CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217686Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

TRYVIO™ (aprocitentan) REMS

I. Administrative Information

Risk: embryo-fetal toxicity

Application Number: NDA 217686

Application Holder: Idorsia Pharmaceuticals Ltd

Initial REMS Approval: 3/2024

II. REMS Goal

The goal of the TRYVIO (aprocitentan) REMS is to mitigate the risk of embryo-fetal toxicity associated with TRYVIO.

Objective: Ensure that prescribers are aware of the risk of embryo-fetal toxicity associated with TRYVIO and the need to counsel patients who can become pregnant on the actions necessary to prevent pregnancy and minimize exposure to a fetus.

III. REMS Requirements

Idorsia Pharmaceuticals Ltd must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare providers who prescribe TRYVIO must:	
To become certified to prescribe	1. Review the drug's Prescribing Information. 2. Review the **Prescriber and Pharmacy Guide**. 3. Successfully complete the **Prescriber Knowledge Assessment** and submit it to the REMS. 4. Enroll in the REMS by completing and submitting the **Prescriber Enrollment Form** to the REMS.
Before treatment initiation (First dose)	5. Assess the patient's reproductive status using the definitions in the **Prescriber and Pharmacy Guide**. 6. For patients who can become pregnant: Counsel the patient on the risk of embryo-fetal toxicity, to use acceptable contraception, pregnancy testing recommendations before initiating treatment, monthly during treatment, and one month after discontinuing treatment, and the use of emergency contraception using the **Patient Guide**. Provide a copy of the material to the patient.
At all times	7. Report pregnancies to the REMS.

2. Patients who are prescribed TRYVIO:	
Before treatment initiation	1. For patients who can become pregnant: Review the **Patient Guide**. 2. For patients who can become pregnant: Receive counseling from the prescriber on the risk of embryo-fetal toxicity, the need to use acceptable contraception, pregnancy testing recommendations before initiating treatment, monthly during treatment, and one month after discontinuing treatment, and the use of emergency contraception using the **Patient Guide**.
During treatment	3. Receive a **Risk of Birth Defects with TRYVIO** from the pharmacy or the prescriber who dispenses the drug.
At all times	4. For patients who can become pregnant: Inform the prescriber immediately if you miss a menstrual period or suspect a pregnancy.

3. Outpatient pharmacies and prescribers that dispense TRYVIO must:	
To become certified to dispense	1. For outpatient pharmacies: Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the TRYVIO REMS on behalf of the outpatient pharmacy. 2. For outpatient pharmacies: Have the authorized representative enroll in the TRYVIO REMS by completing and submitting the **Outpatient Pharmacy Enrollment Form** to the REMS. 3. For prescribers who dispense: Complete the certified dispenser section of the **Prescriber Enrollment Form**. 4. Review the Prescribing Information and the **Prescriber and Pharmacy Guide**. 5. Train all relevant staff involved in dispensing on the REMS requirements, procedures, and REMS materials. 6. Establish processes and procedures to report a pregnancy to the REMS. 7. Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO** to each patient each time TRYVIO is dispensed.
Before dispensing	8. For outpatient pharmacies: Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified. 9. Provide the patient with the **Risk of Birth Defects with TRYVIO** through the processes and procedures established as a requirement of the REMS. 10. For prescribers who dispense: Report dispensing TRYVIO to the REMS.
To maintain certification to dispense	11. Have a new authorized representative enroll by completing and submitting the **Outpatient Pharmacy Enrollment Form**, if the authorized representative changes.

At all times	12. Report pregnancies to the REMS. 13. Not distribute, transfer, loan, or sell TRYVIO except to certified pharmacies. 14. Maintain records that all processes and procedures are in place and are being followed. 15. Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.
4. Inpatient pharmacies that dispense TRYVIO must:	
To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. 2. Have the authorized representative review the Prescribing Information and the **Prescriber and Pharmacy Guide**. 3. Have the authorized representative enroll in the TRYVIO REMS by completing and submitting the **Inpatient Pharmacy Enrollment Form** to the REMS. 4. Train all relevant staff involved in dispensing TRYVIO on the REMS requirements, procedures, and REMS materials. 5. Establish processes and procedures to verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber. 6. Establish processes and procedures to report pregnancies to the REMS. 7. Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO** to each patient each time TRYVIO is dispensed at patient discharge.
Before dispensing	8. Verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber through the processes and procedures established as a requirement of the REMS.
To maintain certification to dispense	9. Have a new authorized representative enroll by completing and submitting the **Inpatient Pharmacy Enrollment Form** if the authorized representative changes.
At discharge	10. Provide the patient with the **Risk of Birth Defects with TRYVIO** through the processes and procedures established as a requirement of the REMS.
At all times	11. Report pregnancies to the REMS. 12. Not distribute, transfer, loan, or sell TRYVIO except to certified pharmacies. 13. Maintain records that all processes and procedures are in place and are being followed. 14. Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are

	being followed.

5. Wholesalers-distributors that distribute TRYVIO must:

To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies and certified prescribers who can dispense. 2. Train all relevant staff involved in distribution on the REMS requirements.
At all times	3. Distribute only to certified pharmacies and certified prescribers who can dispense. 4. Maintain records that all processes and procedures are in place and are being followed. 5. Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

Idorsia Pharmaceuticals Ltd must provide training to healthcare providers who prescribe TRYVIO.

The training includes the following educational materials: Prescribing Information, **Prescriber Knowledge Assessment** and **Prescriber and Pharmacy Guide**. The training must be available online and by calling the REMS.

Idorsia Pharmaceuticals Ltd must provide training to pharmacies that dispense TRYVIO.

The training includes the following educational material: Prescribing Information and **Prescriber and Pharmacy Guide**. The training must be available online and by calling the REMS.

