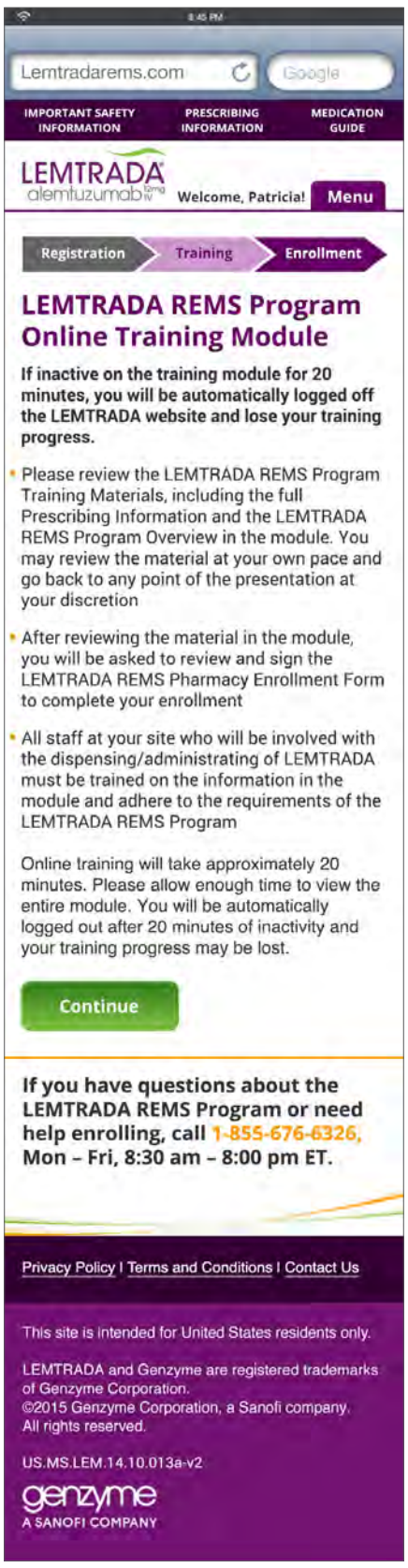
LEMTRADA REMS Mobile - Pharmacy Registration, Password Strength Error



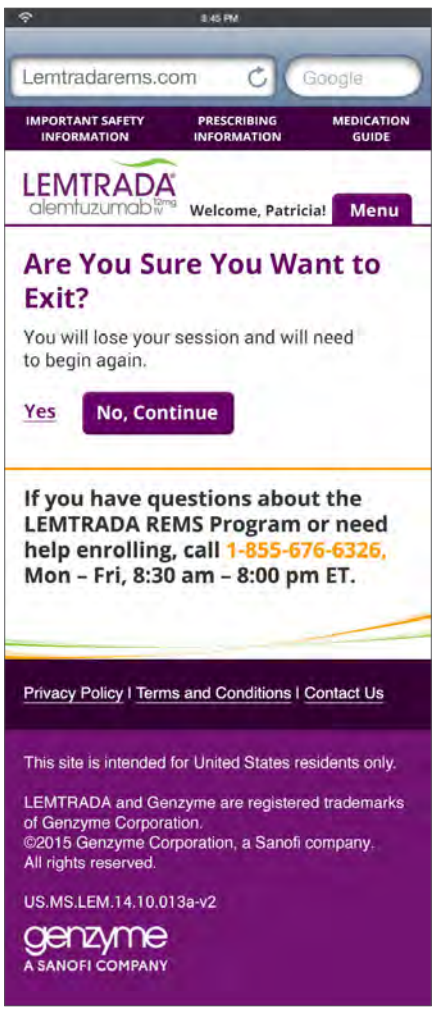
LEMTRADA REMS Mobile - Pharmacy Registration Confirmation



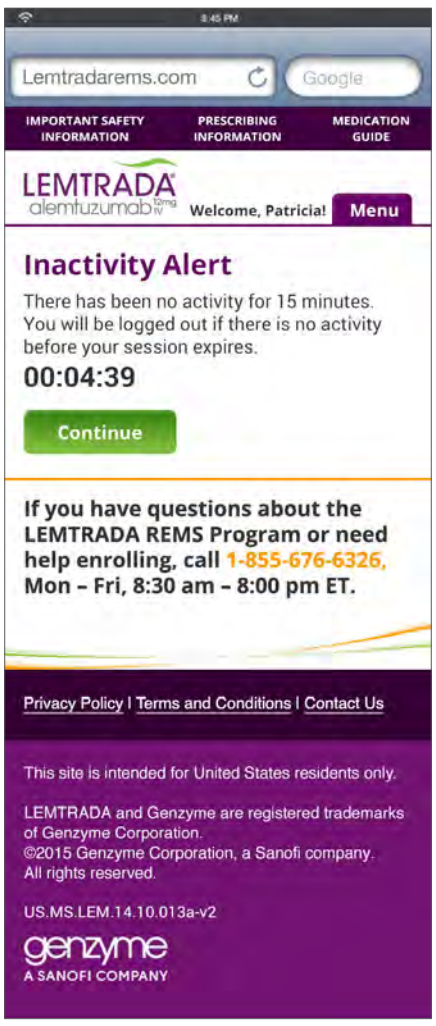
LEMTRADA REMS Mobile - Pharmacy, Training Module



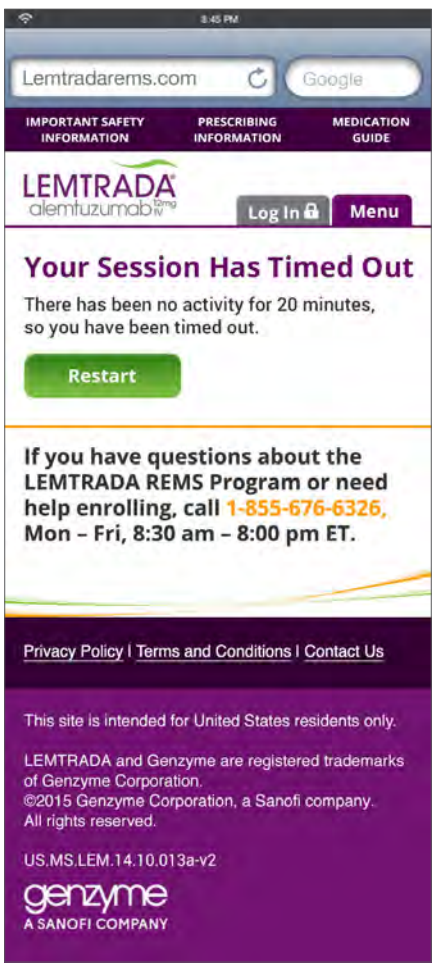
LEMTRADA REMS Mobile - Pharmacy, Training Module Exit



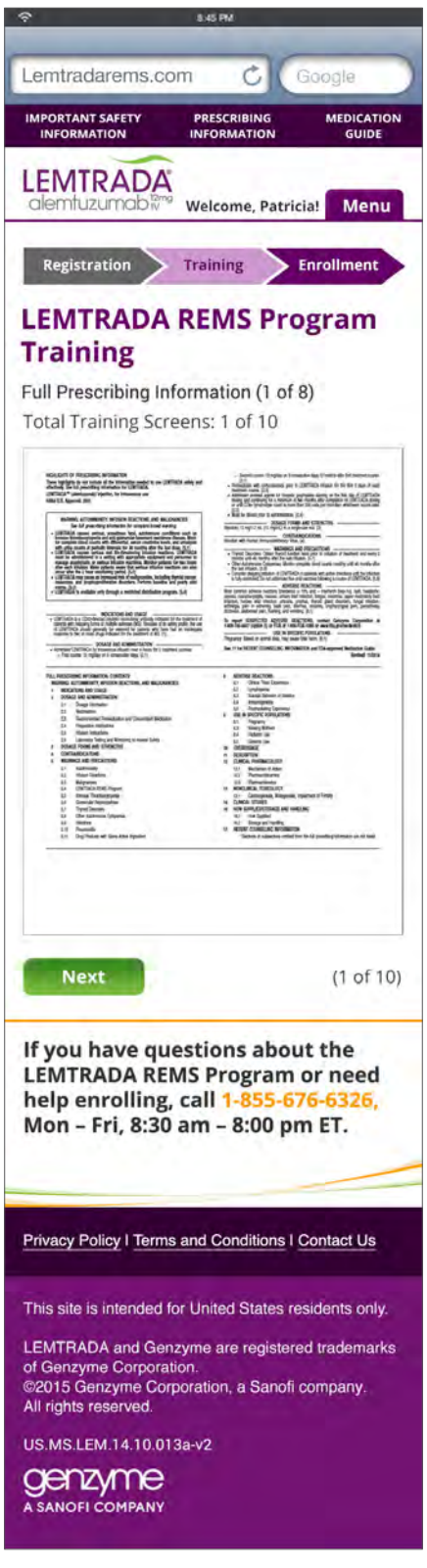
LEMTRADA REMS Mobile - Pharmacy, Training Module Timer



LEMTRADA REMS Mobile - Pharmacy, Training Module Timed Out



LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 1



LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 2



LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 3




8:45 PM
Lemtradarems.com
Google
IMPORTANT SAFETY INFORMATION
PRESCRIBING INFORMATION
MEDICATION GUIDE
LEMTRADA
alemtuzumab 12mg IV
Welcome, Patricia!
Menu
Registration
Training
Enrollment
LEMTRADA REMS Program Training
Full Prescribing Information (4 of 8)
Total Training Screens: 4 of 10
Previous
Next
(4 of 10)
If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.
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8:45 PM
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Google
IMPORTANT SAFETY INFORMATION
PRESCRIBING INFORMATION
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LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 6



LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 7



LEMTRADA REMS Mobile - Pharmacy, Training - PI Page 8



LEMTRADA REMS Mobile - Pharmacy, Training - Program Overview Page 1



LEMTRADA REMS Mobile - Pharmacy, Training - Program Overview Page 2



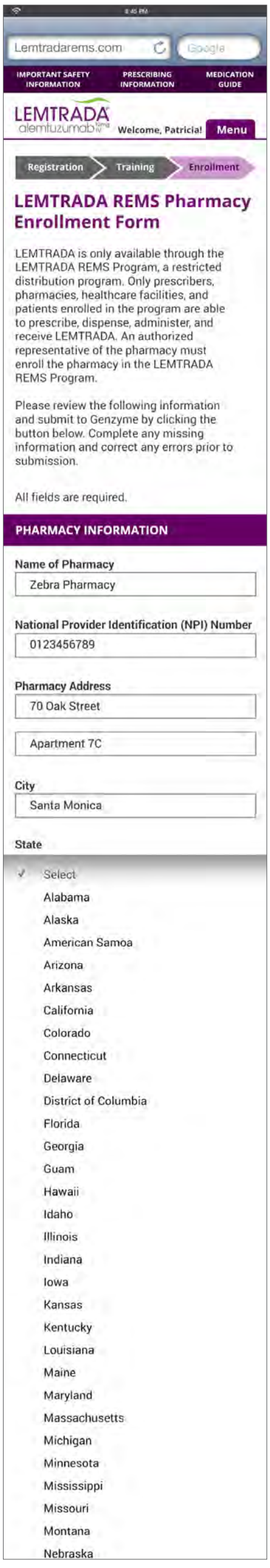
LEMTRADA REMS Mobile - Pharmacy, Training Confirmation



LEMTRADA REMS Mobile - Pharmacy Enrollment



LEMTRADA REMS Mobile - Pharmacy Enrollment, State Selection



LEMTRADA REMS Mobile - Pharmacy Enrollment, Error

Lemtradarems.com

Google

IMPORTANT SAFETY INFORMATION | PRESCRIBING INFORMATION | MEDICATION GUIDE

LEMTRADA alemtuzumab

Welcome, Patricia! Menu

Registration > Training > Enrollment

LEMTRADA REMS Pharmacy Enrollment Form

LEMTRADA is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the pharmacy must enroll the pharmacy in the LEMTRADA REMS Program.

Please review the following information and submit to Genzyme by clicking the button below. Complete any missing information and correct any errors prior to submission.

All fields are required.

PHARMACY INFORMATION

Name of Pharmacy

Please enter name of pharmacy.

National Provider Identification (NPI) Number

Please enter a valid NPI number.

Pharmacy Address

Please enter pharmacy address.

City

Please enter city.

State

Please select a state.

ZIP Code

Please enter a 5-digit ZIP Code.

Name of Authorized Pharmacy Representative

Please enter name of Authorized Pharmacy Representative.

Title

Please enter title.

Phone Number

Please enter a 10-digit phone number.

Fax Number

Please enter a 10-digit fax number.

Email Address

Please enter email address.

PHARMACY AGREEMENT

I am the authorized representative designated by my Pharmacy to coordinate the activities of the LEMTRADA REMS Program. By signing this form, I agree to comply with the following Program requirements:

- I understand that my pharmacy must be certified with the LEMTRADA REMS Program to dispense LEMTRADA.
- I will oversee implementation and compliance with the LEMTRADA REMS Program requirements.
- I have reviewed the LEMTRADA REMS Program Overview.
- I will ensure that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the LEMTRADA REMS Program Overview.
- I will put processes and procedures in place, and follow such processes and procedures, to ensure the following verifications are met prior to dispensing LEMTRADA:
  - The LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program prior to dispensing LEMTRADA.
  - Ensuring LEMTRADA is only dispensed to a certified infusion center.
- This pharmacy will establish procedures and protocols that are subject to audit, to help ensure compliance with the requirements of the LEMTRADA REMS Program.
- I understand that my pharmacy must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.

☐ I have verified that all details are correct.
Please indicate information has been verified.

By providing my e-signature, I attest that I have completed the educational training about LEMTRADA for pharmacies and I understand the benefits and risks of LEMTRADA. I understand that all staff members from my site must be trained on the information in the module and adhere to the requirements of the LEMTRADA REMS Program. I understand that I must complete this LEMTRADA REMS Pharmacy Enrollment Form in order to complete the enrollment process.

By entering my name, NPI number, and password, I confirm that I have completed the LEMTRADA REMS Program training and that I will comply with the requirements of the program.

Full Name

Please enter your full name.

NPI Number

Please enter your NPI number.

Password

Please enter a password.

Cancel Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

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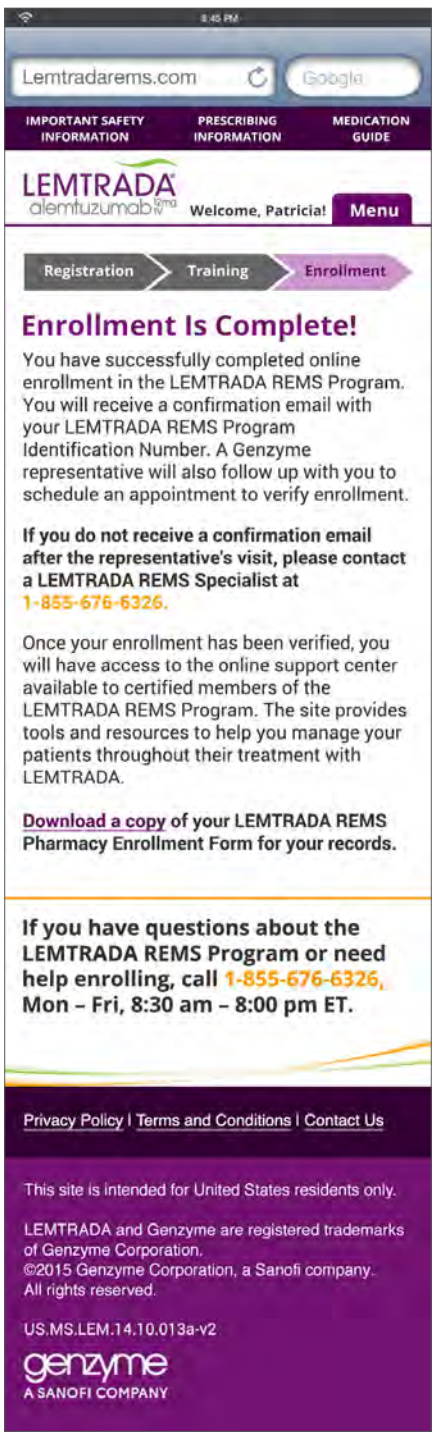
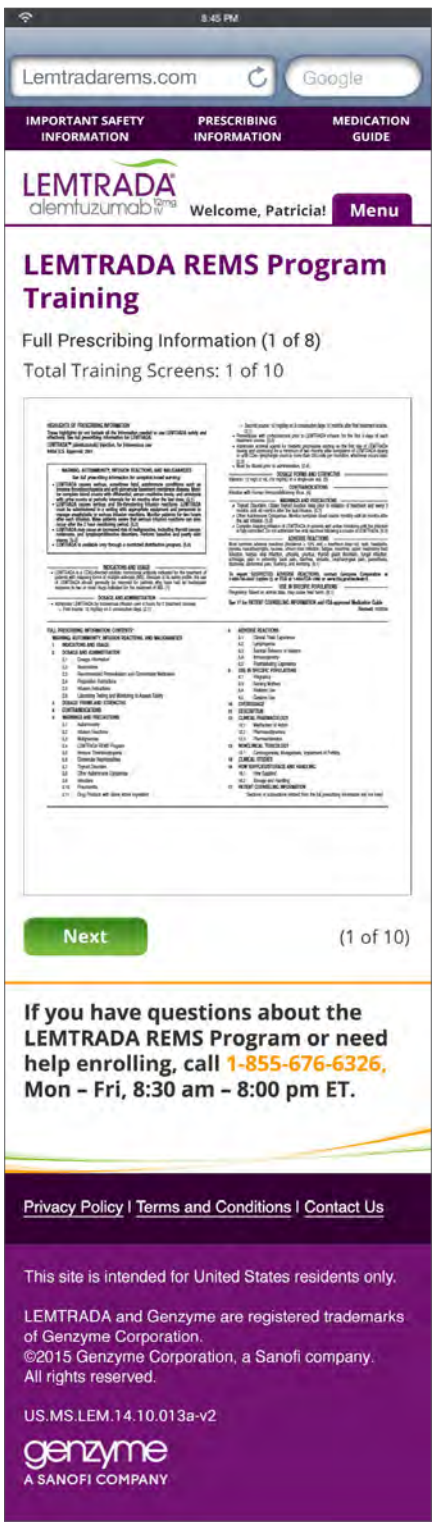
LEMTRADA REMS Mobile - Pharmacy Enrollment, Confirmation



