

# Risk Evaluation and Mitigation Strategy (REMS) Document

## LEMTRADA® (alemtuzumab) REMS

### I. Administrative Information

Application Number: BLA 103948  
Application Holder: Genzyme Corporation  
Initial REMS Approval: 11/2014  
Most Recent REMS Update: 10/2019

### II. REMS Goal

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

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

1. Informing patients about the serious risks of autoimmune conditions, infusion reactions, stroke, and malignancies with LEMTRADA and the need for baseline and periodic monitoring; and
2. Informing healthcare providers about the serious risks of autoimmune conditions, infusion reactions, stroke, 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:

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

### III. REMS Requirements

**Genzyme must ensure that healthcare providers, patients, pharmacies, healthcare facilities, and wholesalers-distributors comply with the following requirements:**

**1. Healthcare Providers who prescribe LEMTRADA must:**

To become certified to prescribe	<ol style="list-style-type: none"><li>1. Review the drug's Prescribing Information.</li><li>2. Review the following: <a href="#">Program Overview</a> and <a href="#">Education Program for Prescribers</a>.</li><li>3. Successfully complete the <a href="#">Knowledge Assessment</a> and submit it to the REMS Program.</li><li>4. Enroll in the REMS by completing the <a href="#">Prescriber Enrollment Form</a> and submitting it to the REMS Program.</li></ol>
Before treatment initiation (first dose)	<ol style="list-style-type: none"><li>5. Counsel the patient on the risks associated with LEMTRADA, including autoimmune conditions, infusion reactions, stroke and malignancies, and the need for baseline and periodic monitoring, using <a href="#">What You Need to Know About LEMTRADA Treatment: A Patient Guide</a>, and the <a href="#">Patient Safety Information Card</a>. Provide a copy of the materials to the patient.</li><li>6. Enroll the patient by completing and submitting the <a href="#">Patient Enrollment Form</a> to the REMS Program. Provide a completed copy to the patient and retain a copy in the patient's record.</li><li>7. Order the prescription using the <a href="#">Prescription Ordering Form</a> and submit it to the REMS Program.</li></ol>
Before treatment initiation and during treatment, within 30 days prior to the first infusion date of each treatment course	<ol style="list-style-type: none"><li>8. Assess the patient's health status by completing the laboratory testing and monitoring as described in the Prescribing Information. Document and submit to the REMS Program using the <a href="#">Patient Authorization and Baseline Lab Form</a>.</li></ol>
During treatment, at periodic intervals	<ol style="list-style-type: none"><li>9. Assess the patient's health status by completing the laboratory testing and monitoring as described in the Prescribing Information.</li><li>10. Order the prescription using the <a href="#">Prescription Ordering Form</a> and submit it to the REMS Program.</li></ol>
During treatment, every 6 months	<ol style="list-style-type: none"><li>11. Assess the patient for adverse events and completion of laboratory testing and monitoring. Document and submit to the REMS Program using the <a href="#">Patient Status Form</a>.</li></ol>
After the last infusion, every 6 months for 48 months	<ol style="list-style-type: none"><li>12. Assess the patient for adverse events and completion of laboratory testing and monitoring. Document and submit to the REMS Program using the <a href="#">Patient Status Form</a>.</li></ol>

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At all times	<p>13. Report any adverse events suggestive of autoimmune conditions, infusion reactions, stroke, and malignancies to Genzyme.</p> <p>14. Report if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care to Genzyme.</p>
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## 2. Patients who are prescribed LEMTRADA:

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Before treatment initiation	<p>1. Receive counseling from the prescriber on the risks associated with LEMTRADA, including autoimmune conditions, infusion reactions, stroke and malignancies, and the need for laboratory testing and monitoring, using <a href="#">What You Need to Know About LEMTRADA Treatment: A Patient Guide</a> and the <a href="#">Patient Safety Information Card</a>.</p> <p>2. Enroll in the REMS Program by completing the <a href="#">Patient Enrollment Form</a> with the prescriber. Enrollment information will be provided to the REMS Program.</p> <p>3. Get a skin exam.</p>
Before treatment initiation, within 30 days prior to the first infusion date of each treatment course	<p>4. Be monitored for autoimmune conditions and/or malignancies.</p>
During treatment; after each infusion for at least 2 hours	<p>5. Be monitored for infusion reactions.</p>
During treatment, at periodic intervals	<p>6. Be monitored for autoimmune conditions and/or malignancies.</p> <p>7. Inform the prescriber if you have had a stroke.</p>
During treatment, yearly	<p>8. Get a skin exam.</p>
After last infusion, at periodic intervals for 48 months	<p>9. Be monitored for autoimmune conditions and/or malignancies.</p> <p>10. Inform the prescriber if you have had a stroke.</p>
At all times	<p>11. Inform the prescriber if any reactions or symptoms are experienced after receiving LEMTRADA.</p> <p>12. Have the <a href="#">Patient Safety Information Card</a> with you.</p>

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## 3. Pharmacies that dispense LEMTRADA must:

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To become certified to dispense	<ol style="list-style-type: none"> <li>1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy.</li> <li>2. Have the authorized representative review the <a href="#">Program Overview</a>.</li> <li>3. Have the authorized representative enroll in the REMS Program by completing the <a href="#">Pharmacy Enrollment Form</a> and submitting it to the REMS Program.</li> <li>4. Train all relevant staff involved in dispensing LEMTRADA using the <a href="#">Program Overview</a>.</li> <li>5. Establish processes and procedures to verify that the <a href="#">Prescription Ordering Form</a> is received for each prescription.</li> </ol>
Before dispensing	<ol style="list-style-type: none"> <li>6. Verify that the <a href="#">Prescription Ordering Form</a> is received for each prescription through the processes and procedures established as a requirement of the REMS Program.</li> <li>7. Obtain authorization to dispense each prescription by contacting the REMS Program to verify that the prescriber is certified, the healthcare facility administering the infusion is certified, and the patient is enrolled and authorized to receive LEMTRADA.</li> </ol>
To maintain certification to dispense, every 2 years	<ol style="list-style-type: none"> <li>8. Have the authorized representative re-enroll in the REMS Program by completing the <a href="#">Pharmacy Enrollment Form</a>.</li> </ol>
At all times	<ol style="list-style-type: none"> <li>9. Maintain records of training.</li> <li>10. Maintain records of all processes and procedures including compliance with those processes and procedures.</li> <li>11. Comply with audits carried out by Genzyme to ensure that all processes and procedures are in place and are being followed.</li> </ol>

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**4. Healthcare facilities that dispense and administer LEMTRADA must:**

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To become certified to dispense and administer	<ol style="list-style-type: none"> <li>1. Have the necessary on-site equipment and personnel available to appropriately manage serious infusion reactions (including anaphylaxis, cardiac and respiratory emergencies).</li> <li>2. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the healthcare facility.</li> <li>3. Have the authorized representative review the <a href="#">REMS Program Overview</a> and <a href="#">Education Program for Healthcare Facilities</a>.</li> <li>4. Have the authorized representative enroll in the REMS Program by completing the <a href="#">Healthcare Facility Enrollment Form</a> and submitting it to the REMS Program.</li> <li>5. Train all relevant staff involved in the dispensing and administration of LEMTRADA using the <a href="#">Program Overview</a> and <a href="#">Education Program for Healthcare Facilities</a>.</li> <li>6. Establish processes and procedures to verify that (1) the Prescription Ordering Form is received for each prescription, (2) patients are counseled, (3) the patient is monitored for infusion reactions during and for at least 2 hours after each infusion, (4) the Infusion Checklist is completed and submitted for each patient, and (5) Lemtrada is not dispensed outside of the certified healthcare facility administering the infusion.</li> </ol>
Before administering	<ol style="list-style-type: none"> <li>7. Verify that the <a href="#">Prescription Ordering Form</a> is received for each prescription through the processes and procedures established as a requirement of the REMS Program.</li> <li>8. Obtain authorization to dispense each prescription by contacting the REMS Program to verify that the prescriber is certified and the patient is enrolled and authorized to receive LEMTRADA.</li> <li>9. Counsel the patient about the risk for infusion reactions using the <a href="#">What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide</a>. Provide a copy of the material to the patient.</li> </ol>
During and after administering for at least 2 hours	<ol style="list-style-type: none"> <li>10. Assess the patient for infusion reactions.</li> </ol>
After the last infusion, within 5 business days	<ol style="list-style-type: none"> <li>11. Complete the <a href="#">Infusion Checklist</a> for each patient and submit it to the REMS Program.</li> </ol>