To support the REMS operations, Idorsia Pharmaceuticals Ltd must:

1. Authorize dispensing for each patient based on verifying the prescriber is certified.
2. Establish and maintain a REMS Website, **<TRYVIOREMS.com>**. The REMS Website must include the capability to complete prescriber, inpatient pharmacy, and outpatient pharmacy enrollment online, 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 Website. The REMS Website must not link back to the promotional product website.
3. Make the REMS Website fully operational, and all REMS materials are available through the REMS website or coordinating center at the time TRYVIO first becomes commercially available.
4. Establish and maintain a coordinating center for REMS participants at (1-866-429-8964).
5. Establish and maintain a validated, secure database of all REMS participants who are certified in the TRYVIO REMS.
6. Ensure prescribers are able to enroll by submitting a completed **Prescriber Enrollment Form** online and by fax.
7. Ensure prescribers are able to report dispensing TRYVIO by phone.
8. Ensure pharmacies are able to enroll as inpatient (including, but not limited to, pharmacies in hospitals, long-term care facilities, prisons, and state psychiatric units) or as outpatient pharmacies.
9. Ensure outpatient pharmacies are able to enroll by submitting a completed **Outpatient Pharmacy Enrollment Form** online and by fax.
10. Ensure outpatient pharmacies are able to obtain authorization to dispense by phone and online.
11. Ensure inpatient pharmacies are able to enroll by submitting a completed **Inpatient Pharmacy Enrollment Form** online and by fax.

12. Ensure prescribers and pharmacies are able to report pregnancies by phone.
13. Provide the **Prescriber Enrollment Form, Prescriber Knowledge Assessment,** and **Prescriber and Pharmacy Guide** to prescribers who (1) attempt to prescribe TRYVIO and are not yet certified or (2) inquire about how to become certified.
14. Provide the **Outpatient Pharmacy Enrollment Form** or **Inpatient Pharmacy Enrollment Form** and **Prescriber and Pharmacy Guide** to pharmacies that (1) receive their first TRYVIO prescription and are not yet certified or (2) inquire about how to become certified.
15. Provide certified prescribers access to the database of certified pharmacies.
16. Provide certified pharmacies access to the database of certified prescribers.
17. Provide authorized wholesalers-distributors access to database of certified pharmacies.

To ensure REMS participants' compliance with the REMS, Idorsia Pharmaceuticals Ltd must:

18. Maintain adequate records to demonstrate that the REMS requirements have been met, including but not limited to records of: TRYVIO distribution and dispensing, certification of prescribers and pharmacies, authorization of wholesalers-distributors; and audits of the REMS participants. These records must be readily available for FDA inspections.
19. Establish and maintain a plan for addressing non-compliance with REMS requirements.
20. Monitor prescribers, pharmacies, and wholesaler-distributors on an ongoing basis to ensure the REMS requirements are being met. Take corrective action if non-compliance is identified, including de-certification.
21. Audit all certified outpatient specialty pharmacies, a representative sample of certified outpatient retail pharmacies (10% or at least 10, whichever is greater yet not to exceed 100), and a representative sample of certified inpatient pharmacies (10% or at least 10, whichever is greater yet not to exceed 100) within 180 days after their first shipment receipt of TRYVIO to ensure that all the REMS processes and procedures are in place, functioning, and support the REMS requirements. Audit a representative sample (10% or at least 10, whichever is greater yet not to exceed 100) of each annually: certified outpatient specialty pharmacies, outpatient retail pharmacies, and inpatient pharmacies, to ensure that all the REMS processes and procedures are in place, functioning, and support the REMS requirements.
22. Audit all wholesaler-distributors within 180 days after they become authorized and audit all wholesaler-distributors annually to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.
23. Take reasonable steps to improve the operations of and compliance with the TRYVIO REMS requirements based on monitoring and evaluation of the TRYVIO REMS.

IV. REMS Assessment Timetable

Idorsia Pharmaceuticals Ltd must submit the REMS Assessments annually. To facilitate the inclusion of as much information as possible while allowing a 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. Idorsia Pharmaceuticals Ltd 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 TRYVIO REMS:

Enrollment Forms:

Prescriber:

1. Prescriber Enrollment Form

Pharmacy:

2. Outpatient Pharmacy Enrollment Form

3. Inpatient Pharmacy Enrollment Form

Training and Educational Materials

Prescriber:

4. Prescriber and Pharmacy Guide
5. Prescriber Knowledge Assessment

Patient:

6. Patient Guide
7. Risk of Birth Defects with TRYVIO

Pharmacy:

8. Prescriber and Pharmacy Guide

Other Materials

9. REMS Website (www.TRYVIOREMS.com)

VI. Statutory Elements

This REMS is required under section 505-1 of the Federal Food, Drug and Cosmetic Act (FD&C Act)(21 U.S.C. 355-1) and consists of the following elements:

1. Elements to Assure Safe Use:
   - Healthcare providers who prescribe TRYVIO are specially certified under 505-1(f)(3)(A).
   - Pharmacies that dispense TRYVIO are specially certified under 505-1(f)(3)(B).
2. Implementation System
3. Timetable for Submission of Assessments

TRYVIO™ REMS
Prescriber Enrollment Form

Placeholder for QR code

Due to the risk of embryo-fetal toxicity for patients who can become pregnant, prescribers who wish to prescribe TRYVIO™ must be certified in the TRYVIO™ REMS (Risk Evaluation and Mitigation Strategy) and agree to comply with the requirements of the program. In order to receive samples of TRYVIO™, prescribers must be enrolled in the TRYVIO™ REMS and agree to comply with the requirements for a Sample Dispensing Prescriber, detailed in the agreement on page 2.

To enroll and become certified in the TRYVIO REMS™, complete this form and the **Prescriber Knowledge Assessment** online at www.TRYVIOREMS.com OR fax this completed form and the completed assessment to 1-800-465-0391.

Contact the TRYVIO™ REMS at 1-866-429-8964 with any questions.

Prescriber Information (*indicates required field)

***First Name** _____ **MI** _____ ***Last Name** _____

***NPI Number** _____

***Specialty:** ☐ **Nephrology** ☐ **Cardiology** ☐ **Endocrinology** ☐ **Internist**
☐ **Other (please specify):** _____

***Professional Designation:** ☐ **MD** ☐ **DO** ☐ **PA** ☐ **NP**

Office Practice / Academic Institution _____

***Address Line #1** _____

Address Line #2 _____

***City** _____ ***State** _____ ***Zip** _____

***Preferred Method of Contact** ☐ **Office Phone** ☐ **Email** ☐ **Mobile Phone** ☐ **Text Message**

By selecting to receive texts, you agree to receive text messages from the TRYVIO™ REMS.