LEMTRADA REMS Mobile - Pharmacy Training Materials - Page 1



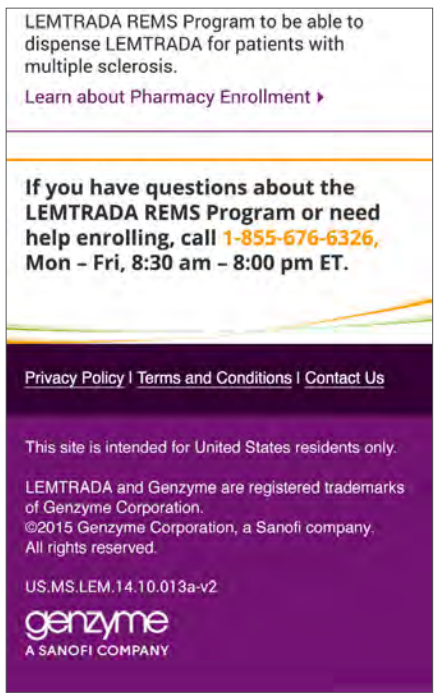
LEMTRADA REMS Mobile - Pharmacy, Temporary Homepage - Training Incomplete





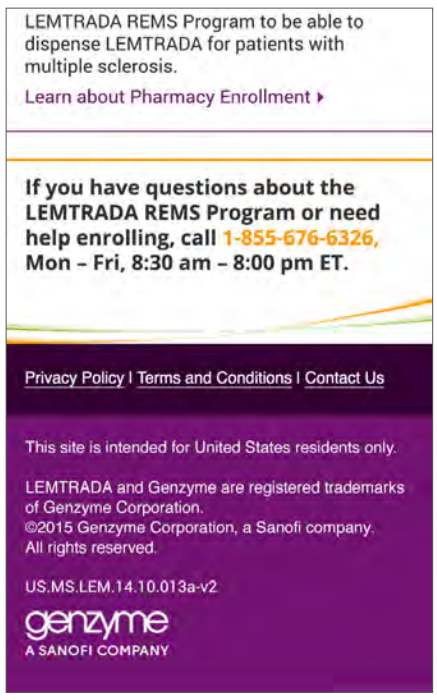
LEMTRADA REMS Mobile - Pharmacy, Temporary Homepage - Training Invalid





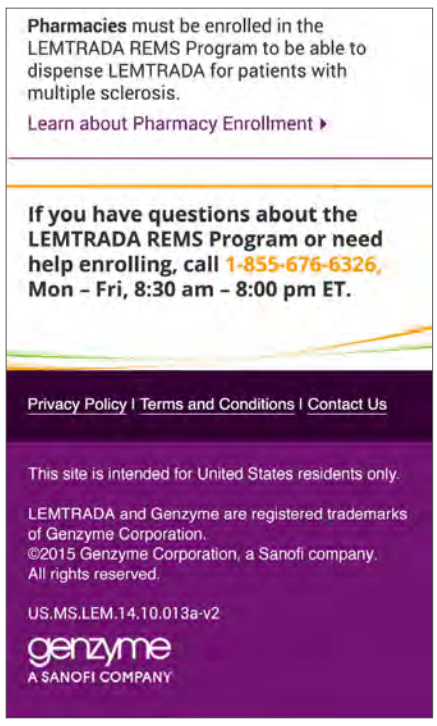
LEMTRADA REMS Mobile - Pharmacy, Temporary Homepage - Enrollment Incomplete





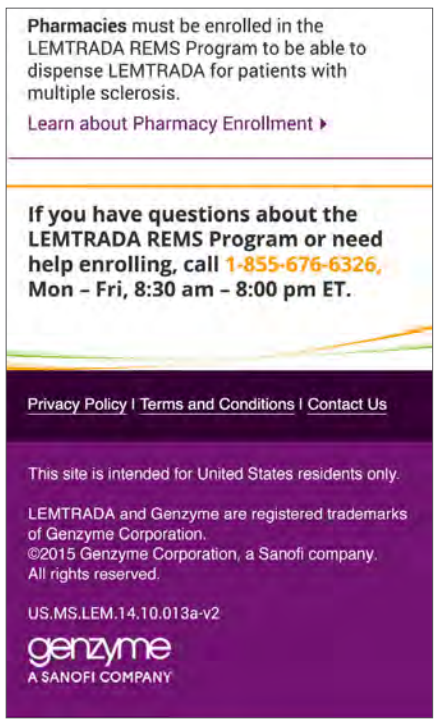
LEMTRADA REMS Mobile - Pharmacy, Temporary Homepage - Enrollment Complete





LEMTRADA REMS Mobile - Pharmacy, Temporary Homepage - Enrollment Complete, Menu Dropdown



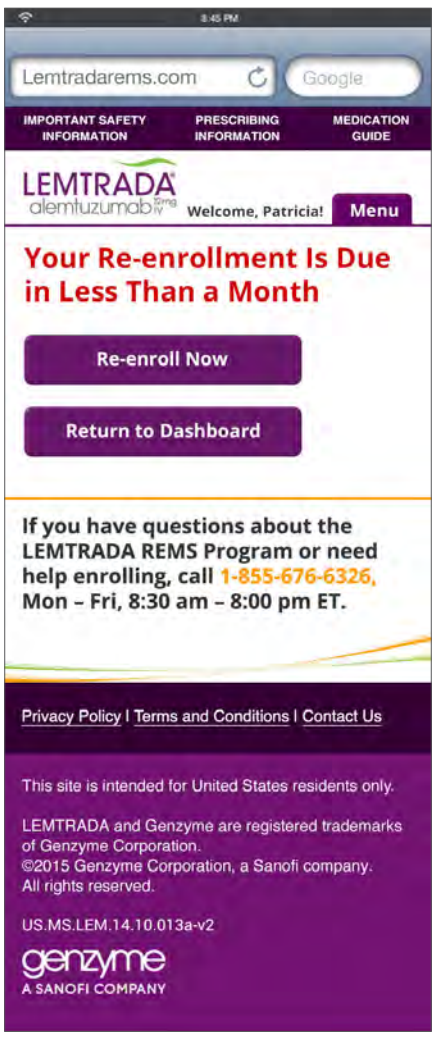


PHARMACY DASHBOARD PAGES

LEMTRADA REMS Mobile - Pharmacy, Dashboard Homepage



LEMTRADA REMS Mobile - Pharmacy, Dashboard Homepage, Re-enrollment Overlay

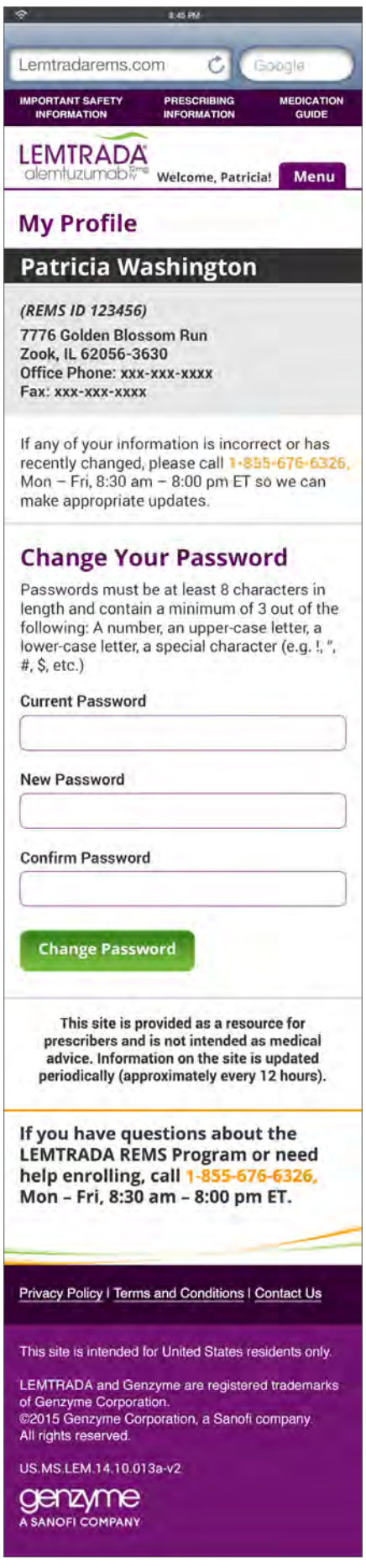


LEMTRADA REMS Mobile - Pharmacy Dashboard - Re-Enrollment Lockout

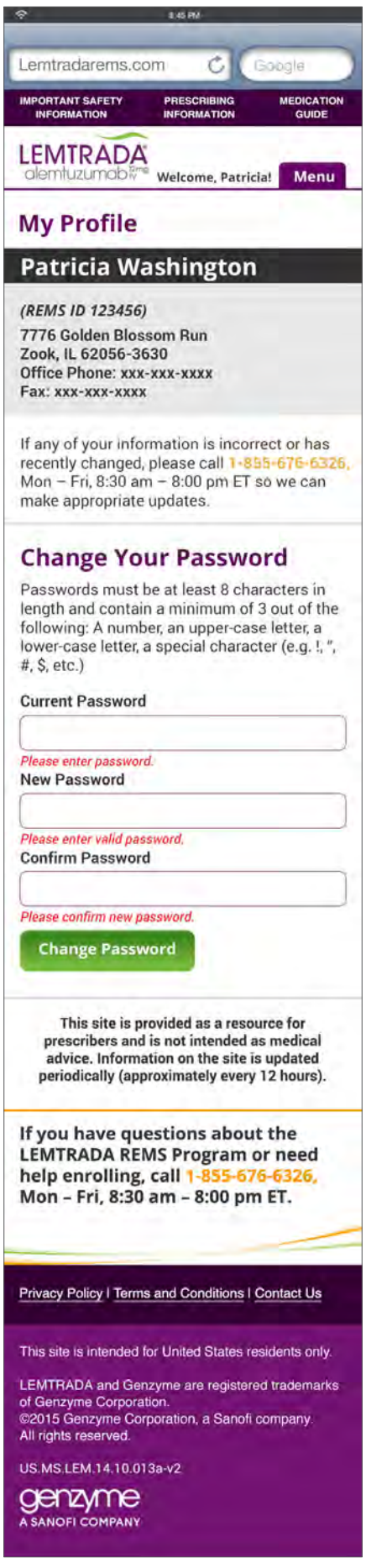




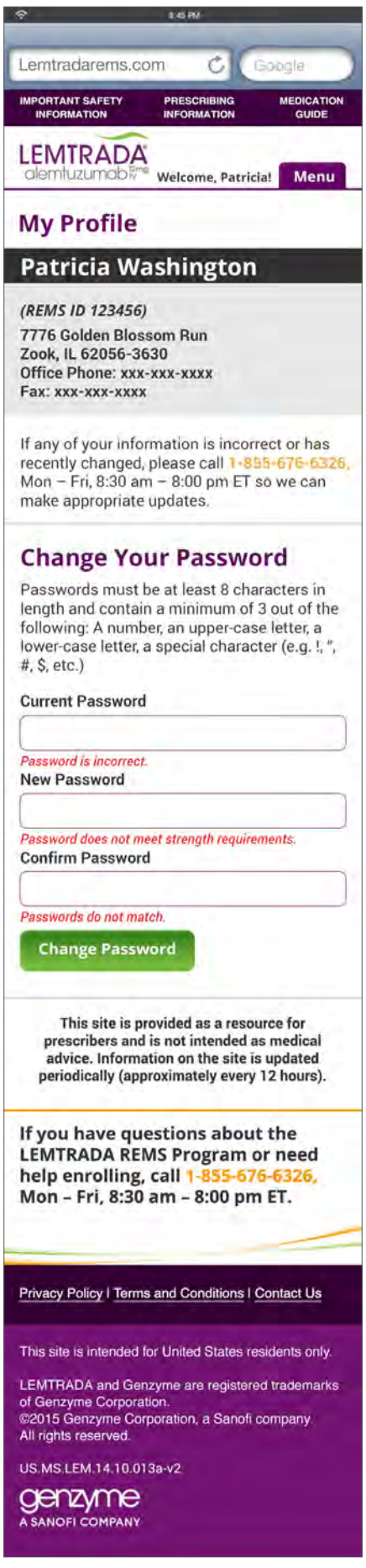
LEMTRADA REMS Mobile - Pharmacy, My Profile



LEMTRADA REMS Mobile - Pharmacy, My Profile, Error



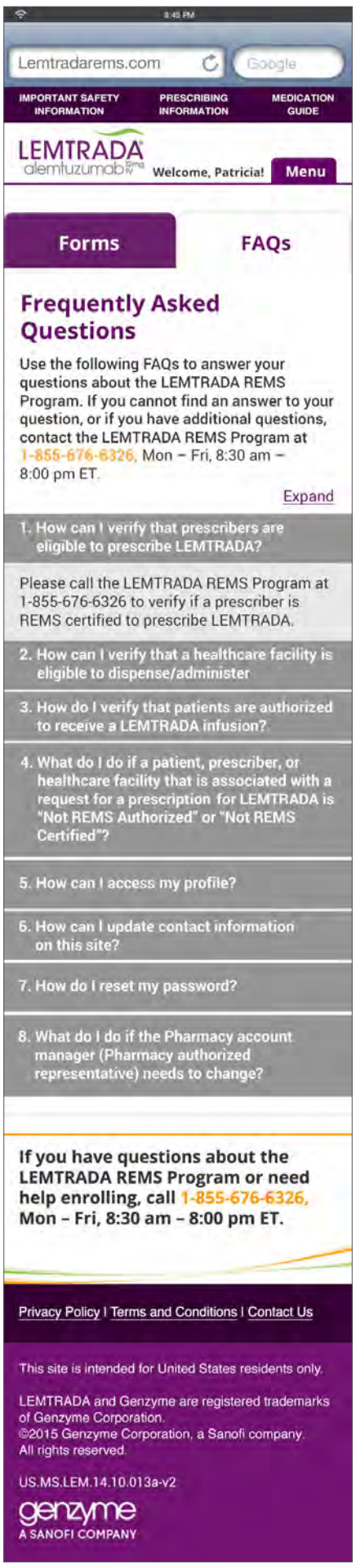
LEMTRADA REMS Mobile - Pharmacy, My Profile, Password Strength Error



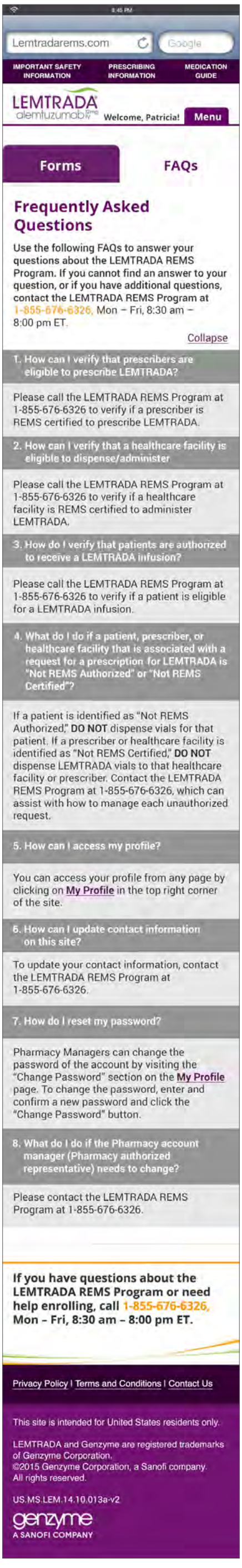
LEMTRADA REMS Mobile - Pharmacy, Support - Forms



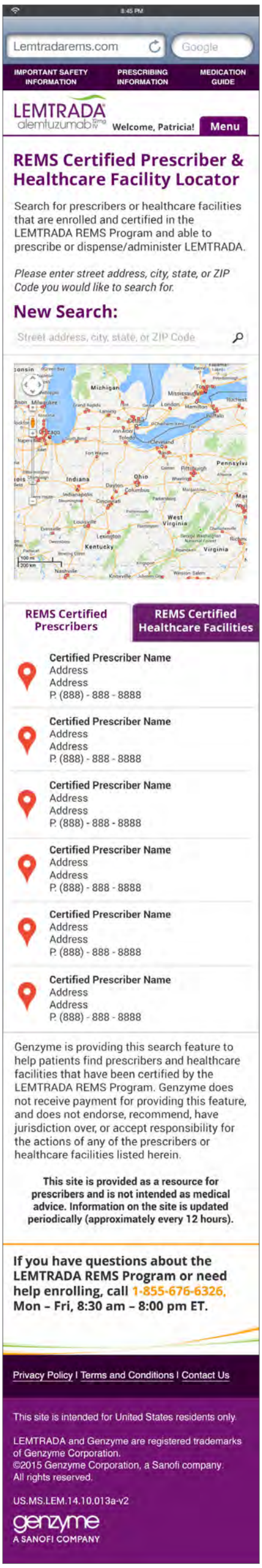
LEMTRADA REMS Mobile - Pharmacy, Support - FAQs



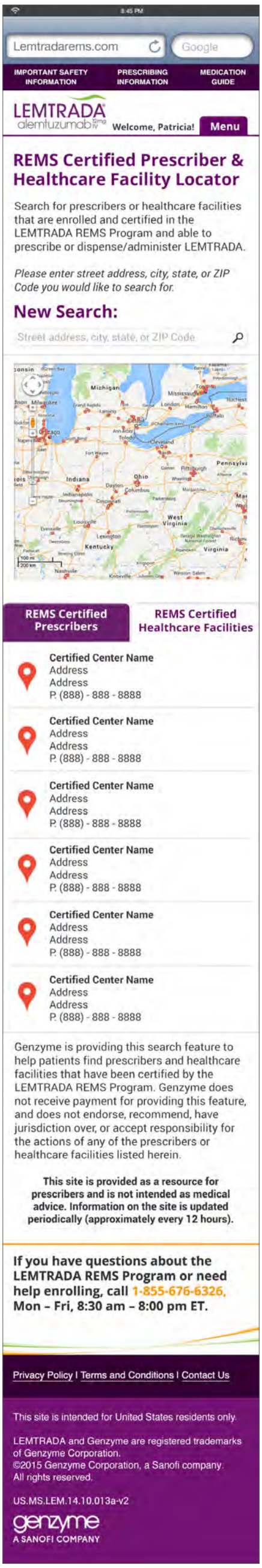
LEMTRADA REMS Mobile - Pharmacy, Support - FAQs, Expanded



LEMTRADA REMS Mobile - Pharmacy, Support - REMS Certified Prescriber & Healthcare Facility Locator