To maintain certification to dispense and administer every 2 years	12. Have the authorized representative enroll in the REMS Program by completing the <a href="#">Healthcare Facility Enrollment Form</a> and submitting it to the REMS Program.
At all times, within 50 business days of submission of the <a href="#">Patient Authorization and Baseline Lab Form</a>	13. Return unused product to the distributor.
At all times	14. Not distribute, transfer, loan, or sell Lemtrada. 15. Maintain records of training. 16. Maintain records of all processes and procedures including compliance with those processes and procedures. 17. Comply with audits carried out by Genzyme to ensure that all training, processes and procedures are in place and are being followed.

**5. Wholesalers-distributors that distribute LEMTRADA must:**

To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies and certified healthcare facilities. 2. Train all relevant staff involved in distributing LEMTRADA on the REMS Program requirements.
At all times	3. Distribute only to certified pharmacies and certified healthcare facilities. 4. Maintain and submit patient level distribution records of all shipments of LEMTRADA to the REMS Program. 5. Maintain records of all processes and procedures including compliance with those processes and procedures. 6. Comply with audits carried out by Genzyme to ensure that all processes and procedures are in place and are being followed.

**Genzyme must provide training to healthcare providers who prescribe LEMTRADA.**

The training includes the following educational materials: [Program Overview](#), [Education Program for Prescribers](#), and [Knowledge Assessment](#). The training must be available online and in hard copy format by calling the REMS call center.

**Genzyme must provide training to pharmacies that dispense LEMTRADA.** The training includes the following educational materials: [Program Overview](#). The training must be available online and in hardcopy format by calling the REMS call center.

**Genzyme must provide training to healthcare facilities that dispense and administer LEMTRADA.**

The training includes the following educational materials: [Program Overview](#) and [Education Program for Healthcare Facilities](#). The training must be available online and in hardcopy format by calling the REMS call center.

**To inform healthcare providers about the REMS Program and the risks and safe use of LEMTRADA, Genzyme must disseminate REMS communication materials according to the table below:**

<b>Target Audience</b>	<b>Communication Materials and Dissemination Plans</b>
Healthcare Providers and Healthcare Facilities enrolled in the LEMTRADA REMS Program.	REMS Letter: <a href="#">REMS Letter 2 for Healthcare Providers</a> <ol style="list-style-type: none"><li>1. Email within 60 calendar days of approval of the REMS modification (04/2019).<ol style="list-style-type: none"><li>a. Send by mail within 30 calendar days of the date the first email was sent if a healthcare provider's email address is not available or the email is undeliverable.</li><li>b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened.</li><li>c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened.</li></ol></li></ol>
Healthcare providers who have written at least one prescription within the previous 2 years for a prescription drug indicated for the treatment of multiple sclerosis	REMS Letter: <a href="#">REMS Letter 1 for Healthcare Providers</a> <ol style="list-style-type: none"><li>1. Email 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 (11/2014).<ol style="list-style-type: none"><li>a. Send by mail within 30 calendar days of the date the first email was sent if a healthcare provider's email address is not available or the email is undeliverable.</li><li>b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened.</li><li>c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened.</li></ol></li></ol>

**To support REMS Program operations, Genzyme must:**

1. Establish and maintain a REMS Program website, [www.LemtradaREMS.com](http://www.LemtradaREMS.com). The REMS Program website must include the capability to complete prescriber, pharmacy, and healthcare facility certification online, the capability to review patient authorization and enrollment status and prescriber and healthcare facility certification status, the capability to search for a REMS certified prescriber or healthcare facility, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).