***Office Phone** _____ **Ext.** _____ ***Fax** _____
(XXX)XXX-XXXX (XXX)XXX-XXXX

***Mobile Phone** _____
(XXX)XXX-XXXX

***Email** _____

Office Contact Information

Primary Contact
First Name _____ **Last Name** _____

Office Phone _____ **Ext.** _____ **Email** _____
(if different than above) (XXX)XXX-XXXX

Secondary Contact
First Name _____ **Last Name** _____

Office Phone _____ **Ext.** _____ **Email** _____
(if different than above) (XXX)XXX-XXXX

By signing you agree that you have read the TRYVIO™ REMS Prescriber Agreement on Page 2 and understand your obligations as a TRYVIO™ prescriber.

_____ _____
***Prescriber Signature** ***Date (MM-DD-YYYY)**

TRYVIO™ REMS
Prescriber Enrollment Form

Placeholder for QR code

TRYVIO™ REMS Prescriber Agreement

By signing this **Prescriber Enrollment Form,** you signify your understanding of the risks of TRYVIO™ treatment and your obligation as a TRYVIO™ prescriber to educate your patients about the TRYVIO™ REMS (Risk Evaluation and Mitigation Strategy) and report any pregnancies to the REMS at 1-866-429-8964. Specifically, you attest to the following:

By signing this form, I agree to become certified and comply with the following TRYVIO REMS requirements:

- Review the drug's Prescribing Information.
- Review the **Prescriber and Pharmacy Guide**.
- Enroll in the REMS by successfully completing the **Prescriber Knowledge Assessment** and completing the **Prescriber Enrollment Form** and submitting both to the TRYVIO™ REMS.

Before treatment initiation (First Dose), I must:

- Assess the patient's reproductive status using the definitions in the **Prescriber and Pharmacy Guide**.
- For patients who can become pregnant, counsel the patient
  - On the risk of embryo-fetal toxicity
  - To use acceptable contraception, pregnancy testing recommendations before initiating treatment, monthly during treatment, and one month after discontinuing treatment.
  - The use of emergency contraception using the **Patient Guide**.
- Provide a copy of the **Patient Guide** to the patient.

At all times, I must:

- Report pregnancies to the REMS at 1-866-429-8964.

Prescriber REMS Agreement for Those Who Dispense Samples

To dispense TRYVIO samples, I must:

- Follow the requirements of a prescriber that I have attested to on the **Prescriber Enrollment Form** above.
- Train all relevant staff involved in dispensing on the REMS requirements, procedures, and REMS materials.
- Establish processes and procedures for providing the **Risk of Birth Defects with TRYVIO** to each patient each time TRYVIO is dispensed.
- Provide the patient with the **Risk of Birth Defects with TRYVIO** with each dispense.
- Report dispenses to the TRYVIO™ REMS by calling 1-866-429-8964.
- Not distribute, transfer, loan, or sell TRYVIO™.
- Maintain records of all processes and procedures including compliance with those processes and procedures.
- Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

* Prescriber Signature

* Date (MM-DD-YYYY)

Healthcare providers should report suspected adverse events or product quality complaints associated with TRYVIO™ to Idorsia Pharmaceuticals at 1-833-400-9611 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

TRYVIO™ REMS
Outpatient Pharmacy Enrollment Form

Placeholder for QR code

Due to the risk of embryo-fetal toxicity for patients who can become pregnant, outpatient pharmacies that wish to dispense TRYVIO™ must be certified in the TRYVIO™ REMS (Risk Evaluation and Mitigation Strategy) and agree to comply with the requirements of the program. An authorized representative must complete and sign this form on behalf of the outpatient pharmacy.

To enroll and become certified in the TRYVIO™ REMS, complete this form online at **www.TRYVIOREMS.com** OR fax this completed form to 1-800-465-0391.

Contact the TRYVIO™ REMS at 1-866-429-8964 with any questions.

Outpatient Pharmacy Information (*indicates required field)

***Outpatient Pharmacy Type:** ☐ **Retail** ☐ **Specialty**

***NPI Number** _____

***Outpatient Pharmacy Name** _____

***Address Line 1** _____

Address Line 2 _____

***City** _____ ***State** _____ ***Zip** _____

***Office Phone** _____ (XXX)XXX-XXXX **Ext.** _____ ***Fax** _____ (XXX)XXX-XXXX

Authorized Representative Information and Agreement (*indicates required field)

***First Name** _____ **MI** _____ ***Last Name** _____

Title _____

*** Credentials:** ☐ **RPh** ☐ **PharmD** ☐ **BCPS** ☐ **Other** _____

***Office Phone** _____ (XXX)XXX-XXXX **Ext.** _____ ***Fax** _____ (XXX)XXX-XXXX

***Email** _____

***Mobile Phone** _____ (XXX)XXX-XXXX

***Preferred Method of Contact** ☐ **Office Phone** ☐ **Email** ☐ **Mobile Phone** ☐ **Text Message**

By selecting to receive texts, you agree to receive text messages from the TRYVIO™ REMS.

By signing below, you agree that you have read the Outpatient Pharmacy Authorized Representative Agreement on Page 2 and understand your obligations as an Authorized Representative.

_____ _____

***Authorized Representative Signature** ***Date** (MM-DD-YYYY)

Reference ID: 5351337

TRYVIO™ REMS
Outpatient Pharmacy Enrollment Form

Placeholder for QR code

Outpatient Pharmacy Authorized Representative Agreement

To become certified to dispense TRYVIO™, my pharmacy must:

- Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the outpatient pharmacy.
- Have the authorized representative enroll in the TRYVIO™ REMS by completing and submitting the **Outpatient Pharmacy Enrollment Form** to the REMS.
- Review the Prescribing Information and the **Prescriber and Pharmacy Guide**.
- Train all relevant staff involved in dispensing TRYVIO™ on the REMS requirements, procedures, and REMS materials.
- Establish processes and procedures to report a pregnancy to the REMS at 1-866-429-8964.
- Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed.

Before dispensing TRYVIO™, my pharmacy must:

- Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.
- Provide the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

To maintain certification to dispense, my pharmacy must:

- Have a new authorized representative complete and submit an updated **Outpatient Pharmacy Enrollment Form** to the REMS if the authorized representative changes.