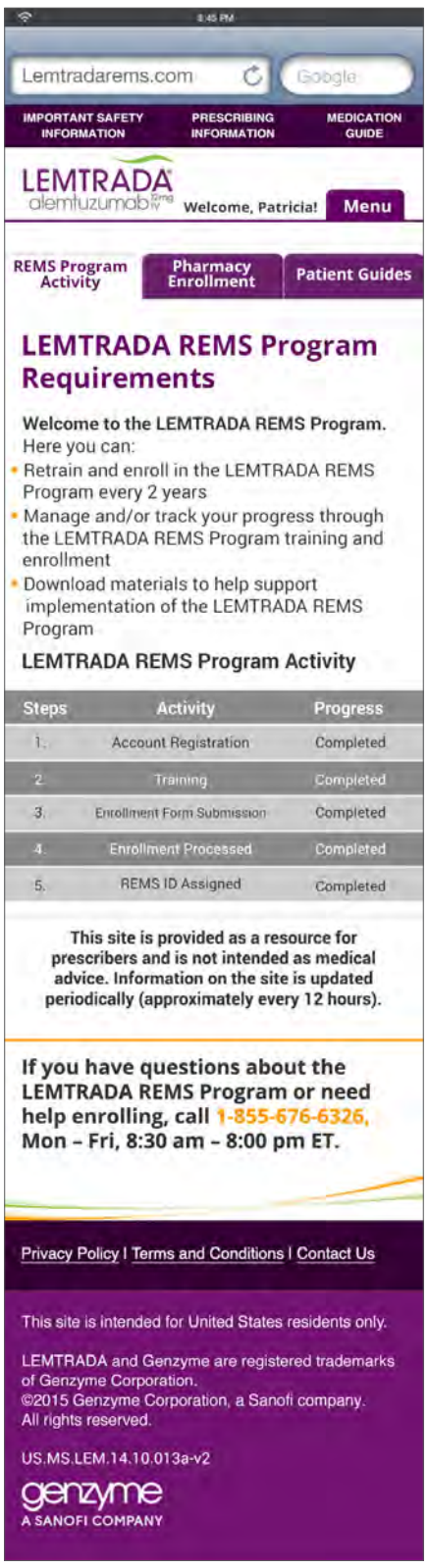


LEMTRADA REMS Mobile - Pharmacy, Support - REMS Certified Prescriber & Healthcare Facility Locator



Reference ID: 3821900

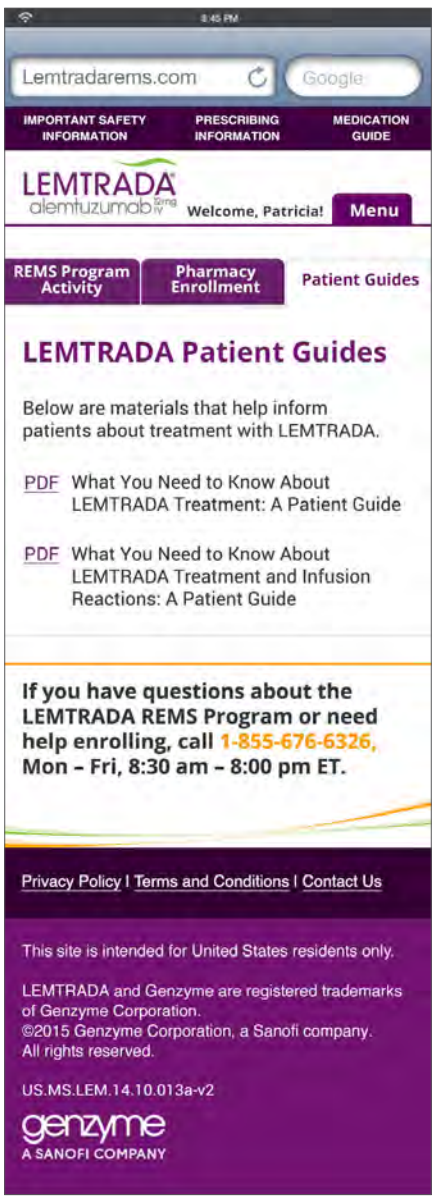
LEMTRADA REMS Mobile - Pharmacy, About REMS - REMS Program Activity



LEMTRADA REMS Mobile - Pharmacy, About REMS - Pharmacy Enrollment



LEMTRADA REMS Mobile - Pharmacy, About REMS - Patient Guide



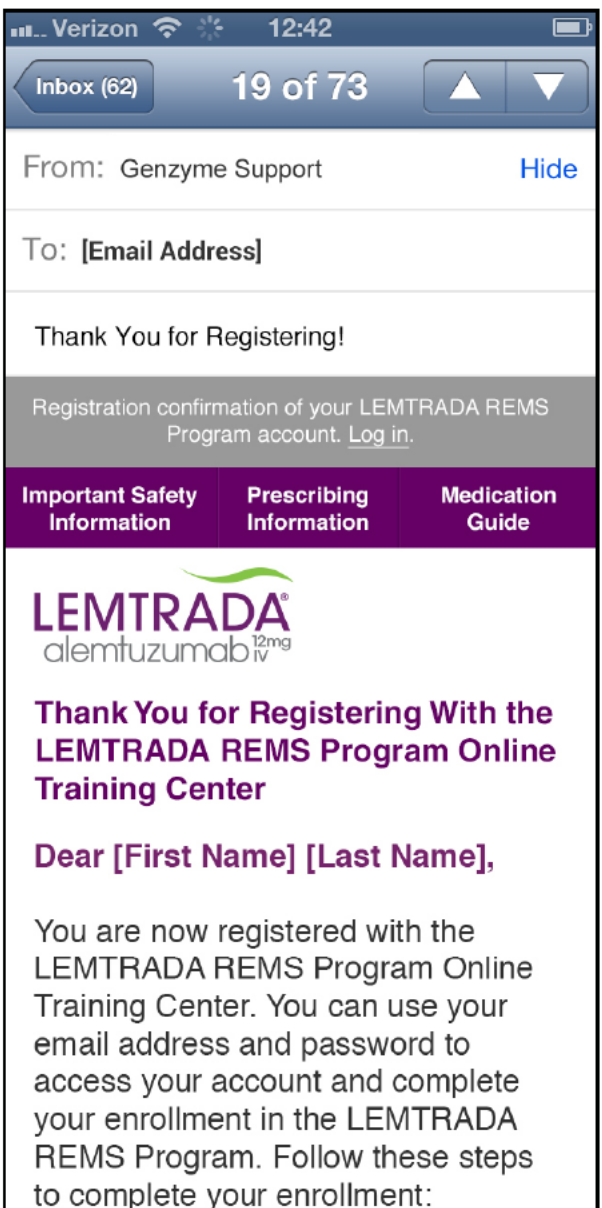
LEMTRADA REMS Mobile - Scheduled Site Maintenance



LEMTRADA REMS

User Emails

A Registration Confirmation [All Users]



B Password Reset Request [All Users]

Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Password Reset Request

Reset your password.

Important Safety Information | **Prescribing Information** | **Medication Guide**

LEMTRADA® alemtuzumab 12mg IV

Password Reset Request Received

Dear [First Name] [Last Name],

We received a request to reset the password for your LEMTRADA REMS Program Account.

Click the link below to reset your password using our secure server:

[http://urltoresetpasswordgoeshereloremipsumdolor.com/@1562162t1]

If clicking the link doesn't seem to work, copy and paste the link into your browser's address window, or retype it there. If you did not request a password reset, you may safely disregard this email.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Last Update: June 2015

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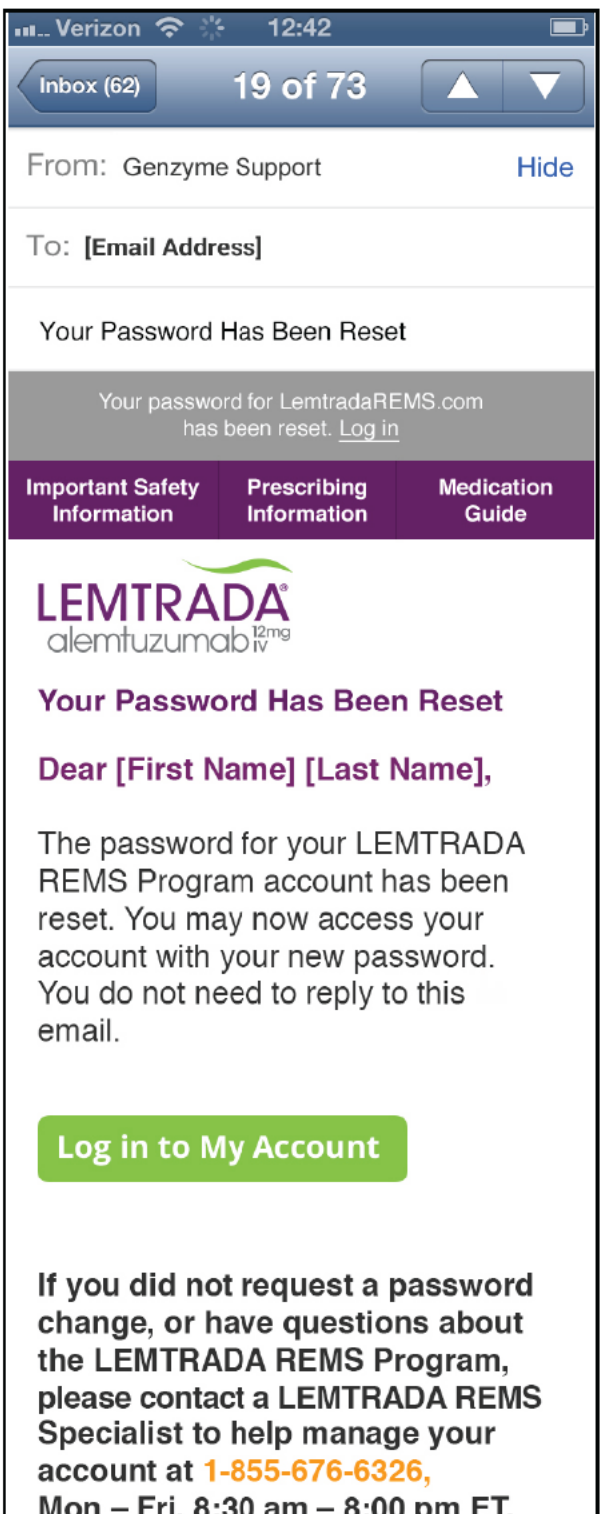
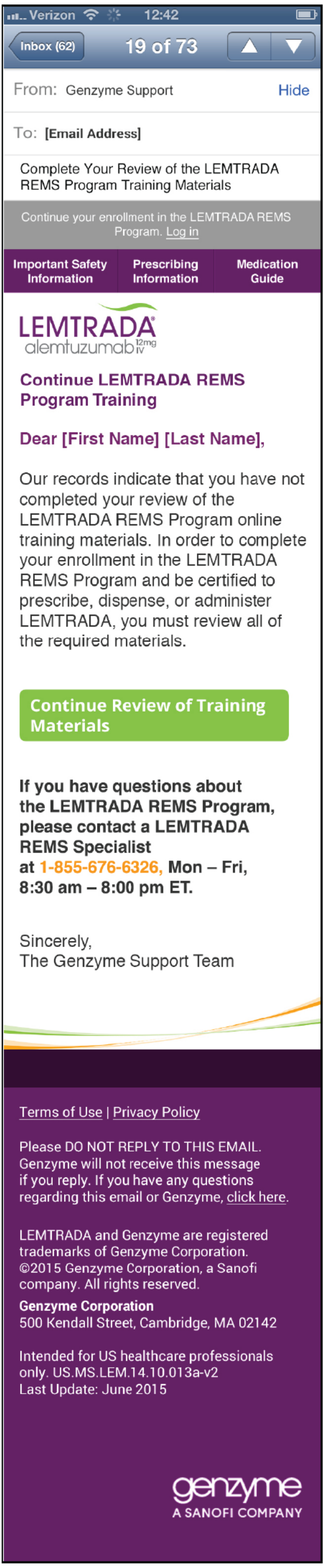
C Password Reset Confirmation [All Users]



D Incomplete Training [All Users]



Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Complete the LEMTRADA REMS Knowledge Assessment

Continue your enrollment in the LEMTRADA REMS Program. Log in

Important Safety Information | **Prescribing Information** | **Medication Guide**

LEMTRADA® alemtuzumab 12mg IV

Please Complete the LEMTRADA REMS Knowledge Assessment

Dear [First Name] [Last Name],

Our records indicate that you have not successfully completed the LEMTRADA REMS Knowledge Assessment. In order to become enrolled in the LEMTRADA REMS Program and be certified to prescribe LEMTRADA, prescribers must successfully complete all questions in the Knowledge Assessment.

Continue the Knowledge Assessment

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Last Update: June 2015

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Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Your Enrollment in the LEMTRADA REMS Program Is Almost Complete

Your enrollment in the LEMTRADA REMS Program is almost complete. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS Program Training Complete

Dear [First Name] [Last Name],

You have successfully reviewed the LEMTRADA REMS Program prescriber training materials! You may log in to review the training materials again at any time.

Please note that you must complete the Knowledge Assessment and LEMTRADA REMS Prescriber Enrollment Form to complete your enrollment.

Complete the Knowledge Assessment

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Last Update: June 2015

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Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Your Enrollment in the LEMTRADA REMS Program Is Almost Complete

Your enrollment in the LEMTRADA REMS Program is almost complete. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS Program Training Complete

Dear [First Name] [Last Name],

You have successfully completed the required training for the LEMTRADA REMS Program! You may log in to review the training materials again at any time.

Please ensure that all staff members involved with the dispensing/administering of LEMTRADA also understand the content in the training materials. Note that you must complete the LEMTRADA REMS Enrollment Form to complete your enrollment.

Complete the Enrollment Form

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Last Update: June 2015

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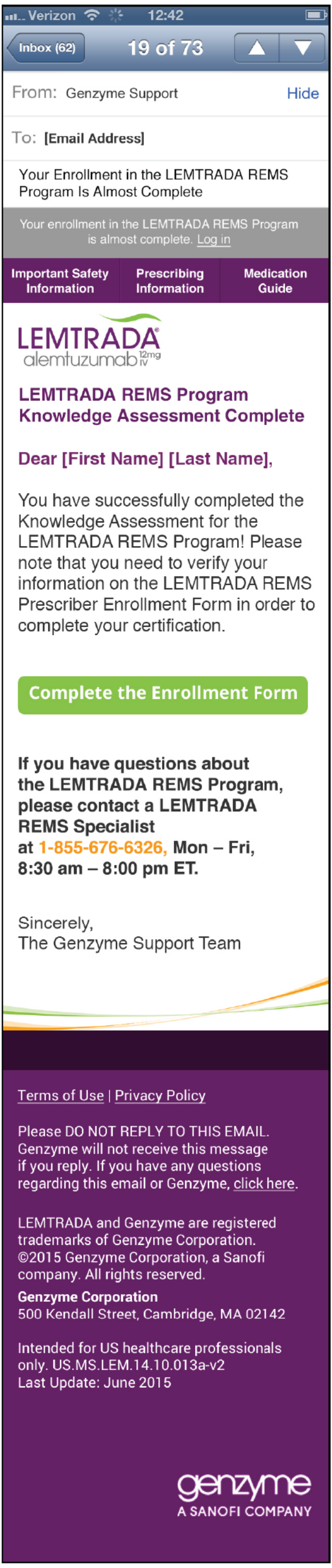
H Knowledge Assessment Complete [HCP only]



I Enrollment Complete [All Users]



J Certification Confirmation [HCF]

Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Congratulations! You Are Certified by the LEMTRADA REMS Program

You are now certified by the LEMTRADA REMS Program. Log in

Important Safety Information | **Prescribing Information** | **Medication Guide**

LEMTRADA® alemtuzumab 12mg IV

Welcome to the LEMTRADA REMS Program!

Dear [First Name] [Last Name],

Congratulations! You are now certified by the LEMTRADA REMS Program to dispense/administer LEMTRADA. Your LEMTRADA REMS Identification Number is [xxxxxxxxx]. This number will be used to verify your activity in the LEMTRADA REMS Program. Please ensure that all staff members of your facility receive the necessary training to comply with the LEMTRADA REMS Program requirements. Use **LemtradaREMS.com** to:

- **View** patient and prescriber information, including REMS status, REMS ID number, and eligibility to receive or prescribe LEMTRADA
- **Download** forms and resources to support you in implementing the requirements of the program
- **Access** educational materials about LEMTRADA for you and your staff

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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500 Kendall Street, Cambridge, MA 02142

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Last Update: June 2015

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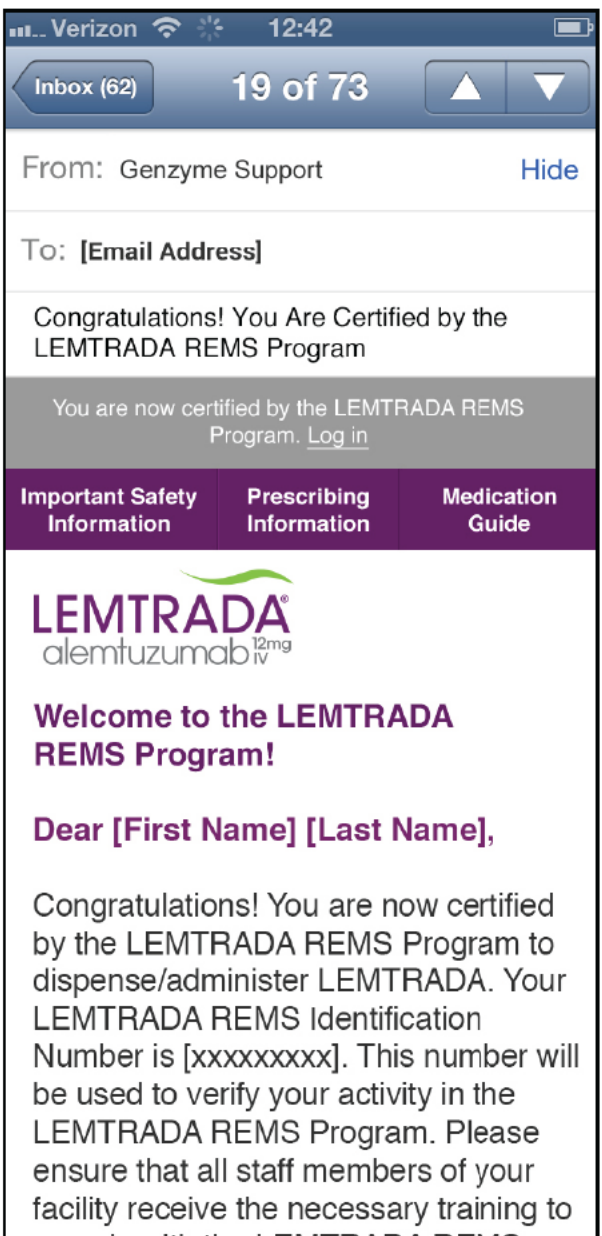
Ja Certification Confirmation [Pharmacy]



K Certification Confirmation [HCP]

Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

Congratulations! You Are Certified by the LEMTRADA REMS Program

You are now certified by the LEMTRADA REMS Program. Log in

Important Safety Information | **Prescribing Information** | **Medication Guide**

LEMTRADA® alemtuzumab 12mg IV

Welcome to the LEMTRADA REMS Program!