2. Make the REMS Program website fully operational and all REMS materials available through [www.LemtradaREMS.com](http://www.LemtradaREMS.com) and the REMS Program call center.
3. Establish and maintain a REMS Program call center for REMS participants at 1-855-676-6326.
4. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program.
5. Ensure prescribers, pharmacies, and healthcare facilities are able to complete enrollment by fax and online.
6. Ensure prescribers are able to complete enrollment of patients by fax.
7. Ensure prescribers are able to provide a [Prescription Ordering Form](#) for each LEMTRADA prescription by fax.
8. Ensure pharmacies and healthcare facilities are able to access and review the database of certified prescribers and enrolled patients to obtain certification status and authorization status via the REMS Program call center and the REMS Program website.
9. Provide the [Prescriber Enrollment Form](#), [Patient Enrollment Form](#), [Program Overview](#), [Education Program for Prescribers](#), [Patient Status Form](#), [Prescription Ordering Form](#), [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.
10. Notify prescribers, pharmacies, and healthcare facilities after they become certified in the REMS Program.
11. Provide certified prescribers access to the database of certified pharmacies, certified healthcare facilities, and enrolled patients.
12. Provide certified pharmacies and certified healthcare facilities access to the database of certified prescribers and enrolled patients.

**To ensure REMS participants' compliance with the REMS Program, Genzyme must:**

13. Verify annually that the authorized representative is the current designated authorized representative for the certified pharmacy and certified healthcare facility. If different, the pharmacy or healthcare facility or both must be required to re-certify with a new authorized representative.
14. Notify healthcare facilities if a completed [Infusion Checklist](#) has not been received by the REMS Program within 40 days from the date of submission of the [Patient Authorization and Baseline Lab Form](#).
15. Send a [Patient Letter: Monitoring Reminder](#) to patients monthly who have received at least one LEMTRADA treatment, reminding them of the requirement for ongoing monitoring.
16. Send a [Healthcare Provider Letter: Patient Status](#) to the prescriber who must submit a completed [Patient Status Form](#) for the patient. Send the letter electronically or by mail 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, for 48 months after the completion of the patient's last infusion of LEMTRADA.
17. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: distribution and dispensing; certification of prescribers, pharmacies, and healthcare facilities; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.
18. Establish a plan for addressing noncompliance with REMS Program requirements.
19. Monitor certified prescribers, certified pharmacies, certified healthcare facilities, and wholesalers-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.

20. Audit wholesalers-distributors no later than 180 days after they become authorized, and annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
21. Audit certified pharmacies no later than 180 days after they become certified and after they have dispensed at least one LEMTRADA prescription, and annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
22. Audit 10% of the certified healthcare facilities that have received at least one shipment of Lemtrada over a 24-month period defined as the current and previous reporting period, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements. A minimum of 50 healthcare facilities must be audited annually.
23. 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.

## IV. REMS Assessment Timetable

Genzyme must submit REMS Assessments at 6 months and 12 months, and annually thereafter from the date of the initial approval of the REMS (11/14/2014). 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 calendar days before the submission date for that assessment. Genzyme must submit each assessment so that it will be received by the FDA on or before the due date.

## V. REMS Materials

The following materials are part of the LEMTRADA REMS:

### Enrollment Forms:

Prescriber:

1. [Prescriber Enrollment Form](#)

Patient:

2. [Patient Enrollment Form](#)

Pharmacy:

3. [Pharmacy Enrollment Form](#)

Healthcare Facility:

4. [Healthcare Facility Enrollment Form](#)

### Training and Educational Materials

Prescriber:

5. [REMS Program Overview](#)
6. [Education Program for Prescribers](#)
7. [Knowledge Assessment](#)

Pharmacy:

8. [REMS Program Overview](#)

Healthcare Facility:

9. [REMS Program Overview](#)
10. [Education Program for Healthcare Facilities](#)

Patient:

11. [What You Need to Know About LEMTRADA Treatment: A Patient Guide](#)

12. [Patient Safety Information Card](#)
13. [What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide](#)

#### **Patient Care Forms**

14. [Patient Authorization and Baseline Lab Form](#)
15. [Prescription Ordering Form](#)
16. [Patient Status Form](#)
17. [Infusion Checklist](#)

#### **Communication Materials**

18. [REMS Letter 1 for Healthcare Providers](#)
19. [REMS Letter 2 for Healthcare Providers](#)

#### **Other Materials**

20. REMS Program website [www.LemtradaREMS.com](http://www.LemtradaREMS.com)
  21. [Healthcare Provider Letter: Patient Status](#)
  22. [Patient Letter: Monitoring Reminder](#)
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