At all times, my pharmacy must:

- Report pregnancies to the REMS at 1-866-429-8964.
- Not distribute, transfer, loan, or sell TRYVIO™ except to certified pharmacies.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

Healthcare providers should report suspected adverse events or product quality complaints associated with TRYVIO™ to Idorsia Pharmaceuticals at 1-833-400-9611 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

TRYVIO™ REMS
Inpatient Pharmacy Enrollment Form

Placeholder for QR code

Due to the risk of embryo-fetal toxicity for patients who can become pregnant, inpatient pharmacies that wish to dispense TRYVIO™ must be certified in the TRYVIO™ REMS (Risk Evaluation and Mitigation Strategy) and agree to comply with the requirements of the program. An authorized representative must complete and submit this form on behalf of the inpatient pharmacy.

To enroll and become certified in the TRYVIO™ REMS, complete this form online at **www.TRYVIOREMS.com** OR fax this completed form to 1-800-465-0391.

Contact the TRYVIO™ REMS at 1-866-429-8964 with any questions.

Inpatient Pharmacy Information (*indicates required field)

***Inpatient Pharmacy Name** _____ ***NPI Number** _____

***Type of Facility** ☐ **Hospital** ☐ **Nursing Home** ☐ **Rehab** ☐ **Mental Facility** ☐ **Assisted Living** ☐ **Prison**

☐ **Other (please specify)** _____

***Address Line 1** _____

Address Line 2 _____

***City** _____ ***State** _____ ***Zip** _____

***Office Phone** _____ (XXX)XXX-XXXX **Ext.** _____ ***Fax** _____ (XXX)XXX-XXXX

Pharmacy Shipping Address, if different from above (*indicates required field)

***First Name** _____ **MI** _____ ***Last Name** _____

***Address Line 1** _____

Address Line 2 _____

***City** _____ ***State** _____ ***Zip** _____

***Office Phone** _____ (XXX)XXX-XXXX **Ext.** _____ ***Fax** _____ (XXX)XXX-XXXX

Authorized Representative Information and Agreement (*indicates required field)

***First Name** _____ **MI** _____ ***Last Name** _____

Position/Title ☐ **Hospital Pharmacist** ☐ **Head of Pharmacy & Therapeutics (P&C) Committee**
(If Other, please specify) ☐ **Other** _____

***Office Phone** _____ (XXX)XXX-XXXX **Ext.** _____ ***Fax** _____ (XXX)XXX-XXXX

***Mobile Phone** _____ (XXX)XXX-XXXX

***Preferred Method of Contact** ☐ **Office Phone** ☐ **Email** ☐ **Mobile Phone** ☐ **Text Message**

By selecting to receive texts, you agree to receive text messages from the TRYVIO™ REMS.

***Email** _____

By signing you agree that you have read the Inpatient Pharmacy Authorized Representative Agreement on Page 2 and understand your obligations as an inpatient pharmacy Authorized Representative.

_____ _____

***Authorized Representative Signature** ***Date** (MM-DD-YYYY)

Reference ID: 5351337

TRYVIO™ REMS
Inpatient Pharmacy Enrollment Form

Placeholder for QR code

Inpatient Pharmacy Authorized Representative Agreement

To become certified to dispense TRYVIO™, my pharmacy must:

- Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy.
- Have the authorized representative review the Prescribing Information and the **Prescriber and Pharmacy Guide**.
- Have the authorized representative enroll in the TRYVIO™ REMS by completing and submitting the **Inpatient Pharmacy Enrollment Form** to the REMS.
- Train all relevant staff involved in dispensing TRYVIO™ on the REMS requirements, procedures, and REMS materials.
- Establish processes and procedures to verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber.
- Establish processes and procedures to report pregnancies to the REMS at 1-866-429-8964.
- Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed at patient discharge.

Before dispensing, my pharmacy must:

- Verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber through the processes and procedures established as a requirement of the REMS.

To maintain certification to dispense, my pharmacy must:

- Have a new authorized representative complete and submit an updated **Inpatient Pharmacy Enrollment Form** to the TRYVIO™ REMS if the authorized representative changes.

At discharge, my pharmacy must:

- Provide the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

At all times, the inpatient pharmacy must:

- Report pregnancies to the REMS at 1-866-429-8964.
- Not distribute, transfer, loan, or sell TRYVIO™ except to certified pharmacies.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals to ensure that all processes and procedures are in place and are being followed.

Healthcare providers should report suspected adverse events or product quality complaints associated with TRYVIO™ to Idorsia Pharmaceuticals at 1-833-400-9611 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Phone: 1-866-429-8964 **www.TRYVIOREMS.com** **Fax: 1-800-465-0391**

TRYVIO™ REMS Prescriber and Pharmacy Guide

Introduction to TRYVIO™ Indication

TRYVIO™ (aprocitentan) is an endothelin receptor antagonist (ERA) indicated for the treatment of hypertension, to lower blood pressure (BP) in patients who are not adequately controlled on other drugs.

TRYVIO™ Risk of Embryo-Fetal Toxicity

TRYVIO™ can cause embryo-fetal toxicity if taken during pregnancy and should not be prescribed for a pregnant patient.

TRYVIO™ is in a class of medications called ERAs and has dual inhibition of Endothelin (ET)-1 binding to ET_A and ET_B receptors. Based on the mechanism of action and animal data of other medications in this class, TRYVIO™ can cause embryo-fetal toxicity when used during pregnancy, including use during **early pregnancy** (first trimester).

Several antihypertensive drugs, from a variety of pharmacologic classes, have been shown to induce embryo-fetal toxicity. Specifically, the use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. These drugs should be stopped as soon as pregnancy is detected. TRYVIO™ should also be stopped as soon as pregnancy is detected, but because of the potential for embryo-fetal toxicity to occur even earlier in pregnancy, TRYVIO™ should not be initiated in pregnant patients.

Patients must not become pregnant while taking TRYVIO™, or for one month after stopping treatment.

Risk Evaluation and Mitigation Strategy (REMS)

Because of the risk of serious birth defects, TRYVIO™ is only available through a restricted distribution program required by the Food and Drug Administration (FDA) called the TRYVIO™ REMS.

The goal of the TRYVIO™ REMS is to mitigate the risk of embryo-fetal toxicity associated with TRYVIO™ by ensuring that prescribers are aware of the risk of embryo-fetal toxicity associated with TRYVIO™ and the need to counsel patients who can become pregnant on the actions necessary to prevent pregnancy and minimize exposure to a fetus.