Dear [First Name] [Last Name],

Congratulations! You are now certified by the LEMTRADA REMS Program to prescribe LEMTRADA. Your LEMTRADA REMS Identification Number is [xxxxxxxxx]. This number will be used to verify your activity in the LEMTRADA REMS Program. As a member of the LEMTRADA REMS Program, you can now access personal online tools to help you manage your LEMTRADA patients. This site will allow you to:

- **View** patient and healthcare facility information, including REMS status, REMS ID number, and eligibility to receive or dispense/administer LEMTRADA
- **Complete** required authorization forms, including the LEMTRADA REMS Patient Status Form and the LEMTRADA REMS Patient Authorization and Baseline Lab Form
- **Download** forms to sign patients up for the LEMTRADA Central Lab Program
- **Access** educational materials about LEMTRADA for you and your staff

Log in to My Account

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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L Authorization Alert [HCP, HCF]

Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: **[Email Address]**

LEMTRADA REMS Program Alert

Important notifications about the status of your LEMTRADA patients. Log in

Important Safety Information | **Prescribing Information** | **Medication Guide**

LEMTRADA® alemtuzumab 12mg IV

You have [Y+Z] patients who have authorization requirements. View Patients

Dear [First Name] [Last Name],

According to our records, [Y+Z] or more of your LEMTRADA patients are in need of authorization in order to receive treatment. Patients must be authorized by their prescriber with:

- The **LEMTRADA REMS Patient Authorization and Baseline Lab Form** 30 days prior to each LEMTRADA infusion
- The **LEMTRADA REMS Patient Status Form** every 6 months after a patient's first infusion, and every 6 months thereafter, until 48 months after the patient's last infusion

See the information below or log in to **View Patients** for more details.

Alert!

[Y] patients are overdue for their authorization requirements.

[Z] patients have authorization requirements due in 1 month.

View My Patients

To change the frequency of Patient Alerts, please update your preferences in your **Profile.**

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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La Authorization Alert [HCP, HCF]

Verizon 12:42

Inbox (62) 19 of 73

From: Genzyme Support Hide

To: [Email Address]

LEMTRADA REMS Program Alert

Important notifications about the status of your LEMTRADA patients. Log in

Important Safety Information | Prescribing Information | Medication Guide

LEMTRADA® alemtuzumab 12mg IV

You have [Y+Z] patient who has authorization requirements. View Patient

Dear [First Name] [Last Name],

According to our records, [Y+Z] of your LEMTRADA patients is in need of authorization in order to receive treatment. Patients must be authorized by their prescriber with:

- The **LEMTRADA REMS Patient Authorization and Baseline Lab Form** 30 days prior to each LEMTRADA infusion
- The **LEMTRADA REMS Patient Status Form** every 6 months after a patient's first infusion, and every 6 months thereafter, until 48 months after the patient's last infusion

See the information below or log in to **View Patients** for more details.

View My Patients

To change the frequency of Patient Alerts, please update your preferences in your **Profile.**

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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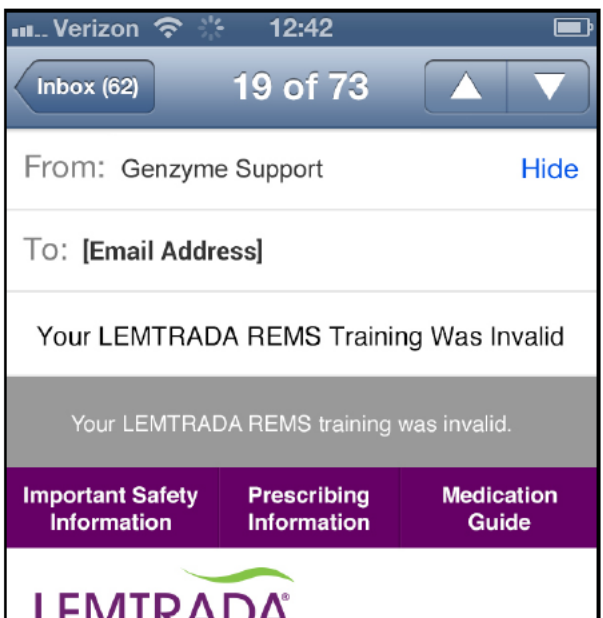

LEMTRADA® alemtuzumab 12mg IV

Your LEMTRADA REMS Training Was Invalid

Dear [First Name] [Last Name],

Thank you for completing your LEMTRADA REMS training. Unfortunately, your training was deemed invalid. In order to proceed, please contact *MS One to One*® at 1-855-676-6326.

If you have questions about the LEMTRADA REMS Program, please contact a LEMTRADA REMS Specialist at 1-855-676-6326, Mon – Fri, 8:30 am – 8:00 pm ET.

Sincerely,
The Genzyme Support Team

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Last Update: June 2015

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LEMTRADA REMS

Online Forms

Printed for User Records

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is available only through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA.

Instructions:

1. Review the LEMTRADA REMS Education Program for Prescribers, including the Prescribing Information
2. Successfully complete the LEMTRADA REMS Knowledge Assessment
3. Complete and submit this LEMTRADA REMS Prescriber Enrollment Form
4. Send your patient to a healthcare facility that is enrolled in the LEMTRADA REMS Program

Please complete all required fields on this form and fax it to 1-855-557-2478. You will receive enrollment confirmation via your preferred method of communication (email or fax) within 2 business days.

*Indicates a mandatory field.

LEMTRADA PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)/Degree* Doe, Dr. John/Doctor Of Osteopathy			
Name of Institution or Healthcare Facility* TheBestHCF			
Street Address* 1234 Intouch DriveSuite 400			
City* Overland Park		State* KS	ZIP Code* 12345
Office Phone Number* 9131112222	Fax Number* 9132223333	Email Address john.doe@gmail.com	Mobile Phone Number 9135551234
National Provider Identification (NPI) Number* 1234567893			

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

PRESCRIBER AGREEMENT

By completing this form, I attest that:

- I understand that LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- I understand that LEMTRADA is only available through the LEMTRADA REMS Program and that I must comply with the program requirements in order to prescribe LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Prescribers*, including a review of the LEMTRADA Prescribing Information, and successfully completed the LEMTRADA REMS Knowledge Assessment.
- I understand that by completing the training program and signing this LEMTRADA REMS Prescriber Enrollment Form, I will be enrolled in the LEMTRADA REMS Program and can prescribe LEMTRADA.
- I understand that I am responsible for reviewing *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with each patient, and counseling each patient on an ongoing basis about the serious risks associated with the use of LEMTRADA and how to mitigate these risks through periodic monitoring.
- I understand that I must enroll all patients being treated with LEMTRADA into the LEMTRADA REMS Program prior to initiating the patient on treatment with LEMTRADA. I am responsible for completing a LEMTRADA REMS Patient Enrollment Form with the patient (or patient's legal representative), obtaining the patient's (or patient's legal representative's) signature on the form, and submitting the signed form to the LEMTRADA REMS Program. A completed copy should be provided to the patient and another copy should be stored in the patient's records.
- I will provide enrolled patients with a LEMTRADA Patient Safety Information Card and instruct patients to carry this card with them at all times in case of an emergency.
- I understand that I must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription. I understand that I am responsible for completing baseline lab monitoring within 30 days prior to infusion of LEMTRADA.

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PRESCRIBER AGREEMENT (CONTINUED)

- I understand that I must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form indicating completion of each patient's baseline labs within 30 days prior to the patient's infusion date.
- I understand the risks of autoimmune conditions and malignancies associated with the use of LEMTRADA, and the need for periodic monitoring in order to identify and mitigate these risks:
  - Complete blood counts with differential obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Serum creatinine levels obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Urinalysis with urine cell counts obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Thyroid function tests, such as thyroid stimulating hormone (TSH) level, obtained within 30 days prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion.
  - Baseline and yearly skin examinations.
- I will report any adverse events of autoimmune conditions, infusion reactions, or malignancies to Genzyme.
- I will complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the Program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

WEBSITE CONSENT

I understand that the LEMTRADA REMS Program will publish my name, business address, and phone number ("Contact Information") on its website in a directory of physicians certified to prescribe and administer LEMTRADA and consent to the foregoing. I understand that I am waiving the right to inspect my Contact Information prior to its inclusion on the website, and I agree to hold harmless and release the LEMTRADA REMS Program and Genzyme Corporation and its affiliates from any and all actions, claims, or demands arising out of or in connection with the use of my Contact Information on the website. I understand that I can request the removal of my Contact Information from the LEMTRADA REMS Program website at any time by contacting the LEMTRADA REMS Program at 1-800-557-2478.

(●) Yes ( ) No

SIGNATURE

6/24/2015

Prescriber Signature* Date*

Dr. John Doe

Print Name*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:12:14 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT STATUS FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed every 6 months for each LEMTRADA® (alemtuzumab) patient under your care. Please complete this form 6 months after your patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the patient's last infusion.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Dr. John

Office Phone Number* 9135551234

Address* 1234 Intouch Drive Suite 400

City* Los Angeles

State* CA

ZIP Code* 90210

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Jane

Patient LEMTRADA REMS Program Identification Number* 1122334455

Date of Birth (MM/DD/YYYY)* 08/18/1969

Date of Last LEMTRADA Infusion (MM/DD/YYYY)* 03/21/2015

Is the above-named patient still under your care?* (Check one) ■ **Yes** ☐ **No**

IF NO, please indicate the name of the healthcare provider now responsible for this patient's care

Healthcare Provider Name

Healthcare Provider Phone Number

Patient's Current Healthcare Provider Is Unknown ☐

IF YES, please complete the following information

The patient has completed the periodic monitoring within the last 6 months. ■ Yes ☐ No

Since submitting the last LEMTRADA REMS Patient Status Form, has the patient been diagnosed with any of the following?

a. Autoimmune conditions ☐ Yes ■ No

b. Infusion reactions ■ Yes ☐ No

c. Malignancies ☐ Yes ■ No

☑ This adverse event has already been reported to Genzyme (specify date of report): 06/04/2015

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

In signing this form, I acknowledge that I have reviewed *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with this patient and counseled the patient about the serious risks associated with the use of LEMTRADA, and how to mitigate these risks through periodic monitoring.

PRESCRIBER'S SIGNATURE

Prescriber Signature*

Date* 6/24/2015

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:08:23 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT AUTHORIZATION AND BASELINE LAB FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed within 30 days prior to the first infusion date of each LEMTRADA® (alemtuzumab) patient's treatment course.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Dr. John

Office Phone Number* 9135551234

Address* 1234 Intouch Drive Suite 400

City* Overland Park

State* KS

ZIP Code* 12345

Prescriber LEMTRADA REMS Program Identification Number* 1234567893

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)* Doe, Jane

Patient LEMTRADA REMS Program Identification Number* 1122334455

Date of Birth (MM/DD/YYYY)* 08/18/1969

AUTHORIZATION AND BASELINE LABS

Do you authorize LEMTRADA treatment for the above-referenced patient?* (●) Yes ( ) No

Do you attest that required baseline laboratory testing has been completed prior to LEMTRADA treatment and within 30 days of the patient's first infusion?* (●) Yes ( ) No

PRESCRIPTION INFORMATION

Check one*

(●) Initial course (1 vial [12 mg/day]) X 5 consecutive days — Total number of vials: 10

( ) Subsequent course (1 vial [12 mg/day]) X 3 consecutive days — Total number of vials: _____

SIGNATURE

Prescriber Signature*

Date* 6/24/2015

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:13:56 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS HEALTHCARE FACILITY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the healthcare facility must enroll the facility in the LEMTRADA REMS Program.

- ○ New Enrollment
- ◉ Re-enrollment (every 2 years)

*Indicates a mandatory field.

Please complete a separate Healthcare Facility Enrollment Form for each facility site, if applicable.

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Name of Institution or Healthcare Facility* TheBestHCF		NPI Number* 1122334455	
Infusion Facility Address* 1234 Intouch Drive Suite 400			
City* Overland Park		State* KS	ZIP Code* 12345
Ship-to Street Address (if different)* 1234 Shipping St.			
City* Leawood		State* KS	ZIP Code* 55555
Phone Number* 9135551234	Fax Number* 9135558888	Email Address thebestHCF@gmail.com	
Name of Authorized Healthcare Facility Representative* John Doe		Title* TheBest	

Site Affiliation

○ Academic ○ Government ○ Ambulatory/Freestanding ◉ Hospital Based ○ Private Practice (in office)

HEALTHCARE FACILITY AGREEMENT

I am the authorized representative designated by my healthcare facility to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following Program requirements:

- I understand that my healthcare facility must be certified with the LEMTRADA REMS Program to receive or administer LEMTRADA.
- I have completed the review of the *LEMTRADA REMS Education Program for Healthcare Facilities* and the LEMTRADA REMS Program Overview.
- I understand that my healthcare facility must confirm that the patient is authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program or verifying online at www.LemtradaREMS.com prior to initiation of each treatment course.
- I understand the risk of serious infusion reactions during and following the administration of LEMTRADA.
- I understand the need to monitor patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
  - To include the monitoring of patient vital signs before the infusion and periodically during the infusion.
- I understand that my healthcare facility must be equipped with the necessary on-site equipment and personnel to manage anaphylaxis or serious infusion reactions.
- I understand that my healthcare facility must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

Reference ID: 3821900

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HEALTHCARE FACILITY AGREEMENT (CONTINUED)

- This healthcare facility will establish procedures and protocols that are subject to audit, to help ensure compliance with the safe use conditions required in the LEMTRADA REMS Program, including the following:
  - Ensure that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - Ensure that the prescriber is certified and the patient is enrolled and authorized by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website prior to dispensing and administering LEMTRADA.
  - Ensure that the infusion site is equipped to manage infusion reactions.
  - Ensure that LEMTRADA is not dispensed outside of the authorized representative's certified healthcare facility.
  - Prior to the first day of each treatment course, counsel and provide a copy of *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* to each patient to inform them about the risk of serious infusion reactions.
  - Observe each patient administered LEMTRADA at my healthcare facility during and for at least 2 hours after each LEMTRADA infusion, in order to provide appropriate medical treatment in the event of serious infusion reactions following LEMTRADA infusion.
  - For each patient, complete and return the LEMTRADA REMS Infusion Checklist to the LEMTRADA REMS Program within 5 business days from the patient's last infusion of LEMTRADA within a specific treatment course.
  - Renew enrollment into the LEMTRADA REMS Program every 2 years from the initial enrollment.
- To make available to Genzyme documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.
- To return to Genzyme any unused vials of LEMTRADA within 50 days from the date of receipt of the LEMTRADA REMS Patient Authorization Baseline Lab Form.
- To ensure that a LEMTRADA REMS Patient Authorization and Baseline Lab Form is received for each prescription by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website.
- To ensure that all non-prescribing HCPs who administer LEMTRADA in my healthcare setting are trained using the LEMTRADA REMS Program Overview and the *LEMTRADA REMS Education Program for Healthcare Facilities*, and a record regarding such training must be maintained.

SIGNATURE

	6/24/2015
Authorized Healthcare Facility Representative Signature*	Date*
John Doe	TheBest
Print Name*	Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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Electronic Signature Details
Electronically Signed by Intouch Tester
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IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Healthcare Facilities to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS INFUSION CHECKLIST

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

As a condition of your healthcare facility's authorization to infuse LEMTRADA® (alemtuzumab), this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and submitted within **5 business days. This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused.** Keep a copy of this checklist in the patient's medical record.

All fields on this form are mandatory.

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First) Doe, Jane

DOB (MM/DD/YYYY) 08/18/1969

Patient LEMTRADA REMS Program Identification Number 1122334455

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (Last, First) Doe, Dr. John

Prescriber LEMTRADA REMS Program Identification Number 1234567893

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Healthcare Facility Name TheBestHCF

Healthcare Facility LEMTRADA REMS Program Identification Number 1234567893

STEP 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course.

Is the patient authorized to receive LEMTRADA? ☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE.** Refer patient back to the LEMTRADA prescriber.

STEP 2: CONFIRM that the patient has been counseled and has received *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

The patient must be counseled about the risk for infusion reactions and provided with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to the first infusion of each treatment course. Has the patient been counseled and received the guide?

☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP** — provide the patient guide. Proceed to the next question after the patient has received this guide and has been counseled.

STEP 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:

1. In case of serious infusion reactions.
2. To monitor patient's vital signs before, during, and post-infusion.

Are the appropriate medical measures listed above available? ☑ **Yes** ☐ **No**

Yes Continue to next question.

No **STOP — DO NOT INFUSE** until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information.

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PATIENT INFORMATION (PLEASE PRINT)

Patient Name (Last, First)	DOB (MM/DD/YYYY)
Doe, Jane	08/18/1969

STEP 4: RECORD infusion information

Was the patient infused with LEMTRADA? ■ **Yes** ☐ **No**

Yes Fill in Dates of Infusion below and then proceed to Step 5.

No Proceed to Step 5.

LEMTRADA Infusions

Dates of Infusion:

Date: 03/21/2014

Date: 07/27/2014

Date: 08/14/2014

Date: _____

Date: _____

STEP 5: RETURN unused vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Baseline Lab Form.

Contact the LEMTRADA REMS Program at 1-855-676-6326 for additional information.

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch

STEP 6: SIGNATURE

	6/24/2015
Signature of staff completing checklist	Date
Dr. John Doe	
Name of staff completing checklist (Please Print)	

STEP 7: Fax the Infusion Checklist to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com within 5 business days

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326.

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Reference ID: 3821900

Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:06:36 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

For Pharmacy

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PHARMACY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the pharmacy must enroll the pharmacy in the LEMTRADA REMS Program.

☒ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

PHARMACY INFORMATION (PLEASE PRINT)

Name of Pharmacy* TheBestSPP		NPI Number* 1234567893	
Pharmacy Address* 1234 Intouch Drive			
City* Overland Park		State* KS	ZIP Code* 64129
Name of Authorized Pharmacy Representative* John Doe		Title* TheBestRep	
Phone Number* 9134441234	Fax Number* 9138881234	Email Address john.doe@gmail.com	

PHARMACY AGREEMENT

I am the authorized representative designated by my Pharmacy to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following program requirements:

- I understand that my pharmacy must be certified with the LEMTRADA REMS Program to dispense LEMTRADA.
- I will oversee implementation and compliance with the LEMTRADA REMS Program requirements.
- I have reviewed the LEMTRADA REMS Program Overview.
- I will ensure that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the LEMTRADA REMS Program Overview.
- I will put processes and procedures in place, and follow such processes and procedures, to ensure the following verifications are met prior to dispensing LEMTRADA:
  - The LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program prior to dispensing LEMTRADA.
  - Ensuring LEMTRADA is only dispensed to a certified infusion center.
- This pharmacy will establish procedures and protocols that are subject to audit, to help ensure compliance with the requirements of the LEMTRADA REMS Program.
- I understand that my pharmacy must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.

SIGNATURE

Authorized Pharmacy Representative Signature* John Doe	Date* 6/24/2015
Print Name*	Title TheBestRep

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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Electronic Signature Details
Electronically Signed by Intouch Tester
Date/Time: 6/24/2015 5:10:10 PM
IP: ::1
LemtradaREMS.com User Account: test7049@testing.com
Verified Identity by correct entry of user account password
Verified identity by correct entry of NPI
Signature Reason: I wish to approve this document electronically.
I attest to the accuracy and integrity of this document.