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Prescriber Requirements

Important information for prescribers of patients who can become pregnant:

- **Counsel patients about acceptable contraception and about medical options in the event of unprotected sex or known or suspected contraceptive failure.**
- **Remind patients about pregnancy testing before, monthly during treatment, and for one month after discontinuing treatment.**
- **Remind patients to report missing a menstrual period or any other reason for suspected pregnancy to you immediately.**

Prescriber Steps in TRYVIO™ REMS

1. **Review** the TRYVIO™ Prescribing Information.

2. **Review** the **Prescriber and Pharmacy Guide.**

3. **Enroll** in the TRYVIO™ REMS:
   - ☐ Complete the **Prescriber Knowledge Assessment**
   - ☐ Complete the **Prescriber Enrollment Form**
   - ☐ Submit both to the TRYVIO™ REMS either online at www.TRYVIOREMS.com or via fax at 1-800-465-0391.

4. **Assess** the patient's reproductive status. You should identify patients as one of the following categories based on the definitions provided.
   - Prescribers should follow-up with patients during treatment to reassess reproductive status and the need for patient counseling.

   For the purposes of the REMS, the following definitions apply:

   Patients Who Cannot Become Pregnant:
   - Patients with a uterus who are at Tanner Stages 1 and 2 and are not considered to be of reproductive potential
   - Patients with a uterus who have passed through Menopause (as defined below)
   - Patients with other medical reasons for permanent, irreversible infertility
   - Patients without a uterus (including patients who were born male)

   Patients Who Can Become Pregnant:
   - Patients with a uterus who have entered puberty and all patients with a uterus that have not passed through Menopause (as defined below).
   - For the purpose of the TRYVIO™ REMS, puberty includes those patients with a uterus who are at least Tanner State 3 and have not yet had a menses (premenarchal).
   - For the purpose of the TRYVIO™ REMS, patients who have undergone tubal sterilization are classified as patients who can become pregnant.

   Definition of Menopause:
   - Menopause is defined as 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition of medical therapy) or post-surgical from a bilateral oophorectomy.

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5. **Confirm** that patients who can become pregnant are not pregnant before starting treatment.

6. **Counsel** patients who can become pregnant about:
   - The risk of embryo-fetal toxicity.
   - Pregnancy testing recommendations before initiating treatment, monthly during treatment, and for one month after discontinuing treatment.
   - The need to use acceptable contraception.
   - The use of emergency contraception using the **Patient Guide.**

7. **Report** pregnancies to the REMS at 1-866-429-8964.

Birth Control Options for Patients Who Can Become Pregnant

Prescribers must counsel patients about acceptable contraception and about medical options in the event of unprotected sex or known or suspected contraceptive failure.

Please refer to the table below for a complete list of acceptable contraceptive options. The same diagram appears in the **Patient Guide** and should be used to discuss acceptable contraceptive options with patients. Patients must adhere to (at least) any one of the following four Options for contraception:

Option 1	Option 2	Option 3	Option 4
One method from this list:	One method from this list:	One method from this list:	One method from this list:
Standard intrauterine device (Copper T 380A IUD)	Estrogen and progesterone oral contraceptives ("the pill")	Diaphragm with spermicide	Partner's vasectomy
Intrauterine system (LNG-20 IUS: progesterone IUS)	Estrogen and progesterone transdermal patch	Cervical cap with spermicide	PLUS One method from this list:
Progesterone implant	Vaginal ring	PLUS One method from this list:	Male condom
Tubal sterilization	Progesterone injection	Male condom	Diaphragm with spermicide
	PLUS One method from this list:		Cervical cap with spermicide
	Male condom		Estrogen and progesterone oral contraceptives ("the pill")
	Diaphragm with spermicide		Estrogen and progesterone transdermal patch
	Cervical cap with spermicide		Vaginal ring
			Progesterone injection

Pharmacy Requirements

Outpatient Pharmacy Steps for TRYVIO™ REMS

For certified outpatient pharmacies, the designated authorized representative must complete the following steps to become certified in the TRYVIO™ REMS and receive TRYVIO™:

1. **Review** the Prescribing Information and **Prescriber and Pharmacy Guide.**

2. **Enroll** in the TRYVIO™ REMS by completing the **Outpatient Pharmacy Enrollment Form** and submitting it to the TRYVIO™ REMS online at www.TRYVIOREMS.com or via fax at 1-800-465-0391.
   - By signing the form, the authorized representative attests to understanding the risk of TRYVIO™ and agrees to comply with the TRYVIO™ REMS.

3. **Train** all relevant staff involved in dispensing TRYVIO™ on the TRYVIO™ REMS requirements, procedures, and REMS materials.
   - Establish processes and procedures to report pregnancies to the REMS at 1-866-429-8964.
   - Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed.

Certified outpatient pharmacies must:

1. **Obtain authorization** to dispense each prescription by contacting the REMS to verify the prescriber is certified.

2. **Provide** the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

3. **Have** a new authorized representative complete and submit an updated **Outpatient Pharmacy Enrollment Form** to the TRYVIO™ REMS immediately if the authorized representative changes.

4. **Report** pregnancies to the REMS at 1-866-429-8964. .

5. **Not distribute, transfer, loan, or sell** TRYVIO™ to any person or entity other than certified pharmacies.

6. **Maintain** records that all processes and procedures are in place and being followed.

7. **Comply** with audits carried out by Idorsia Pharmaceuticals or a third party acting on behalf of Idorsia Pharmaceuticals to ensure that all processes and procedures are in place and are being followed.

Reference ID: 5351337

Pharmacy Requirements (Continued)

Inpatient Pharmacy Steps for TRYVIO™ REMS

For inpatient pharmacies, the designated authorized representative must complete the following steps to become certified in the TRYVIO™ REMS and receive TRYVIO™:

1. **Review** the **Prescriber and Pharmacy Guide**.

2. **Enroll** in the TRYVIO™ REMS by completing the **Inpatient Pharmacy Enrollment Form** and submitting it to the TRYVIO™ REMS online at www.TRYVIOREMS.com or via fax at 1-800-465-0391.

3. **Train** all relevant staff involved in dispensing TRYVIO™ on the TRYVIO™ REMS requirements, procedures, and REMS materials.
   - Establish processes and procedures to verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber.
   - Establish processes and procedures to report pregnancies to the REMS at 1-866-429-8964.
   - Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed at patient discharge.

Certified inpatient pharmacies must:

1. **Verify** the prescriber is certified or the patient is under the supervision and care of a certified prescriber through processes and procedures established as a requirement of the REMS.

2. **Provide** the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

3. **Have** a new authorized representative complete and submit and updated **Inpatient Pharmacy Enrollment Form** to the TRYVIO™ REMS immediately if the authorized representative changes.

4. **Report** pregnancies to the REMS at 1-866-429-8964.

5. **Not distribute, transfer, loan, or sell** TRYVIO™ to any person or entity other than certified pharmacies.

6. **Maintain** records that all processes and procedures are in place and being followed.

7. **Comply** with audits carried out by Idorsia Pharmaceuticals or a third party acting on behalf of Idorsia Pharmaceuticals to verify that all processes and procedures are in place and being followed.

TRYVIO™ REMS

For further information about the TRYVIO™ REMS:
Online: www.TRYVIOREMS.com **Phone:** 1-866-429-8964

Healthcare providers should report suspected adverse events or product quality complaints associated with TRYVIO™ to Idorsia Pharmaceuticals at 1-833-400-9611 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Reference ID: 5351337

TRYVIO™ REMS Prescriber Knowledge Assessment

TRYVIO™ (aprocitentan) is available only through the TRYVIO™ Risk Evaluation and Mitigation Strategy (REMS).

Instructions

1. Review the **Prescriber and Pharmacy Guide** and the TRYVIO™ US Prescribing Information.
2. Complete and submit this **Prescriber Knowledge Assessment** and **Prescriber Enrollment Form** online or print and complete the **Prescriber Knowledge Assessment** and **Prescriber Enrollment Form** and submit them to the TRYVIO™ REMS via fax to 1-800-465-0391.
3. Complete all required fields on this form to avoid a delay in the enrollment process. **You must answer ALL eight questions of this Prescriber Knowledge Assessment correctly to become certified.**

PRESCRIBER INFORMATION

* indicates required field.

First Name*: _____ Phone*: _____

Last Name*: _____ Email*: _____

National Provider Identifier (NPI)*: _____

PRESCRIBER ASSESSMENT

Answer the following questions by selecting the single best answer. You must answer ALL eight questions correctly to become certified in the TRYVIO™ REMS.

1. To prescribe TRYVIO™, prescribers do not need to be certified in the TRYVIO™ REMS.
   a. True
   b. False

2. Which of the following is true for TRYVIO™?
   a. TRYVIO™ is indicated for the treatment of hypertension, to lower blood pressure in patients who are not adequately controlled on other drugs.
   b. TRYVIO™ is contraindicated for pregnancy and hypersensitivity.
   c. TRYVIO™ carries a risk of embryo-fetal toxicity.
   d. All of the above.

3. Based on the mechanism of action, TRYVIO™ has a risk of embryo-fetal toxicity as early as which trimester during pregnancy?
   a. Only during the third trimester.
   b. Only during the second trimester.
   c. During the first trimester, even before a patient knows they are pregnant.
   d. None of the above.

4. A patient should inform their prescriber immediately if they suspect they are pregnant.
   a. True
   b. False

5. Patients who can become pregnant should continue to take a pregnancy test for one month after treatment.
   a. True
   b. False

6. Before treatment with TRYVIO™, prescribers must inform patients who can become pregnant:
   a. To report a missing menstrual period or any other suspected pregnancy to their healthcare provider.
   b. To have a pregnancy test before and monthly during treatment.
   c. About the acceptable contraception and medical options in the event of unprotected sex or known contraceptive failure.
   d. All of the above.

7. Prescribers must report pregnancies of patients exposed to TRYVIO™ to the REMS.
   a. True
   b. False

8. Prior to initiating treatment with TRYVIO™, a prescriber must assess a patient's reproductive status.
   a. True
   b. False

If you have any questions or need additional information, please visit www.TRYVIOREMS.com or call 1-866-429-8964, Monday through Friday, 8am – 8pm ET.

TRYVIO™ REMS Patient Guide

What is TRYVIO™?

TRYVIO™ (aprocitentan) is a prescription medicine for the treatment of high blood pressure, to lower blood pressure in patients who are not adequately controlled on other drugs. TRYVIO™ is for use in combination with other blood pressure lowering medications.

What are the serious risks of TRYVIO™?

TRYVIO™ can cause serious birth defects if taken during pregnancy, including when taken before you know you are pregnant or during the first trimester.

- You cannot take TRYVIO™ if you are pregnant.
- You must not become pregnant while taking TRYVIO™, or
- Within one month after stopping TRYVIO™.
- **Your doctor will tell you about serious birth defects (embryo-fetal toxicity) associated with taking Tryvio™ while pregnant.**

What is the TRYVIO™ Risk Evaluation and Mitigation Strategy (REMS)?

Because of the risk of serious birth defects, the FDA has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for TRYVIO™. The purpose of the REMS is to make sure the benefits of TRYVIO™ outweigh the risks. The TRYVIO™ REMS provides patients and healthcare providers with information and requirements to manage the risk of birth defects associated with taking TRYVIO™.

Before you begin treatment with TRYVIO™

- ☐ Read this guide.
- ☐ Ask your healthcare provider any questions you have about TRYVIO™, its benefits and risks, and the TRYVIO™ REMS requirements.
- ☐ Receiving counseling about the risk of serious birth defects.

Your healthcare provider has determined that you can become pregnant using the definitions that apply to the TRYVIO REMS shown below:

Patients Who Can Become Pregnant:

- Patients with a uterus who have entered puberty and all patients with a uterus that have not passed through Menopause (as defined to the right).
- For the purpose of the TRYVIO™ REMS, puberty includes those patients with a uterus who have undergone noticeable bodily changes (continued breast budding and pubic hair growth) and have not yet had a menstrual period.
- For the purpose of the TRYVIO™ REMS, patients who have undergone tubal sterilization are classified as patients who can become pregnant.

Patients Who Cannot Become Pregnant:

- Patients with a uterus who have not yet undergone noticeable bodily changes and are not considered to be of reproductive potential
- Patients with a uterus who have passed through Menopause (as defined below)
- Patients with other medical reasons for permanent, irreversible infertility
- Patients without a uterus (including patients who were born male)

Definition of Menopause:

- Menopause is defined as 12 months without menstruation (not induced by a medical condition or medical therapy) or post-surgical from removal of ovaries.