What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide

LEMTRADA® (alemtuzumab) Infusion Reactions: What You Need to Know

- Infusion reactions are side effects linked to the infusion of LEMTRADA® (alemtuzumab). LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.
- Most patients treated with LEMTRADA will experience side effects at the time of the infusion.
- The most common infusion reactions for patients who receive LEMTRADA were nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness, and pain.
- Some serious reactions are possible, such as life-threatening allergic reactions, swelling, wheezing, low blood pressure, chest pain, a fast, slow, or irregular heartbeat, transient neurologic symptoms, high blood pressure, headache, fever, and rash.
- A serious allergic reaction called anaphylaxis, which can cause death if not properly treated, was reported rarely.

LEMTRADA can only be given at a certified healthcare facility that has the necessary equipment and personnel to manage infusion reactions.

Steps you and your healthcare provider can take to help manage infusion reactions

- The healthcare facility where you receive LEMTRADA has personnel who are trained and medical equipment needed to treat infusion reactions.
- Your healthcare provider will give you medication called a corticosteroid, and possibly other medications—such as anti-allergy medications (antihistamines) and anti-fever medications (antipyretics)—to help avoid infusion reactions or make them milder. Corticosteroids are usually given through a vein in your arm on the first 3 days of your infusions—just before your LEMTRADA infusion.

LEMTRADA® alemtuzumab 12mg IV

Reference ID: 3821900

- You will be closely monitored during the infusion and for at least 2 hours following the completion of the infusion to watch for any infusion reactions. Your healthcare provider may continue to monitor you for longer if needed.
- Should an infusion reaction occur, your healthcare provider will likely provide treatment as needed.
  - Medication may be given for relief of your symptoms. For example, antihistamines may help relieve an itchy rash.
  - Infusions usually take about 4 hours; however, your healthcare provider may slow down the infusion or stop it temporarily.
  - If an infusion is stopped, your healthcare provider might try to administer LEMTRADA again, but more slowly and with additional medicine to try to stop an infusion reaction from happening again.
  - If your healthcare provider suspects you might be having a serious allergic reaction, the LEMTRADA infusion will be stopped, and you may receive medication or other measures to treat this reaction. In addition to medication, IV fluids may be given.

Make sure to speak up

If you experience any discomfort or anything that feels out of the ordinary during your infusion, be sure to immediately tell the healthcare provider providing the infusion. If symptoms occur after you have left the healthcare facility, be sure to notify your doctor as soon as possible.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion or after you have left the healthcare facility:

- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heart beat
- chest pain
- rash

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For Healthcare Facilities

LEMTRADA REMS Education Program for Healthcare Facilities

This Educational Piece Includes Information About:

- The LEMTRADA REMS Program requirements to implement in your healthcare facility
- Serious risks of autoimmune conditions, infusion reactions, and malignancies
- Proper administration of LEMTRADA® (alemtuzumab)

The *LEMTRADA REMS Education Program for Prescribers* Includes Additional Information About:

- Steps for PRESCRIBER enrollment
- Ordering of LEMTRADA
- Patient Counseling

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Reference ID: 3821900

What Is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS Program is a strategy to manage known or potential risks associated with a drug and is required by FDA to ensure that the benefits of the drug outweigh its risks. LEMTRADA is only available under a restricted program called the LEMTRADA REMS Program because of the risks of infusion reactions, autoimmune conditions, and malignancies. The *LEMTRADA REMS Education Program for Healthcare Facilities* is designed to educate and train healthcare facilities' authorized representatives on the serious risks associated with LEMTRADA, the LEMTRADA REMS Program requirements, and how to properly administer LEMTRADA.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

Steps for Healthcare Facility Certification	
1	Designate an authorized representative.
2	Review the *LEMTRADA REMS Education Program for Healthcare Facilities*, including the Prescribing Information.
3	Complete and sign the LEMTRADA REMS Healthcare Facility Enrollment Form. This enrollment must be renewed every 2 years.
4	Implement the necessary staff training and processes to comply with the LEMTRADA REMS Program requirements.

The *LEMTRADA REMS Education Program for Healthcare Facilities*, LEMTRADA REMS Healthcare Facility Enrollment Form, and other LEMTRADA REMS Program tools are available online at **www.LemtradaREMS.com** or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program, call 1-855-676-6326 or enroll online at **www.LemtradaREMS.com**

Who Can Be An Authorized Representative?

An authorized representative at the healthcare facility can be a:

- Pharmacist
- Director of infusion center
- Prescriber
- Nurse
- Or any responsible individual in the healthcare facility

Please check with your manager to ensure the appropriate person represents the healthcare facility and attests to the enrollment requirements as stated on the LEMTRADA REMS Healthcare Facility Enrollment Form.

- One representative needs to enroll per healthcare facility (the "authorized representative"). One authorized representative can manage more than one healthcare facility.
- Please note, there are no LEMTRADA REMS requirements for staff at a healthcare facility who will not be involved with dispensing or administering LEMTRADA.

Overview of Important Safety Information

INDICATION

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA.

Please see the Prescribing Information for complete safety information, including BOXED WARNING.

SERIOUS RISKS ASSOCIATED WITH LEMTRADA

Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients, including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate patients with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

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Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. If the infusion is not well tolerated, the duration of the infusion may be extended. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

Autoimmune Conditions

LEMTRADA has been associated with risk of autoimmune conditions, including immune thrombocytopenia, thyroid disorders, and glomerular nephropathies, which may occur many years after treatment and may be serious or life-threatening. Early detection can help to improve the outcomes of patients experiencing these events.

Please review the sections that follow to gain a better understanding of the risks of autoimmune conditions.

Immune Thrombocytopenia (ITP)

Immune thrombocytopenia (ITP) is an autoimmune disorder usually associated with anti-platelet antibodies. Platelet depletion reduces the ability of the blood to clot.

ITP was reported in 2% of patients in clinical trials in MS. ITP can be a serious condition leading to morbidity and mortality, and may occur several years after dosing. Prescribers are required to monitor all patients for ITP by obtaining complete blood counts with differential ≤30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the patient's last infusion of LEMTRADA. After this period of time, testing should be performed based on clinical findings suggestive of ITP. Patients should also be monitored for clinical symptoms of ITP. Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. These clinical signs of ITP may be apparent before serious bleeding develops.

Potential Clinical Presentations of ITP

Note: These pictures are only a guide in order to show examples of bruises or petechiae.
The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

Petechiae are small, scattered, "pinprick" spots under the skin that are red, pink, or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

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Other Autoimmune Cytopenias (including neutropenia, hemolytic anemia, and pancytopenia)

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Monthly CBC results will also be used to monitor for cytopenias. If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

Glomerular Nephropathies

Glomerular nephropathies, including anti-glomerular basement membrane (anti-GBM) disease, have been reported after treatment with LEMTRADA in MS patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation, and this may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria. While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, prescribers are required to monitor patients by obtaining serum creatinine levels and urinalysis with microscopy ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

Thyroid Disorders

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention. Prescribers are required to monitor all patients for thyroid disorders by obtaining thyroid function tests, such as thyroid-stimulating hormone (TSH) levels ≤30 days prior to the first infusion of LEMTRADA, and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

Prescribers should also monitor for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness, and newly occurring constipation (hypothyroidism).

Malignancies

LEMTRADA may increase the risk of thyroid cancer. Patients and prescribers should monitor for symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

LEMTRADA may increase the risk of melanoma. Prescribers should perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA. Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS.

Strategies to Implement in Your Healthcare Facility to Mitigate Risk of Infusion Reactions

- Ensure the infusion site is equipped with the necessary equipment and personnel to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).
- Premedicate patients with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment.
- Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
- Consider longer periods of observation if clinically indicated. Monitor vital signs before and periodically during the infusion.
- Provide appropriate symptomatic treatment as needed if an infusion reaction occurs.
- Consider extending the duration of the infusion if the infusion is not well tolerated.
- Consider immediate discontinuation of the infusion if severe infusion reactions occur.
- Do not administer LEMTRADA outside of the authorized representative's certified healthcare facility.

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Proper Storage and Administration

STORAGE OF LEMTRADA

- LEMTRADA is packaged in 12 mg/1.2 mL (10 mg/mL) single-dose vials.
- LEMTRADA vials should be stored at 2° to 8°C (36° to 46°F). Do not freeze or shake. Protect from light.

PRIOR TO EACH TREATMENT COURSE OF LEMTRADA

- Confirm prescriber is certified and patient is enrolled and authorized to receive LEMTRADA.
- Counsel each patient about the risk for infusion reactions.
- Provide the patient with *What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to dispensing LEMTRADA.
- Administer corticosteroids immediately prior to LEMTRADA administration for the first 3 days of each treatment course.
- Ensure oral prophylaxis for herpes infection is available or has been prescribed to start on the first day of each treatment course. Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed.
- Monitor vital signs before and periodically during the infusion.

ADMINISTRATION OF LEMTRADA

1. Inspect vial for particulate matter/discoloration prior to use.
2. Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique.
3. Inject into 100 mL sterile 0.9% Sodium Chloride USP or 5% Dextrose in Water USP. Gently invert the bag to mix the solution.
4. Cover IV solution bag to protect from light.
5. Administer 12 mg/day over approximately 4 hours.
6. Do not administer as IV push or bolus.
7. If infusion is not well tolerated, infusion duration may be extended.
8. Use the LEMTRADA diluted product within 8 hours after dilution. LEMTRADA diluted product may be stored at room temperature (15° to 25°C) or refrigerated conditions (2° to 8°C). Protect from light.
9. Monitor patient vital signs before and periodically during the infusion, and provide appropriate symptomatic treatment for infusion reactions as needed.
10. Monitor patients for at least 2 hours after each LEMTRADA infusion or longer if clinically indicated.

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FOLLOWING THE CONCLUSION OF EACH LEMTRADA TREATMENT COURSE

- Complete a LEMTRADA REMS Infusion Checklist for each patient at the conclusion of each treatment course and fax it to the LEMTRADA REMS Program (1-855-557-2478) or submit online at **www.LemtradaREMS.com** within 5 business days of the last infusion.
- Return unused vials of LEMTRADA to Genzyme within 50 days of receipt of the LEMTRADA REMS Patient Authorization and Baseline Lab Form.

Adverse Event Reporting

Report suspected adverse events to Genzyme at Medical Information at 1-800-745-4447 (option 2) or to FDA at 1-800-FDA-1088 or **www.FDA.gov/medwatch**

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For Prescribers

LEMTRADA REMS Education Program for Prescribers

This education program includes information about:

- The LEMTRADA REMS Program requirements
- Serious risks of autoimmune conditions, infusion reactions, and malignancies
- Counseling and management of your patient

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What Is the LEMTRADA REMS Program?

A REMS (Risk Evaluation and Mitigation Strategy) is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions and malignancy, LEMTRADA is only available through a restricted program called the LEMTRADA REMS Program.

This brochure has been developed as part of the LEMTRADA REMS Program to help educate prescribers about the risks associated with LEMTRADA and how to help mitigate these risks through periodic monitoring for, and prompt identification of, signs and symptoms of these events.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA.
- **Healthcare Facilities** must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

Steps for Prescriber Certification and Enrollment in the LEMTRADA REMS Program

1. Complete the training program, which includes reviewing the following materials:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - *LEMTRADA REMS Education Program for Prescribers*
2. Successfully complete the 8-question Knowledge Assessment
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form
4. Submit the completed and signed forms to the LEMTRADA REMS Program

The LEMTRADA REMS Program Overview, Knowledge Assessment, LEMTRADA Prescribing Information, and other REMS materials are available online at **www.LemtradaREMS.com** or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program, call 1-855-676-6326 or go to **www.LemtradaREMS.com**

Genzyme will send confirmation of a prescriber's enrollment in the LEMTRADA REMS Program, including the prescriber's assigned LEMTRADA REMS Program identification number.

You will not be able to prescribe LEMTRADA without completing your certification in the LEMTRADA REMS Program.

You should understand that if you fail to comply with the Program requirements, you may no longer be able to participate in the Program.

Reference ID: 3821900

Overview of Important Safety Information

INDICATION

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA.

Please see the Prescribing Information for complete safety information, including BOXED WARNING.

SERIOUS RISKS ASSOCIATED WITH LEMTRADA

Autoimmune Conditions

LEMTRADA has been associated with risk of autoimmune conditions, including immune thrombocytopenia, other cytopenias (including neutropenia, hemolytic anemia, and pancytopenia), thyroid disorders and glomerular nephropathies, which may occur many years after treatment and may be serious or life-threatening. Early detection can help to improve the outcomes of patients experiencing these events.

Please review the sections that follow to gain a better understanding of the risks of autoimmune conditions.

Immune Thrombocytopenia (ITP)

Immune thrombocytopenia occurred in 2% of LEMTRADA-treated patients in clinical studies in MS. Immune thrombocytopenia is an autoimmune disorder usually associated with anti-platelet antibodies. Platelet depletion reduces the ability of the blood to clot. Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. These clinical signs of ITP may be apparent before serious bleeding develops.

ITP can be a serious condition leading to morbidity and mortality, and may occur several years after dosing. It is important to monitor all patients for ITP as follows:

- Complete blood counts with differential should be obtained ≤30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the patient's last infusion of LEMTRADA. After this period of time, testing should be performed based on clinical findings suggestive of ITP.
- Check the patient for clinical symptoms of ITP.
- Counsel the patient on the importance of complying with monthly monitoring of their blood and the need to continue for 48 months after their last infusion.
- Educate the patient on how to recognize ITP-related symptoms, and emphasize the need to remain vigilant for them.
- If ITP is suspected, appropriate medical intervention should be promptly initiated, including immediate referral to a specialist. Severe or widespread bleeding is life-threatening and demands immediate care.

The potential risk associated with retreatment with LEMTRADA following the occurrence of ITP is unknown.

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Reference ID: 3821900

Potential Clinical Presentations of ITP

Note: These pictures are only a guide in order to show examples of bruises or petechiae.
The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

Petechiae are small, scattered, "pinprick" spots under the skin that are red, pink or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

Images ©2015 Genzyme Corporation.

Other Autoimmune Cytopenias

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Use the monthly CBC results to monitor for cytopenias.
If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

Glomerular Nephropathies

Glomerular nephropathies, including anti-glomerular basement membrane (anti-GBM) disease, have been reported after treatment with LEMTRADA in multiple sclerosis patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation, and this may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria.

While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, it is important that the monthly tests are conducted.

- Serum creatinine levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.
- Urinalysis with urine cell counts should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies. In menstruating females, consider the timing of urinalysis to avoid false positives. The observation of clinically significant changes from baseline in serum creatinine, unexplained hematuria, and/or proteinuria should prompt further evaluation for nephropathies, including referral to a specialist.
- Early detection and treatment of nephropathies may decrease the risk of poor outcomes.
- Immediate referral to a specialist for further assessment for patients with suspected nephropathy is strongly recommended.

Thyroid Disorders

During clinical trials, autoimmune thyroid disorders including Graves' disease, hyperthyroidism, and hypothyroidism were reported. Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies.

Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention.

It is important to monitor all patients for thyroid disorders as follows:

- Thyroid function tests such as thyroid-stimulating hormone (TSH) levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.
- Additionally, watch out for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness, and newly occurring constipation (hypothyroidism).

- Thyroid disease poses special risks in women who become pregnant. Untreated thyroid disease can cause harm to the unborn and newborn baby. Special caution should be taken for pregnant women with Graves' disease, as maternal thyroid-stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause transient neonatal Graves' disease. The HCP responsible for managing the patient's pregnancy must be made aware of the increased risk of thyroid disorders due to the patient's LEMTRADA treatment, and the need for these to be appropriately treated.

Strategies to Mitigate the Risk of Autoimmune Conditions

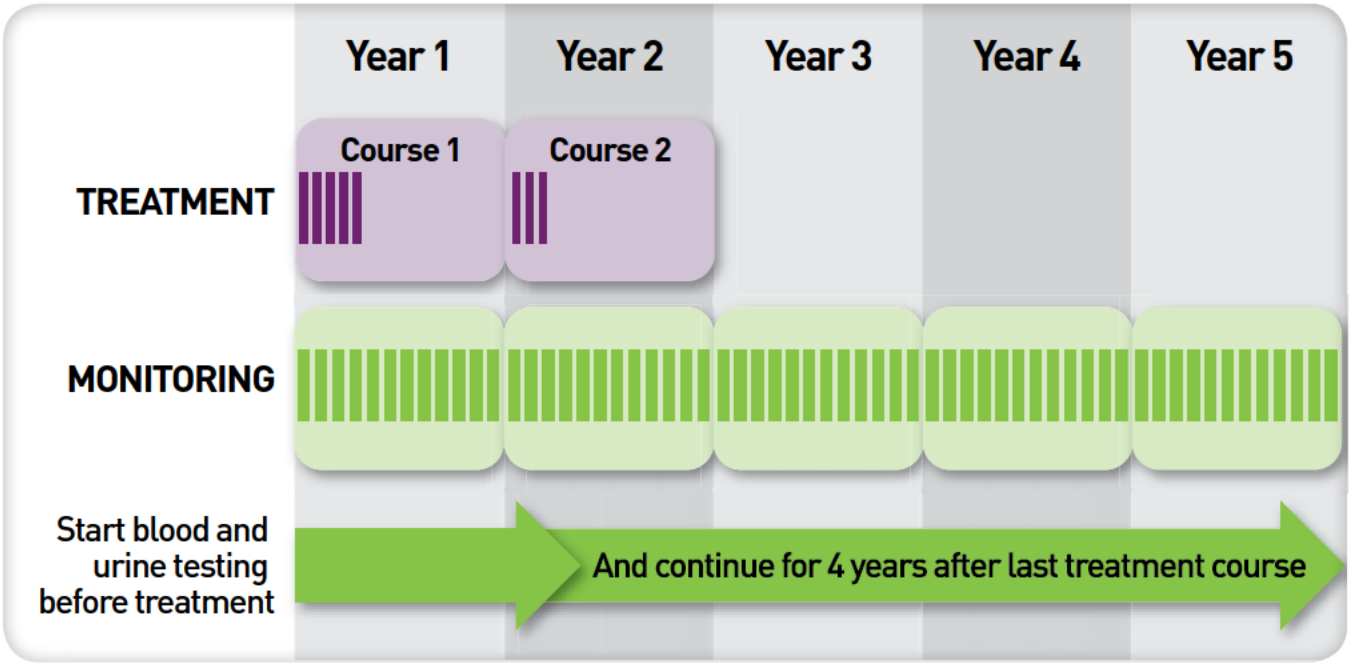
In order to minimize possible risks and side effects of LEMTRADA, prescribers and patients must commit to 48 months of follow-up after the last infusion of LEMTRADA. It is important that patients understand that they should continue with the monitoring, even if they are feeling well.