Reference ID: 5351337

If you are a patient who can become pregnant, you should:

- ☐ Have a negative pregnancy test immediately before starting TRYVIO™.
- ☐ Have a negative pregnancy test each month while taking TRYVIO™ and for one month after discontinuing treatment.
- ☐ Use acceptable birth control at all times while taking TRYVIO™ and for one month after stopping TRYVIO™ using one of the four options in the chart below.
- ☐ **Report possible pregnancy immediately.**

Option 1	Option 2	Option 3	Option 4
One method from this list:	One method from this list:	One method from this list:	One method from this list:
Standard intrauterine device (Copper T 380A IUD)	Estrogen and progesterone oral contraceptives ("the pill")	Diaphragm with spermicide	Partner's vasectomy
Intrauterine system (LNG-20 IUS: progesterone IUS)	Estrogen and progesterone transdermal patch	Cervical cap with spermicide	PLUS One method from this list:
Progesterone implant	Vaginal ring	PLUS One method from this list:	Male condom
Tubal sterilization	Progesterone injection	Male condom	Diaphragm with spermicide
	PLUS One method from this list:		Cervical cap with spermicide
	Male condom		Estrogen and progesterone oral contraceptives ("the pill")
	Diaphragm with spermicide		Estrogen and progesterone transdermal patch
	Cervical cap with spermicide		Vaginal ring
			Progesterone injection

Talk to your healthcare provider right away if:

- You have a positive pregnancy test.
- You think your birth control has failed. Your healthcare provider may discuss medical options with you, such as emergency contraception.
- You missed your period.
- You think you are pregnant.

How will I receive TRYVIO™?

TRYVIO™ is only available at certified pharmacies. You must receive TRYVIO™ through a certified pharmacy and will receive a **Risk of Birth Defects with TRYVIO™** with your prescription.

For support while taking TRYVIO™:

Online: www.TRYVIOREMS.com

Phone: 1-866-429-8964

Risk of Birth Defects with TRYVIO™ (aprocitentan)

TRYVIO™ can cause serious birth defects if taken during pregnancy.

These defects can happen early in pregnancy, sometimes even before you know you are pregnant.

Please read the following important safety information about the use of TRYVIO™ in patients who can become pregnant.

You are considered a patient who can become pregnant if:

- You have a uterus, **and**
- You have entered puberty, even if you haven't had a period, **and**
- You have not gone through menopause (have not had a period for at least 12 months for natural reasons, or have had your ovaries removed)

If you are a patient who can become pregnant:

Before starting TRYVIO™	• You should get a pregnancy test immediately before starting TRYIVIO™. • Do not start TRYVIO if you have a positive pregnancy test, miss a period, or think you might be pregnant. • Talk to your healthcare provider to help decide which birth control options are best for you using the chart on page 2.
During TRYVIO™ treatment	• You should get a pregnancy test each month. • Stop treatment immediately and tell your healthcare provider right away if you have a positive pregnancy test, miss a period, or think you might be pregnant. • Always use acceptable birth control methods, including every time you have any sex (penis-vaginal) with a partner who could get you pregnant.
One month after TRYVIO™ treatment discontinuation	• You should continue to use acceptable birth control and get a pregnancy test one month after stopping treatment with TRYVIO™ because the medicine may still be in your body.

Acceptable Birth Control Options

Certain birth control methods are effective when used alone. Other birth control methods are not as effective by themselves, and you should use multiple methods of birth control together. Choose one option below for birth control.

Option 1	Option 2	Option 3	Option 4
One method from this list:	One method from this list:	One method from this list:	One method from this list:
Standard intrauterine device (Copper T 380A IUD)	Estrogen and progesterone oral contraceptives ("the pill")	Diaphragm with spermicide	Partner's vasectomy
Intrauterine system (LNG-20 IUS: progesterone IUS)	Estrogen and progesterone transdermal patch	Cervical cap with spermicide	PLUS One method from this list:
Progesterone implant	Vaginal ring	PLUS One method from this list:	Male condom
Tubal sterilization	Progesterone injection	Male condom	Diaphragm with spermicide
	PLUS One method from this list:		Cervical cap with spermicide
	Male condom		Estrogen and progesterone oral contraceptives ("the pill")
	Diaphragm with spermicide		Estrogen and progesterone transdermal patch
	Cervical cap with spermicide		Vaginal ring
			Progesterone injection

Talk to your healthcare provider right away if you think your birth control has failed. Your healthcare provider may discuss medical options with you, such as emergency contraception.

Please read the accompanying TRYVIO™ Medication Guide as it contains additional important safety information about your treatment. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about TRYVIO™, talk to your healthcare provider or pharmacist, contact Idorsia Pharmaceuticals Medical Information at 1-833-400-9611, or visit the website www.TRYVIOREMS.com.