Creating a partnership between you and your patient, along with careful review of the patient education tool (*What You Need to Know About LEMTRADA Treatment: A Patient Guide*) with your patient, will help patients to:

- Comply with periodic tests
- Identify and report symptoms early
- Receive prompt and appropriate treatment if needed

To enhance your understanding of the duration of the effects of treatment and the length of required follow-up, please refer to the diagrams below titled ***Overview of LEMTRADA Treatment*** and ***Overview of LEMTRADA Monitoring.***

Overview of LEMTRADA Treatment



Overview of LEMTRADA Monitoring

Condition	Activity	Timing	
Immune Thrombocytopenia (ITP)	Complete blood count with differential	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Serum creatinine	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Urinalysis with microscopy	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Thyroid Disorders	Thyroid function tests (such as TSH)	Prior to initiating LEMTRADA treatment	Every 3 months until 48 months after last infusion

Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients, including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate with high-dose corticosteroids (1000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before the infusion and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. The duration of the infusion may be extended if clinically indicated. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

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Malignancies

LEMTRADA is an immunomodulatory therapy, and caution should be exercised in initiating LEMTRADA in patients with pre-existing or ongoing malignancies.

Thyroid Cancer

LEMTRADA may increase the risk of thyroid cancer. In controlled clinical studies, 0.3% of LEMTRADA-treated patients developed thyroid cancer, compared to none in the interferon beta-1a–treated group. However, screening for thyroid cancer was performed more frequently in the LEMTRADA-treated group, because of the higher incidence of autoimmune thyroid disorders in those patients. Two additional cases of thyroid cancer in LEMTRADA-treated patients occurred in uncontrolled studies.

Melanoma

LEMTRADA may increase the risk of melanoma. In uncontrolled studies, 0.3% of LEMTRADA-treated patients developed melanoma or melanoma in situ. One of those patients had evidence of locally advanced disease.

Lymphoproliferative Disorders and Lymphoma

Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS, including a MALT lymphoma, Castleman's Disease, and a fatality following treatment of non-Epstein Barr Virus–associated Burkitt's lymphoma. There are postmarketing reports of Epstein Barr Virus-associated lymphoproliferative disorders in non-MS patients.

Monitoring for Malignancies

Patients and healthcare providers should monitor for symptoms of thyroid cancer, including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

Perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.

Reference ID: 3821900

Patient Enrollment, Counseling, and Management

To enroll your patient in the LEMTRADA REMS Program, you must:

- Complete the LEMTRADA REMS Patient Enrollment Form for each patient and provide a completed copy to the patient. The completed form should be submitted to the LEMTRADA REMS Program and a copy stored in the patient's records.
- Enrollment forms can be obtained online **(www.LemtradaREMS.com)** or by phone (1-855-676-6326).
- Completed forms should be faxed to 1-855-557-2478.
- Genzyme will provide confirmation of patient enrollment.

As part of patient management and counseling, you must:

- Inform your patient about the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies, and the need for baseline and periodic monitoring. A patient-directed educational guide has been developed for you to use in counseling your patients on the risks associated with LEMTRADA (*What You Need to Know About LEMTRADA Treatment: A Patient Guide*). You should review this guide with your patient on an ongoing basis. You must provide each patient with a copy of this guide and a LEMTRADA Patient Safety Information Card.
- Perform the baseline and periodic monitoring described above and in the Prescribing Information for LEMTRADA.
- Complete the LEMTRADA REMS Patient Status Form 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the completion of the patient's last infusion of LEMTRADA, and submit the completed form to the LEMTRADA REMS Program.
- Notify Genzyme if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care.

Ordering LEMTRADA

To order LEMTRADA, you must submit a LEMTRADA REMS Prescription Ordering Form for each LEMTRADA prescription to the LEMTRADA REMS Program. The ordering form can be obtained online **(www.LemtradaREMS.com)** or by phone (1-855-676-6326).

Completed forms should be faxed to 1-855-557-2478.

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Administering LEMTRADA

As part of the LEMTRADA REMS Program, a healthcare facility must be enrolled in the LEMTRADA REMS Program to be able to dispense/administer LEMTRADA. It is important that you select a healthcare facility that is enrolled and active in the LEMTRADA REMS Program for your patient's infusion. A database of certified healthcare facilities is available by phone at 1-855-676-6326.

Prior to your patient's infusion, you must submit a LEMTRADA REMS Patient Authorization and Baseline Lab Form to the LEMTRADA REMS Program indicating completion of each patient's baseline labs within 30 days of the infusion date.

PRIOR TO EACH TREATMENT COURSE OF LEMTRADA

- Administer corticosteroids (1000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA administration for the first 3 days of any treatment course
- Administer anti-viral prophylaxis for herpetic viral infection starting on the first day of each treatment course and continuing for a minimum of 2 months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥200 cells per microliter, whichever occurs later
- Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed

Adverse Event Reporting

Report suspected adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or to FDA at 1-800-FDA-1088 or **www.FDA.gov/medwatch**

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For Healthcare Providers

LEMTRADA REMS Knowledge Assessment

To become a certified prescriber in the LEMTRADA REMS Program, you will need to answer ALL 8 questions correctly.

- Complete the Knowledge Assessment, populate and sign the one-time LEMTRADA REMS Prescriber Enrollment Form. Fax your responses to the 8 Knowledge Assessment questions and the LEMTRADA REMS Prescriber Enrollment Form to 1-855-557-2478. You can also complete the Knowledge Assessment online at **www.LemtradaREMS.com**

- You will receive correspondence from the LEMTRADA REMS Program via the preferred communication method (email or fax) selected on your enrollment form within two business days. Correspondence may include:
  - How to retake the Knowledge Assessment, if necessary
  - A confirmation of your enrollment and certification in the LEMTRADA REMS Program (which requires no further action)

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QUESTIONS 1-8

QUESTION 1 (check one)

Which of the following laboratory tests are required prior to initiating LEMTRADA treatment and within 30 days of the first infusion?

- ☐ A. Complete blood count (CBC) with differential
- ☐ B. Serum creatinine and urinalysis with urine cell counts
- ☐ C. Thyroid function test
- ☐ D. All of the above

QUESTION 2 (check one)

My patient must have monthly blood and urine tests for:

- ☐ A. 12 months after their last infusion
- ☐ B. 24 months after their last infusion
- ☐ C. 36 months after their last infusion
- ☐ D. 48 months after their last infusion

QUESTION 3

I should assess my patient's compliance with required lab testing on an ongoing basis and document their compliance on the LEMTRADA REMS Patient Status Form every 6 months.

- ☐ True
- ☐ False

QUESTION 4 (check one)

Which of the following symptoms could be associated with immune thrombocytopenia (ITP)?

- ☐ A. Headache, rash, pyrexia, nausea
- ☐ B. Easy bruising, petechiae, purpura, spontaneous mucocutaneous bleeding
- ☐ C. Weight gain, fatigue, constipation
- ☐ D. Pyrexia, chills, swollen glands

QUESTION 5 (check one)

Which of the following could be associated with glomerular nephropathy?

- ☐ A. Elevation in serum creatinine, hematuria, or proteinuria
- ☐ B. Easy bruising, petechiae, purpura, spontaneous mucocutaneous bleeding (e.g., epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding
- ☐ C. Weight gain, fatigue, constipation
- ☐ D. Weight loss, tachycardia, nervousness

QUESTION 6 (check one)

Prior to enrolling a patient in the LEMTRADA REMS Program, you should:

- ☐ A. Provide *What You Need to Know About LEMTRADA Treatment: A Patient Guide* to the patient
- ☐ B. Counsel the patient on the serious risks associated with LEMTRADA and how to mitigate these risks through periodic monitoring
- ☐ C. Provide a LEMTRADA Patient Safety Information Card to the patient
- ☐ D. All of the above

QUESTION 7

The healthcare facility that will administer LEMTRADA infusions to my patient is not required to be REMS certified and enrolled.

- ☐ True
- ☐ False

QUESTION 8

LEMTRADA treatment should be administered in a setting that has the necessary equipment and personnel to manage serious infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

- ☐ True
- ☐ False

Please provide your prescriber name and NPI number so we can associate your progress with your stakeholder record. You can provide this information below.

Prescriber Name: _____

Prescriber NPI: _____

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[Date]

[Treating Provider First Name] [Treating Provider Last Name], [Treating Provider Title]
[Treating Correspondence Primary Contact First Name] [Treating Correspondence Primary Contact Last Name]
[Treating Site Name]
[Treating Site Address 2]
[Treating Site Address 1]
[Treating Site City, State ZIP]

RE: Prescriber LEMTRADA® (alemtuzumab) REMS Program Responsibilities Reminder

Dear Dr. [Provider Last Name],

This letter is to remind you of your responsibilities as a prescriber enrolled in the LEMTRADA REMS Program. Please remember that you must:

1. **Keep Track of Needed Lab Monitoring**: Prescribers are required to keep track of the laboratory monitoring status of all patients who have been infused with LEMTRADA (alemtuzumab) from first infusion until 48 months after the last infusion.
2. **Complete LEMTRADA REMS Status Forms**: For every patient who is infused with LEMTRADA, prescribers are required to complete a LEMTRADA REMS Patient Status Form 6 months after the first infusion, and then every subsequent 6 months until 48 months after the patient's last infusion.

If you have any questions about requirements, please call the LEMTRADA REMS Program at 1-855-676-6326, Monday through Friday, 8:30 am to 8:00 pm Eastern Time.

Sincerely,

LEMTRADA REMS Program

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LEMTRADA REMS Prescription Ordering Form

Please fax this completed form to 1-855-557-2478

*Indicates a mandatory field.

I: PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)*

Date of Birth (MM/DD/YYYY)* | Gender* ☐ Male ☐ Female

Street Address 1*

Street Address 2*

City* | State* | ZIP Code*

Phone Number*

THIS SECTION SHOULD BE FILLED OUT BY THE PRESCRIBER

II: INSURANCE INFORMATION

Patient does not have insurance. ☐

Primary Insurance Company*	Phone Number*	Name of Insured*	Policy Number*	Group/Policy Number*
Secondary Insurance Company	Phone Number	Name of Insured	Policy Number	Group/Policy Number

III: PRESCRIBER INFORMATION

Prescriber Name (Last, First)*	NPI Number*	Name of Institution or Facility*		Tax ID*	
Office Contact*		Street Address*	City*	State*	ZIP Code*
Email Address		Phone Number*	Fax Number*		

IV: PRESCRIPTION INFORMATION

LEMTRADA® (alemtuzumab) 12 mg IV

Check one* ☐ Initial course (1 vial [12 mg/day]) X 5 consecutive days — Total number of vials ordered: _____

☐ Subsequent course (1 vial [12 mg/day]) X 3 consecutive days — Total number of vials ordered: _____

Primary diagnosis: ICD-9 CM340 / ICD-10 G35

V: INFUSION CENTER INFORMATION†

Infusion Center Where Patient Is Referred* | Phone Number*

Street Address*

City* | State* | ZIP Code*

†**Note:** LEMTRADA can only be infused at REMS Certified infusion sites. Genzyme Corporation will contact you if the infusion center you have indicated is not certified to infuse LEMTRADA.

VI: SIGNATURE

Note to Prescribers: This form does not authorize the certified pharmacy or infusion center to dispense LEMTRADA. The LEMTRADA REMS Patient Authorization and Baseline Lab Form must be submitted in order to authorize LEMTRADA to be dispensed.

By signing below, I authorize the LEMTRADA REMS Program and its agents and representatives to forward this prescription on my behalf to a certified pharmacy or infusion center to dispense LEMTRADA to the patient named above.

X

Licensed Prescriber Signature* (Signature required; no stamps accepted) | Print Name* | Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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For Patients

What You Need to Know About LEMTRADA® (alemtuzumab) Treatment: A Patient Guide

Patients: Your doctor or nurse will go over this patient guide with you. It is important to ask any questions you might have prior to each time LEMTRADA® (alemtuzumab) is given to you. Keep this guide for important safety information about the serious risks and reactions of LEMTRADA.

Healthcare Providers: Review this patient guide with your patient prior to each treatment course, and provide your patient a copy to take home.

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What Is LEMTRADA?

LEMTRADA is a prescription medicine approved to treat adult patients with relapsing forms of multiple sclerosis. Because of serious risks with LEMTRADA, it is generally reserved for patients that have not been helped enough by 2 or more MS treatments. You and your healthcare provider have determined that LEMTRADA is an appropriate treatment for you.

LEMTRADA is only available at your doctor's office, clinic, or hospital. It is not a medicine you will give yourself at home because of the serious risks of LEMTRADA.

What Is the Most Serious Risk Information About LEMTRADA Treatment?

LEMTRADA may cause serious side effects, including infusion reactions, autoimmune conditions, and malignancy.

- Most patients treated with LEMTRADA will experience side effects at the time of the infusion or within 24 hours after the infusion **(infusion reactions)**. Common infusion reactions include nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness, and pain.
- Patients receiving LEMTRADA are at risk of **autoimmune conditions**. Your body's immune system contains particular cells that help fight infections. Autoimmune side effects are illnesses that occur when these cells of the immune system fight against your own body.
- Receiving LEMTRADA may increase your chance of getting some kinds of cancers **(malignancies)**, including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:
  - new lump
  - swelling in your neck
  - pain in the front of your neck
  - hoarseness or other voice changes that do not go away
  - trouble swallowing or breathing
  - cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA, and each year while you are receiving treatment, to monitor for symptoms of skin cancer.

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What Are the Signs and Symptoms of Infusion Reactions and Autoimmune Conditions After LEMTRADA Treatment, and What Should I Do?

INFUSION REACTIONS

Most patients treated with LEMTRADA will experience side effects at the time of the infusion, some of which may be serious or life-threatening. Serious infusion reactions may happen while you receive LEMTRADA, or up to 24 hours or longer after you receive LEMTRADA.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion or after you have left the healthcare facility:

- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heart beat
- chest pain
- rash

In order to try to reduce these effects, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before or after the infusion to try to reduce your chances of these reactions or to treat them after they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed, or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.

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DELAYED SIDE EFFECTS

As mentioned previously, patients receiving LEMTRADA are at risk of certain autoimmune conditions. The autoimmune conditions include:

- Immune thrombocytopenia (ITP, or low platelets)
- Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)
- Certain types of kidney diseases
- Thyroid disorders

All of these conditions can be treated when identified early, but delaying treatment increases the risk of complications. This is why it is so important to recognize and immediately report any signs or symptoms of these conditions to your doctor.

In the following pages, you will learn more about each of these side effects, including the signs and symptoms that you may experience and what to do if they happen.

Immune Thrombocytopenia (ITP, or low platelets)

ITP is a condition which results in a decrease in the number of platelets in the blood. ITP has been observed in approximately 2% of patients treated with LEMTRADA in MS clinical trials. Platelets are necessary for normal blood clotting. ITP can cause severe bleeding. If detected early, ITP is usually treatable, but if left untreated it may lead to serious health problems and possibly death.

A blood test will help your doctor watch for changes in your platelet count in order to catch this side effect early. Therefore, your doctor will have your blood tested before starting LEMTRADA and on a monthly basis after your first infusion. The monthly testing must continue for 4 years after your last infusion, or longer if you have signs or symptoms of ITP.

Importantly, ITP may also be detected by certain signs or symptoms that you need to be aware of.

What are the signs and symptoms of ITP?

- Small, scattered spots on your skin that are red, pink, or purple
- Easy bruising
- Bleeding from a cut that is harder to stop
- Heavier, longer, or more frequent menstrual periods than normal. Bleeding between your menstrual periods could also be a sign of ITP
- Bleeding from your gums or nose that is new or takes longer than usual to stop

Call your doctor immediately if you have any of these signs or symptoms. If you cannot reach your doctor, seek immediate medical attention.

Reference ID: 3821900

These pictures show examples of spots and bruises caused by ITP.



This is an example of a leg with scattered spots under the skin that are red, pink, or purple. They might look like pinpricks.

It is important to note that the spots could occur anywhere on your body, not just on your leg.



This is an example of arms with easy or excessive bruising.

It is important to note bruises could occur anywhere on your body, not just on your arms.



This is an example of spots due to bleeding under the tongue.

It is important to note that this could occur anywhere in your mouth—under the tongue, on the roof of your mouth, on your inner cheeks, on your tongue, or on your gums.

Note: These pictures are only a guide in order to show examples of bruises or rashes.

Images ©2015 Genzyme Corporation.

What if I develop ITP?

It is best to identify and treat ITP as early as possible. That is why it is so important that you continue to have your monthly blood test and check for symptoms, which could detect a problem before you have symptoms. It is also important that you, your family members, and/or caregivers are watching for any of the signs or symptoms described in this guide. Delaying treatment of ITP raises the chance of more serious problems.

If detected early, ITP is usually treatable. If you develop ITP, you and your doctor will decide which treatment is best for you.

If you notice any of the signs or symptoms as described above, call your healthcare provider right away to report the symptoms. If you cannot reach your healthcare provider, seek immediate medical attention.

Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)

LEMTRADA may cause a decrease in some types of blood cells. Symptoms may include weakness, dark urine, chest pain, yellowing of the skin or whites of your eyes (jaundice), or fast heartbeat. Your healthcare provider will do blood tests to check for low blood counts.

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Kidney disorders (such as anti-glomerular basement membrane disease)

LEMTRADA may cause a condition known as anti-glomerular basement membrane disease, or anti-GBM disease. Kidney disorders, including anti-GBM disease, have been observed in 0.3% (3 per 1000) patients treated with LEMTRADA in MS clinical trials. Anti-GBM disease is an autoimmune side effect that can result in severe damage to the kidneys. Anti-GBM disease can also damage the lungs, although this was not seen in clinical trials with LEMTRADA. If untreated it can cause kidney failure requiring chronic dialysis or transplant, and may lead to death. Most of the time, doctors can treat kidney problems. It is best to begin treatment as early as possible.

A blood test and a urine test will help your doctor watch for signs of kidney disease to help catch this potential side effect early. Your doctor will have your blood and urine tested in the month before you start treatment with LEMTRADA, and on a monthly basis after your initial infusion. Your doctor will test your urine monthly, so if you are a woman, it is important to avoid urine testing during your menstrual period as this may give a false result. This testing will continue for 4 years after your last infusion, or longer if you have signs or symptoms of a kidney disorder.

Importantly, anti-GBM disease can also be detected by certain signs and symptoms that you need to be aware of.

What are the signs and symptoms of kidney problems or anti-GBM disease?

- Blood in the urine (red or tea-colored urine)
- Swelling in your legs or feet
- Coughing up blood

What if I develop kidney problems?

It is best to begin treatment as early as possible. It is important that you are familiar with the signs and symptoms of kidney problems and anti-GBM disease, and complete your regular laboratory tests (blood and urine tests). Kidney problems will almost always need treatment.

If you notice any of the signs or symptoms as described above, call your doctor right away to report the symptoms. If you cannot reach your doctor, seek immediate medical attention.

Reference ID: 3821900

Thyroid disorders

The thyroid is a gland found in the lower part of the neck. This gland produces hormones that are important throughout your body. In some people, the immune system may mistakenly attack the cells of the thyroid gland (autoimmune thyroid condition), which affects its ability to make and control the level of hormones.

LEMTRADA may cause development of thyroid disorders including:

- Overactive thyroid gland, or hyperthyroidism, when the thyroid produces too much hormone
- Underactive thyroid gland, or hypothyroidism, when the thyroid does not produce enough hormone

An estimated 34% of patients experienced autoimmune thyroid disorders following treatment with LEMTRADA, in MS clinical trials.

Your blood will be checked in the month before you start treatment with LEMTRADA, and every 3 months after your initial infusion, until 4 years after your last LEMTRADA infusion, or longer if you show signs or symptoms of a thyroid disorder. This blood test will help your doctor detect thyroid disorders early.

What are the signs and symptoms of a thyroid disorder?

Overactive thyroid, or hyperthyroidism	Underactive thyroid, or hypothyroidism
Excessive sweating	Unexplained weight gain
Unexplained weight loss	Feeling cold
Eye swelling	Worsening tiredness
Nervousness	Newly occurring constipation
Fast heartbeat	

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What if I develop a thyroid disorder?

Tell your doctor if you experience these symptoms. Most of the time, thyroid disorders are manageable with treatment. Depending on the type of thyroid disorder, your doctor will decide which treatment is best for you. It will be important to follow your doctor's recommendations to be sure to benefit the most from your treatment. In some cases, you may have to take medication for the rest of your life for your thyroid disorder. In some situations, your thyroid may need to be removed.

If you develop a thyroid disorder, it is very important that you are properly treated for it, especially if you become pregnant after using LEMTRADA. Having an untreated thyroid disorder could harm your unborn baby, or harm your baby after birth.

IMPORTANT!

Since all of these autoimmune conditions could occur long after you received a course of treatment with LEMTRADA, it is very important that you continue to have your monthly blood and urine tests (even if you are feeling well).

You must continue to watch for signs and symptoms

Do this for 4 years after your last LEMTRADA infusion

Early detection and prompt treatment may give you the best opportunity for improvement

Carry your LEMTRADA Patient Safety Information Card with you at all times and show it to any healthcare professionals who are providing you with treatment (including for non-MS conditions) or in the event of a medical emergency.

These are **NOT** all the possible side effects of LEMTRADA. Refer to the LEMTRADA Medication Guide that you were given or talk to your doctor or nurse for medical advice about other side effects.

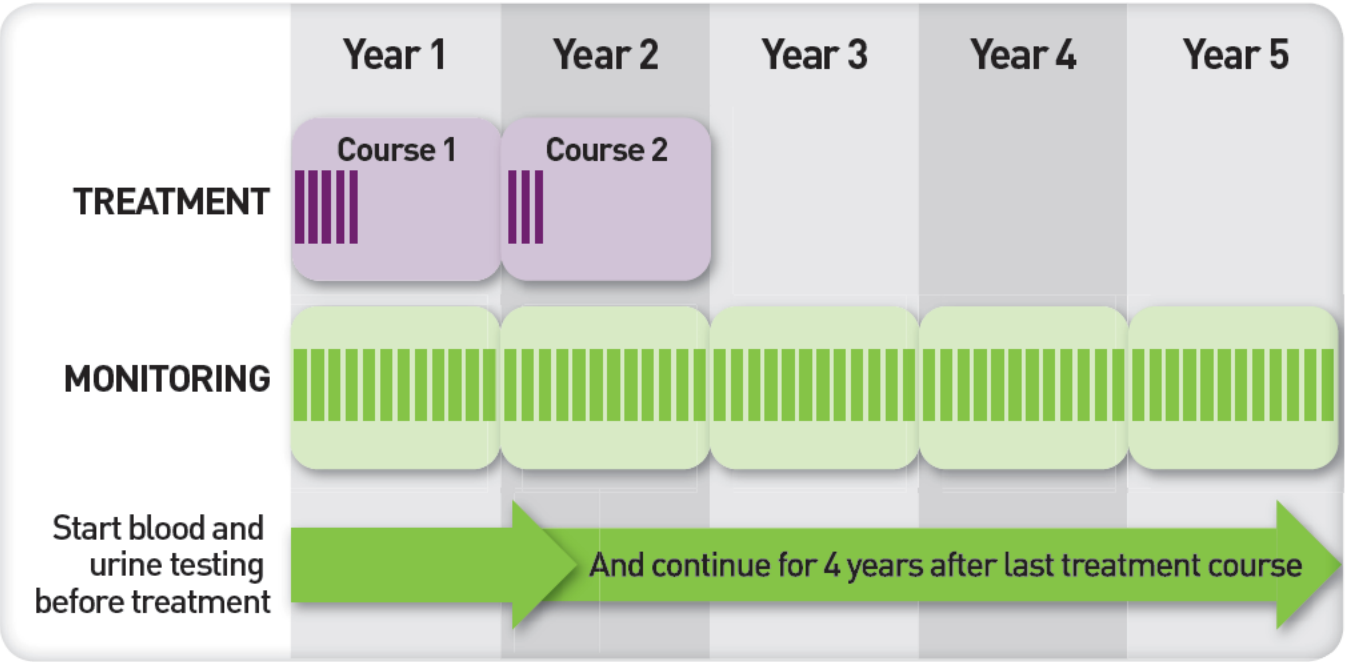
How Can I Detect the Delayed Side Effects from LEMTRADA?

To check for the development of autoimmune conditions (previously described), you will have to be monitored monthly by having your blood and urine tested. Your doctor will order blood and urine tests in the month before you start LEMTRADA treatment, and these tests will continue each month for 4 years after your last LEMTRADA infusion. Monitoring may need to continue for longer if you have signs or symptoms of autoimmune conditions. Your doctor will check the results of these tests to see if you have developed any side effects.

It is very important that you continue to have these tests for 4 years after your last LEMTRADA infusion, even if you are feeling well (no symptoms or side effects). Side effects may occur many months to years after your LEMTRADA infusion and may be (in rare cases) life-threatening, so it is very important that you continue to be checked and that you watch out for symptoms. This will help allow a problem to be detected and treatment to begin right away.

This means that you commit to the monthly blood and urine laboratory tests, continuing for 4 years after your last infusion with LEMTRADA. You and your doctor will work together as a team to make sure you get these tests done, and to plan them around your normal activities. If you are a woman, it is also important to avoid urine testing during your menstrual period, as this may give a false result.

To help you better understand the duration of the effects of LEMTRADA treatment and the length of required follow-up, please refer to the diagram below.



LEMTRADA® alemtuzumab 12mg IV

The following table shows you which laboratory tests are done, when, and for how long.

Test	When?	For how long?
Blood tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion
Urine tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion

How Is LEMTRADA Given?

You will receive LEMTRADA through an intravenous line in your vein (infusion). LEMTRADA is given in two treatment courses. Generally, you will receive LEMTRADA for 5 days for the first treatment course and then for 3 days approximately 1 year later (second treatment course).

The infusion takes place in a healthcare facility or infusion center. It takes about 4 hours to receive a full dose each day, but can take longer if you have side effects (infusion reactions), in which case the infusion may need to be slowed down or stopped. In order to try to reduce some of these reactions, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before, during, or after the infusion to try to avoid these reactions or to treat them once they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.

Where Can I Get More Information on LEMTRADA?

There is a LEMTRADA Medication Guide that your doctor or nurse will give you at the beginning of your treatment course. You can also find additional information at **www.LemtradaREMS.com** or call the LEMTRADA REMS Program at 1-855-676-6326.

How Can I Reach My Doctors?

To make it easier to contact your doctor(s) or your healthcare team, please fill in their telephone numbers and addresses in the chart below.

Doctor/Healthcare Team	Telephone Number	Address

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LEMTRADA®
alemtuzumab 12mg IV

For Prescribers to Complete

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PATIENT AUTHORIZATION AND BASELINE LAB FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

This form must be completed within 30 days prior to the first infusion date of each LEMTRADA® (alemtuzumab) patient's treatment course.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (Last, First)* | Office Phone Number*

Address*

City* | State* | ZIP Code*

Prescriber LEMTRADA REMS Program Identification Number*

PATIENT INFORMATION (PLEASE PRINT)

Name (Last, First)*

Patient LEMTRADA REMS Program Identification Number*

Date of Birth (MM/DD/YYYY)*

AUTHORIZATION AND BASELINE LABS

Do you authorize LEMTRADA treatment for the above-referenced patient?* ☐ **Yes** ☐ **No**

Do you attest that required baseline laboratory testing has been completed prior to LEMTRADA treatment and within 30 days of the patient's first infusion?* ☐ **Yes** ☐ **No**

PRESCRIPTION INFORMATION

Check one* ☐ Initial course (1 vial [12 mg/day]) X 5 consecutive days — Total number of vials: _____

☐ Subsequent course (1 vial [12 mg/day]) X 3 consecutive days — Total number of vials: _____

SIGNATURE

Prescriber Signature* | Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or submit online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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For Pharmacy

LEMTRADA® alemtuzumab 12mg IV

LEMTRADA REMS PHARMACY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

LEMTRADA® (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the pharmacy must enroll the pharmacy in the LEMTRADA REMS Program.

☐ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

PHARMACY INFORMATION (PLEASE PRINT)

Name of Pharmacy*		NPI Number*	
Pharmacy Address*			
City*		State*	ZIP Code*
Name of Authorized Pharmacy Representative*		Title*	
Phone Number*	Fax Number*	Email Address	

PHARMACY AGREEMENT

I am the authorized representative designated by my Pharmacy to coordinate the activities of the LEMTRADA REMS Program.
By signing this form, I agree to comply with the following program requirements:

- I understand that my pharmacy must be certified with the LEMTRADA REMS Program to dispense LEMTRADA.
- I will oversee implementation and compliance with the LEMTRADA REMS Program requirements.
- I have reviewed the LEMTRADA REMS Program Overview.
- I will ensure that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the LEMTRADA REMS Program Overview.
- I will put processes and procedures in place, and follow such processes and procedures, to ensure the following verifications are met prior to dispensing LEMTRADA:
  - The LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program prior to dispensing LEMTRADA.
  - Ensuring LEMTRADA is only dispensed to a certified infusion center.
- This pharmacy will establish procedures and protocols that are subject to audit, to help ensure compliance with the requirements of the LEMTRADA REMS Program.
- I understand that my pharmacy must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.

SIGNATURE

Authorized Pharmacy Representative Signature* Date*

Print Name* Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478 or enroll online at www.LemtradaREMS.com

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

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Reference ID: 3821900

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[Date]

[Patient_First_Name] [Patient_Last_Name]
[Patient Primary_Address_2]
[Patient Primary_Address_1]
[Patient Primary_City», «Patient_State» «Patient_ZIP]

Dear [Patient_First_Name] [Patient_Last_Name]:

When enrolling in the LEMTRADA REMS Program, you and your doctor agreed that you will participate in monthly laboratory monitoring for 4 years after your last infusion to monitor for possible side effects.

The lab tests, which are required every 30 days, are important to identify side effects like autoimmune conditions. Please make sure to continue to schedule and go to your monthly lab appointments.

It is also important that you look for symptoms of these side effects by doing your own symptom self-checks, as described in *What You Need to Know About LEMTRADA Treatment: A Patient Guide* that your doctor gave you before you started your LEMTRADA treatment.

As part of the program, you are receiving these monthly reminders for your lab tests. For your convenience, the program offers options on how you can receive your monthly reminders:

- By mail
- By phone
- By email

If you wish to change the way you receive these reminders, please call the LEMTRADA REMS Program at 1-855-676-6326.

If you have questions about LEMTRADA or your monthly lab monitoring, please call the LEMTRADA REMS Program at 1-855-676-6326, Monday through Friday, 8:30 am to 8:00 pm ET. In addition, please contact the LEMTRADA REMS Program if your contact information has changed.

Sincerely,

LEMTRADA REMS Program

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alemtuzumab 12mg IV

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Reference ID: 3821900

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 103-948/S-5151

OTHER REVIEW(S)

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

RISK EVALUATION AND MITIGATION STRATEGY (REMS) MODIFICATION REVIEW

Date:	September 17, 2015
Reviewer:	Jasminder Kumar, Pharm.D. Risk Management Analyst Division of Risk Management
Acting Team Leader:	Jamie Wilkins-Parker, Pharm.D. Division of Risk Management
Acting Deputy Division Director:	Reema Mehta, Pharm.D., M.P.H. Division of Risk Management
Subject:	Evaluation of proposed REMS minor modification
Drug Name(s):	Lemtrada (alemtuzumab)
Therapeutic class:	CD52-directed cytolytic monoclonal antibody
Dosage forms:	12 mg/1.2 mL (10 mg/mL) injection
OND Review Division:	Division of Neurology Products
Application Type/Number:	BLA 103948 Suppl. 5151
Applicant/sponsor:	Genzyme, a Sanofi Company
OSE RCM #:	2015-1937

1. INTRODUCTION

This review provides the Division of Risk Management's (DRISK) evaluation of the proposed minor modification to the risk evaluation and mitigation strategy (REMS) for Lemtrada (alemtuzumab), BLA 103948, submitted by Genzyme, a Sanofi Company on July 22, 2015 and amended on September 10, 2015. The purpose of the modification is to update the Lemtrada REMS website to provide the option to complete and submit the required REMS forms online, with the exception of the Lemtrada REMS Patient Enrollment Form and the Lemtrada REMS Prescription Ordering Form. In addition, the modification includes an update to the Lemtrada logo per Office of Prescription Drug Promotion (OPDP) feedback[1], along with other minor updates.

1.1 REGULATORY HISTORY

The regulatory history that relates to the proposed REMS minor modification for Lemtrada (Supplement 5151) is briefly summarized below:

October 22, 2014: A teleconference between the Agency and the Sponsor took place during the development of the Lemtrada REMS Program website. During this meeting, the Agency informed the Sponsor that the Lemtrada REMS Program website should not only provide access to downloadable versions of all approved REMS materials, but that the website should all the electronic completion and submission of the REMS Documents. The Sponsor informed the Agency that it was not possible to incorporate this functionality into the website prior to the REMS approved and therefore proposed a REMS modification submission within 9 months of the initial approval of the REMS that would include this website functionality.

November 14, 2014: The Agency approved Lemtrada (alemtuzumab), BLA 103948, for the treatment of patients with relapsing forms of MS. The approval included a REMS which contained a CP, ETASU (A, B, C, D), an implementation system, and a timetable for submission of assessments.

July 22, 2015: The Sponsor submitted a proposed Minor REMS Modification (eCTD Sequence 0267, Supplement 5151), which updated the Lemtrada REMS website to increase its functionality as discussed during the October 22, 2014 teleconference with the Agency and included other minor edits to the REMS program

September 3, 2015: The Agency provided Genzyme with interim comments based on the Agency's preliminary review of the proposed minor REMS modification for Lemtrada, as well as a redlined version of the REMS document.

September 10, 2015: Genzyme submitted an amended REMS proposal with a revised REMS document, REMS appended materials, and a revised REMS supporting document.

2. MATERIALS REVIEWED

2.1. SUBMISSIONS

- Genzyme, a Sanofi Company. Proposed Minor REMS Modification for Lemtrada, eCTD Sequence 0267, Supplement 5151, dated July 22, 2015.

[1] Moukhtara A. OPDP. Advisory for Launch Professional for Lemtrada, dated April 9, 2015.

Reference ID: 3821574

- Genzyme, a Sanofi Company. Proposed Minor REMS Modification for Lemtrada, Response to Agency's feedback, eCTD Sequence 076, Supplement 5151, dated September 10, 2015.

2.2. OTHER MATERIALS INFORMING OUR REVIEW

- FDA. Lemtrada, BLA 103948 REMS Approval Letter, dated November 14, 2014.
- Moukhtara A. Office of Prescription Drug Promotion, Advisory for Launch Professional for Lemtrada, dated April 9, 2015.
- Kumar J, DRISK. REMS Minor Modification Review for Lemtrada, dated September 3, 2015

3. RESULTS OF THE REVIEW OF THE PROPOSED REMS MODIFICATION

3.1. REMS DOCUMENT AND APPENDED MATERIALS

The Sponsor's submission received on September 10, 2015 incorporated the Agency's recommendations and revisions included in the September 3, 2015 DRISK review. This includes revision of the term (b) (4) within the Lemtrada REMS document, revision of the case text of (b) (4) to "BOXED WARNING" within appended REMS materials, inclusion of audit parameters in the Supporting Document versus within the REMS document of Lemtrada, and other minor edits as outlined in the red-line REMS document provided by the Agency on September 3, 2015.

3.2. REMS SUPPORTING DOCUMENT AND ASSESSMENT PLAN

Genzyme's revised REMS supporting document and assessment plan is consistent with the REMS and appended REMS materials. Genzyme submitted updated text relevant to sections regarding the Lemtrada REMS website and other minor changes.

4. CONCLUSION AND RECOMMENDATION

DRISK finds the proposed REMS modification for the Lemtrada REMS, as received on September 10, 2015, acceptable. The REMS assessment plan will remain the same as that approved on November 14, 2014. Therefore, the Office of Surveillance and Epidemiology, Office of Medication Error Prevention and Risk Management, DRISK recommends approval of the REMS modification received on September 10, 2015 and as appended to this review.

5. ATTACHMENTS

Lemtrada REMS Document and appended materials

661 pages has been Withheld has duplicate information

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JASMINDER N KUMAR
09/17/2015

REEMA J MEHTA
09/17/2015
I concur.

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

REMS MINOR MODIFICATION REVIEW

Date:	September 3, 2015
Reviewer:	Jasminder Kumar, Pharm.D. Risk Management Analyst Division of Risk Management
Acting Team Leader:	Jamie Wilkins-Parker, Pharm.D. Division of Risk Management
Acting Deputy Division Director:	Reema Mehta, Pharm.D., M.P.H. Division of Risk Management
Subject:	Evaluation of proposed REMS minor modification
Drug Name(s):	Lemtrada (alemtuzumab)
Therapeutic class:	CD52-directed cytolytic monoclonal antibody
Dosage forms:	12 mg/1.2 mL (10 mg/mL) injection
OND Review Division:	Division of Neurology Products
Application Type/Number:	BLA 103948 Suppl. 5151
Applicant/Sponsor:	Genzyme Corporation
OSE RCM #:	2015-1937

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Reference ID: 3815681

1. INTRODUCTION

This review provides the Division of Risk Management's (DRISK) evaluation of the proposed minor modification to the risk evaluation and mitigation strategy (REMS) for Lemtrada (alemtuzumab), BLA 103948, submitted by Genzyme Corporation on July 22, 2015. The purpose of the modification is to update the Lemtrada REMS website to provide the option to complete and submit the required REMS forms online, with the exception of the Lemtrada REMS Patient Enrollment Form and the Lemtrada REMS Prescription Ordering Form. In addition, the Lemtrada logo was updated on all REMS documents, along with other minor updates.

1.1 PRODUCT BACKGROUND

Lemtrada is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. Lemtrada was approved in November 2015 with a REMS to ensure the benefits of the drug outweigh the risks of autoimmune conditions, infusion reactions, and malignancies. The currently approved REMS includes a communication plan (CP), elements to assure safe use (ETASU) that include prescriber certification (ETASU A), pharmacy certification (ETASU B), dispensing only in certain healthcare settings (ETASU C), documentation of safe use conditions (ETASU D), and documentation of periodic monitoring of patients (ETASU E), an implementation system, and a timetable for submission of assessments.

The goal of the current REMS for Lemtrada is to mitigate the risks of autoimmune conditions, infusion reactions, and malignancies associated with Lemtrada by:

- Helping to ensure informed decisions about the safe use of Lemtrada by:
    - Informing patients about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA and the need for baseline and periodic monitoring; and
    - Informing healthcare providers about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA, the need to counsel patients, and the need for baseline and periodic monitoring, and
- Helping to ensure the safe use of Lemtrada by:
    - Ensuring that only certified prescribers prescribe Lemtrada;
    - Ensuring that Lemtrada is dispensed only in certain healthcare settings, by certified pharmacies, and certified infusion sites, which have on-site access to equipment and personnel trained to manage infusion reactions; and
    - Ensuring that only enrolled and authorized patients receive Lemtrada;
    - Ensuring that certified prescribers submit documentation of periodic monitoring of patients who receive Lemtrada to identify autoimmune conditions and malignancies

1.2 REGULATORY HISTORY

The following is a summary of the regulatory history for BLA 103948 relevant to this review:

October 22, 2014: A teleconference between the Agency and the Sponsor took place during the development of the Lemtrada REMS Program website. During this meeting, the Agency informed the Sponsor that the Lemtrada REMS Program website should not only provide access to downloadable versions of all approved REMS materials, but that the website should all the electronic completion and submission of the REMS Documents. The Sponsor informed the Agency that it was not possible to incorporate this functionality into the website prior to the REMS approved and therefore proposed a REMS modification submission within 9 months of the initial approval of the REMS that would include this website functionality.

November 14, 2014: The Agency approved Lemtrada (alemtuzumab), BLA 103948, for the treatment of patients with relapsing forms of MS. The approval included a REMS which contained a CP, ETASU (A, B, C, D, E), an implementation system, and a timetable for submission of assessments.

May 12, 2015: The Sponsor submitted the first REMS Assessment Report for Lemtrada (reporting period from November 14, 2014 through March 19, 2015).

July 20, 215: The Agency sent an Information Request (IR) requesting clarification on data submitted by the Sponsor in their first REMS Assessment Report. In addition, the Agency requested a status update on the expected date of submission for the proposed REMS modification discussed during the November 11, 2014 teleconference with the Agency.

July 22, 2015: The Sponsor submitted a proposed Minor REMS Modification (eCTD Sequence 0267, Supplement 5151), which updated the Lemtrada REMS website to increase its functionality as discussed during the November 11, 2014 teleconference with the Agency and included other minor edits to the REMS program.

2. MATERIALS REVIEWED

- Genzyme Corporation. Proposed Minor REMS Modification for Lemtrada, eCT Sequence 0267, Supplement 5151, dated July 22, 2015.

- FDA. REMS Approval Letter, dated November 14, 2014.

3. RESULTS OF THE REVIEW OF THE PROPOSED REMS MODIFICATION

The Sponsor proposed a minor REMS modification to provide the option to complete and submit the required REMS forms online (with the exception of the Lemtrada REMS Patient Enrollment Form and the Lemtrada REMS Prescription Ordering Form). The proposed Lemtrada REMS website will also provide the ability to search for REMS certified prescribers and healthcare facilities within the US and its territories. In addition, the submission included proposed updates to the Lemtrada logo and other minor edits. A summary of the proposed changes is as follows:

3.1 REMS DOCUMENT

- Revision of Lemtrada logo from "™" to "®"
- Revision of type case of the Lemtrada REMS website URL from "www.LEMTRADAREMS.com" to "www.LemtradaREMS.com"
- Addition of Lemtrada REMS website to include functionality:
    1. For Prescribers and Healthcare Facilities to review the:
        a. REMS required training documents
        b. enrollment and authorization status of their patients
        c. certification status of the Prescriber and Healthcare Facility intended to treat a specific patient
        d. status of the required REMS forms
    2. To provide the option for Prescribers and Healthcare Facilities to complete the required REMS forms online (except the LEMTRADA REMS Patient Enrollment Form and the LEMTRADA REMS Prescription Ordering Form)
    3. To provide the ability to search for a REMS certified Prescriber and Healthcare Facility within the US and its territories.
- Revision of "infusion site(s)" to (b) (4)
- Addition of "and/or administer" to describe certain healthcare settings that must be specially certified in order to dispense Lemtrada
- Addition of "and authorized…and who have received at least one Lemtrada treatment" to describe patients in the Lemtrada REMS program who will receive monthly reminders
- Deletion of "and infusion sites" to describe who Genzyme will monitor and audit within 180 days after certification
- Addition of Genzyme monitoring and audit plan for (b) (4)

3.2 REMS APPENDED MATERIALS

- Revision of Lemtrada logo from "™" to "®"
- Revision of Lemtrada REMS website URL from "www.LEMTRADAREMS.com" to "www.LemtradaREMS.com"
- Revision of "BOXED WARNING" (b) (4)
- Updated registration and version information
- Addition of "Medical Information" to describe where to report suspected adverse events to Genzyme

1. <u>LEMTRADA REMS Program Overview</u>

a. Revision to separate the following bullet into two bullets, "Healthcare facilities and Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA" to "Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA//Healthcare facilities must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA"

b. Rearranged the order of the REMS Program requirements sections

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2. ***LEMTRADA REMS Education Program for Prescribers***
    a. Addition of tab on top "For Prescribers"
    b. Revision to separate the following bullet into two bullets, "Healthcare facilities and Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA" to "Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA//Healthcare facilities must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA"
    c. Website address added to form
    d. Revision of heading above pictures from "Examples of ITP" to "Potential Clinical Presentation of ITP"
    e. Revision of diagram to reflect the number of treatments per course and 12 months per year
3. ***LEMTRADA REMS Education for Healthcare Facilities***
    a. Addition of tab "For Healthcare Facilities"
    b. Revision to separate the following bullet into two bullets, "Healthcare facilities and Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA" to "Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA//Healthcare facilities must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA"
    c. Revision of "Authorized Representative" to "authorized representative"
    d. Deletion of (b) (4) from "The LEMTRADA REMS Education Program for (b) (4) Healthcare Facilities"
    e. Addition of website address to form
    f. Revision of heading above picture from "Examples of ITP" to "Potential Clinical Presentations of ITP"
    g. Deletion of "and" to describe when to pre-medicate patients with high-dose corticosteroids in relation to their treatment course
    h. Addition of "or submit online at www.LemtradaREMS.com within 5 business days of the last infusion" to describe where to submit the LEMTRADA REMS Infusion Checklist at the conclusion of each treatment course
4. ***LEMTRADA REMS Knowledge Assessment***
    a. Website address added to the instructions
5. ***LEMTRADA REMS Healthcare Facility Enrollment Form***
    a. Addition of website address to the front top side and the back bottom side of the form
    b. Addition of "I understand that my healthcare facility must confirm that the patient is authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program or verifying online at www.LemtradaREMS.com prior to initiation of each treatment course."
    c. Addition of "Ensure that a LEMTRADA REMS Prescription ordering Form is received for each prescription."
    d. Addition of "Ensure that the prescriber is certified and the patient is enrolled and authorized by either calling the LEMTRADA REMS Program or verifying this information via the LEMTRADA REMS website prior to dispensing and administering LEMTRADA."

e. Addition of "Ensure that the infusion site is equipped to manage infusion reactions."
f. Addition of "Renew enrollment into the LEMTRADA REMS Program every 2 years from the initial enrollment."
g. Addition of signature box

6. LEMTRADA REMS Pharmacy Enrollment Form

a. Addition of website address to the top and bottom of form
b. Addition of signature box

7. LEMTRADA REMS Prescriber Enrollment Form

a. Addition of website address to the front top side and the back bottom side of the form
b. Revision of "Healthcare Providers" to "Healthcare Prescribers" to describe who must review LEMTRADA REMS Education Program for Prescribers
c. Addition of a street address box in the prescriber information section
d. Addition of website consent box for prescriber information
e. Addition of signature box

8. LEMTRADA REMS Patient Enrollment Form

a. Revision of name order from "first, last" to "Last, First"
b. Revision of "from" to "prior to" to describe when patient will receive yearly skin exams from the time of their first Lemtrada treatment
c. Addition of signature box

9. LEMTRADA REMS Patient Status Form

a. Addition of website address to the top and the bottom of the form
b. Revision of name order from "first, last" to "Last, First"

10. LEMTRADA REMS Patient Status Reminder Letter

a. No additional significant changes

11. LEMTRADA REMS Patient Reminder Letter

a. No additional significant changes

12. What You Need to Know About LEMTRADA Treatment: A Patient Guide

a. Revision of diagram to reflect the number of treatments per course and 12 months per year

13. What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide

a. No additional significant changes

14. LEMTRADA REMS Prescription Ordering Form

a. Addition of "REMS" to the form's title
b. Revision of name order from "first, last" to "Last, First"
c. Revision of "Your Healthcare Provider" to "The Prescriber"
d. Addition of ICD-10 to and total number of vials to Prescription Information section
e. Addition of signature box
f. Addition of instructions for submission of form

15. *LEMTRADA REMS Patient Authorization and Baseline Lab Form*

a. Website address added to the top and the bottom of the form
b. Revision of name order from "first, last" to "Last, First"
c. Addition of (b) (4) to and total number of vials to Prescription Information section

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d. Addition of signature box
e. Addition of instructions for submission of form

16. LEMTRADA Patient Safety Information Card

a. No additional significant changes

17. LEMTRADA REMS Infusion Checklist

a. Website address added to the front top side and the back bottom site of the form
b. Revision of "faxed" to "submitted" to describe how the Infusion Checklist must be completed and sent
c. Revision of name order from "first, last" to "Last, First"
d. Addition of "before" to describe when to monitors patient's vital sign in relation to infusion
e. Addition of patient identifier to the top of second page of the form
f. Addition of signature box to separate the vial return box from the signature

18. LEMTRADA REMS Letter for Healthcare Providers

a. Revision to separate the following bullet into two bullets, "Healthcare facilities and Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA" to "Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA//Healthcare facilities must be enrolled in the LEMTRADA REMS Program to be able to dispense and administer LEMTRADA"

3.3 REMS SUPPORTING DOCUMENT AND ASSESSMENT PLAN

The Sponsor submitted updated text relevant to sections regarding the Lemtrada REMS website and other minor changes.

4. DISCUSSION

During the negotiations for the initial approval of the Lemtrada REMS, the Sponsor agreed to submit a REMS modification to include an online functionality for submission of completed REMS forms through the Lemtrada REMS website. Therefore, this modification to the Lemtrada REMS was submitted on July 22, 2015 in response to this agreement with the Sponsor. In addition to the previously mentioned website functionalities, the proposed modification also provides the ability to search for REMS certified prescribers and healthcare facilities within the US and its territories. Finally, the submission includes proposed updates to the Lemtrada logo and other minor edits.

DRISK agrees that language updating the website functionality should be included in the REMS document and respective appended materials. This addition also provides direction to stakeholders on how they can review, complete, and submit appropriate REMS materials.

DRISK also agrees with the Sponsors addition of the term "authorized" to describe patients who receive Lemtrada in the appended materials, to align with their description in the REMS document.

We also note the Sponsor also revised the term "infusion site(s)" to (b) (4) within the REMS document. Based on the currently available data, DRISK believes that infusion site adequately characterizes the type of setting in which Lemtrada should be administered. The Sponsor should provide rationale for this revision for further consideration.

Reference ID: 3815681

The Sponsor also proposed revision of "BOXED WARNING" to [redacted] throughout appended materials. This revision may inadvertently minimize the attention paid to the messaging contained in the boxed warning, and the Sponsor has not provided any adequate rationale for their proposed change.

In addition, the Sponsor proposed deletion of word [redacted] when describing the "Lemtrada REMS Education Program for [redacted] Healthcare Facilities." DRISK agrees with this change, as this aligns the title of this document in the appended materials to how it appears in the REMS document.

The Sponsor has also proposed changes to the logo. Their rationale was that this was in response to a request by the Office of Prescription Drug Promotion. DRISK agrees with this change.

Furthermore, the Sponsor has added audit specifications in the REMS document under the implementation system. The audit plan specifications should be housed in the Supporting Document, and are already included in the Supporting Document for Lemtrada.

Finally, DRISK agrees with all other previously mentioned revisions, additions, and deletions made to the REMS Document, appended materials, Supporting Document, and Assessment Plan, unless otherwise noted above.

5. CONCLUSION

DRISK does not agree with all the Sponsor's proposed modifications to the Lemtrada REMS. We agree with the inclusion of website functionality updates and with the addition of "authorized" to describe patients in the LEMTRADA REMS Program. However, we do not agree with the revision of "infusion site(s)" to [redacted] the revision of "BOXED WARNING" to [redacted] and the addition of the Genzyme monitoring and audit plan for [redacted] We do agree with the remaining revisions and modifications made to the REMS and appended materials. Comments for the Sponsor are provided in Section 6.

6. RECOMMENDATIONS FOR THE REVIEW DIVISION

DRISK recommends that the comments listed below on the proposed minor modification to the REMS for Lemtrada, BLA 103948 be sent to the Sponsor. Please request that the Sponsor respond to these comments within 3 business days, to facilitate further review.

7. COMMENTS FOR THE SPONSOR

The comments below and in the attached red-lined REMS document are based on the Agency's preliminary review of the proposed minor REMS modification for Lemtrada submitted under NDA 103948 S-5151. In order to facilitate further review, we ask that you respond to these comments within 3 business days. We agree with the remaining revisions and modifications made to the REMS and appended materials.

1. We note that you have changed the term "infusion site(s)" to [redacted] within the REMS document. Based on the currently available data, the Agency believes that infusion site adequately characterizes the type of setting in which Lemtrada should be administered. Provide rationale for this revision for further

consideration, otherwise revise and include in your response to these comments as reflected in the attached REMS document.

2. We also note you proposed revision of "BOXED WARNING" to (b) (4) throughout the appended materials. This revision may inadvertently minimize the attention paid to the messaging contained in the boxed warning, and have not provided any adequate rationale for the proposed change.

3. Audit parameters should be specified in the Supporting Document, and not within the REMS document. Therefore remove the audit specifications from the REMS document as reflected in the attached redlined REMS document, as they already appear in your Supporting Document.

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Reference ID: 3815681

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/s/

JAMIE C WILKINS PARKER on behalf of JASMINDER N KUMAR
09/03/2015

JAMIE C WILKINS PARKER
09/03/2015

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 103-948/S-5151

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Lopez, Nahleen (FDA)

From: Lopez, Nahleen (FDA)
Sent: Friday, September 04, 2015 2:43 PM
To: 'Mara.Kochaba@genzyme.com'
Subject: BLA 103948_Information Advice
Attachments: REMS Lemtrada.doc

Dear Ms. Kochaba,

Please refer to BLA 103948.

The comments below and in the attached red-lined REMS document are based on the Agency's preliminary review of the proposed minor REMS modification for Lemtrada submitted under NDA 103948 S-5151. In order to facilitate further review, we ask that you respond to these comments within 3 business days. We agree with the remaining revisions and modifications made to the REMS and appended materials.

1. We note that you have changed the term "infusion site(s)" to [redacted] (b) (4) within the REMS document. Based on the currently available data, the Agency believes that "infusion site" adequately characterizes the type of setting in which Lemtrada should be administered. Provide your rationale for this revision for our further consideration. Otherwise, revise as we recommend and include the revision in your response to these comments as reflected in the attached REMS document.

2. We also note you proposed revision of "BOXED WARNING" to [redacted] (b) (4) throughout the appended materials. This revision may [redacted] (b) (4) the attention paid to the messaging contained in the boxed warning. Please revise or provide adequate rationale for the proposed change.

3. Audit parameters should be specified in the Supporting Document, [redacted] (b) (4) Therefore [redacted] (b) (4) as they already appear in your Supporting Document.

Kind Regards,

Nahleen Lopez, PharmD
LCDR, United States Public Health Service

Regulatory Project Manager
Food and Drug Administration
Office of Drug Evaluation – Division of Neurology Products
Bldg. 22, Room 4202
10903 New Hampshire Ave
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/s/

REBECCA N LOPEZ
09/04/2015

Lopez, Nahleen (FDA)

From: Lopez, Nahleen (FDA)
Sent: Thursday, August 13, 2015 4:49 PM
To: 'mara.kochaba@genzyme.com'
Subject: RE: BLA 103948_Information Advice

Dear Ms. Kochaba,

Please refer to BLA 103948.

Please provide an expected timeline for your response to the Agency's Information Request sent on August 4, 2015. We request that you provide this timeline within 14 business days.

Kind Regards,

Nahleen Lopez, PharmD
LCDR, United States Public Health Service

Regulatory Project Manager
Food and Drug Administration
Office of Drug Evaluation – Division of Neurology Products
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10903 New Hampshire Ave
Silver Spring, MD 20993
Office: 240-402-2659
Fax: 301-796-9842
Nahleen.Lopez@fda.hhs.gov

From: Lopez, Nahleen (FDA)
Sent: Tuesday, August 04, 2015 3:22 PM
To: 'mara.kochaba@genzyme.com'
Subject: BLA 103948_Information Advice

Dear Ms. Kochaba,

Please refer to BLA 103948.

Please refer to the risk evaluation mitigation strategy (REMS) Minor Modification submitted on July 22, 2015, the first REMS Assessment Report for the LEMTRADA REMS Program (reporting period from November 14, 2014 through March 19, 2015) submitted on May 12, 2015, and your responses to the Agency's Information Requests (IRs), received on July 23, 2015, and July 28, 2015.

We note that your proposed REMS Modification submission updated the LEMTRADA REMS website to provide the functionality for prescribers and healthcare facilities to review the required training documents, the enrollment and authorization status of patients, the certification status of the prescriber and healthcare facility intended to treat a specific patient, and the status of the required REMS forms online. It also provided the option to complete and submit the required REMS forms online. The submission also included logo updates and additional editorial changes.

Based on your response to the IR dated July 23, 2015, the implementation system in the Lemtrada REMS document does not accurately reflect the curren (b) (4) Therefore, we request that you amend Supplement 5151 to include your proposed revisions to the implementation system. This amendment would change the modification type to a Major Modification; therefore, the supplement should be submitted as a prior approval supplement.

Kind Regards,

Nahleen Lopez, PharmD
LCDR, United States Public Health Service

Regulatory Project Manager
Food and Drug Administration
Office of Drug Evaluation – Division of Neurology Products
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/s/

REBECCA N LOPEZ
08/13/2015

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Kind Regards,

Nahleen Lopez, PharmD
LCDR, United States Public Health Service

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/s/

REBECCA N LOPEZ
08/04/2015