TRYVIO™ REMS Website Screenshots_Draft v5.0

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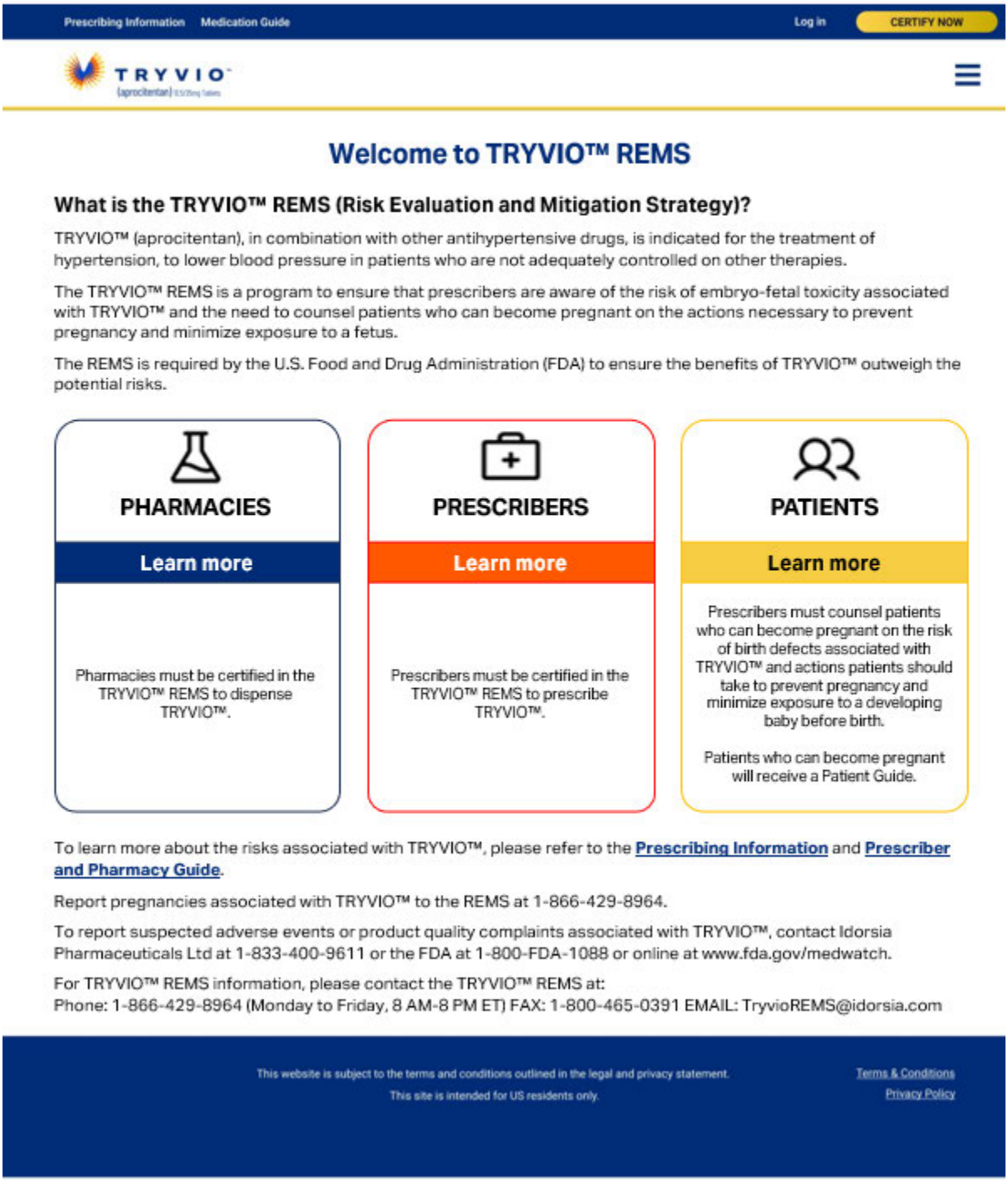
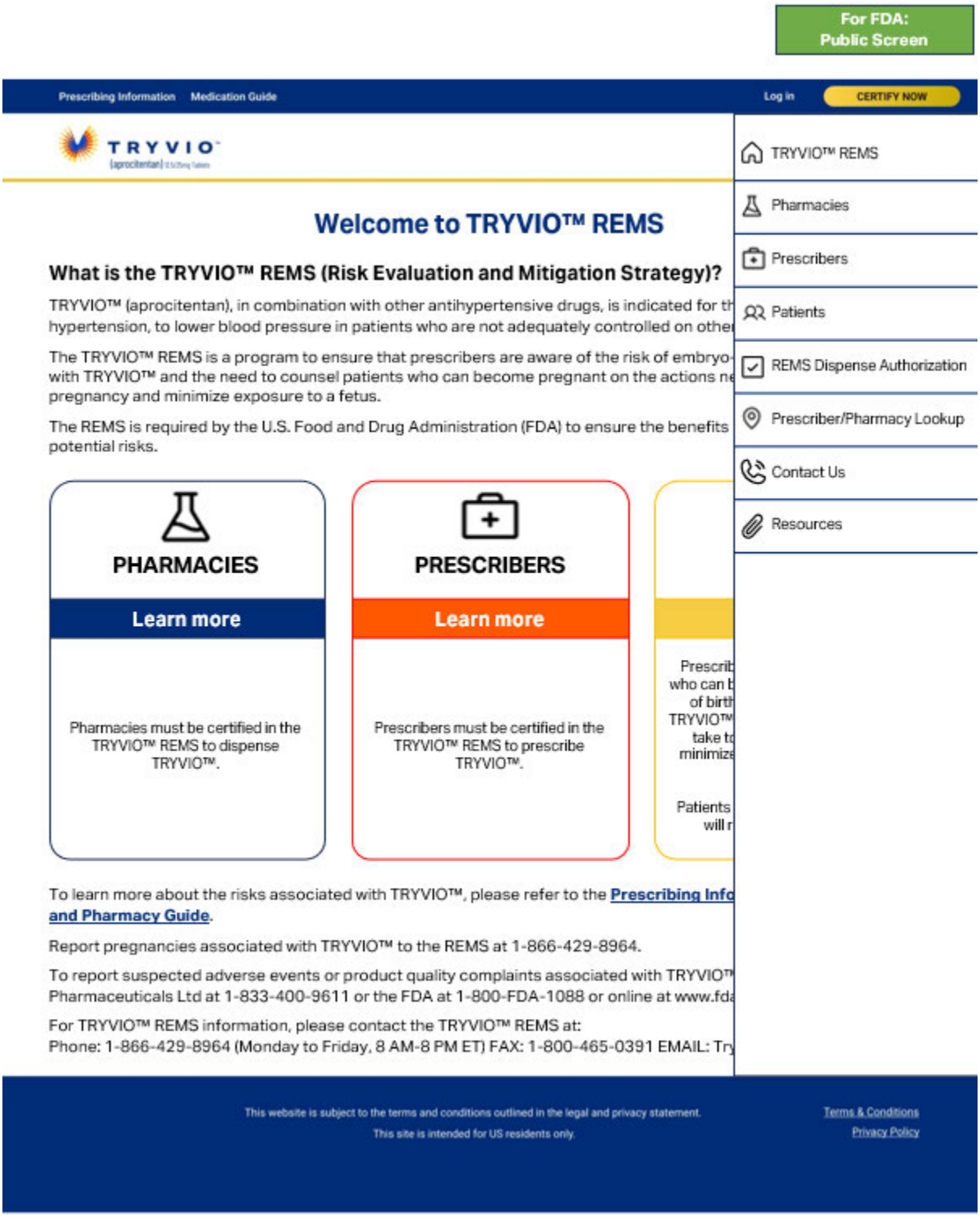
Home

For FDA:
Public Screen

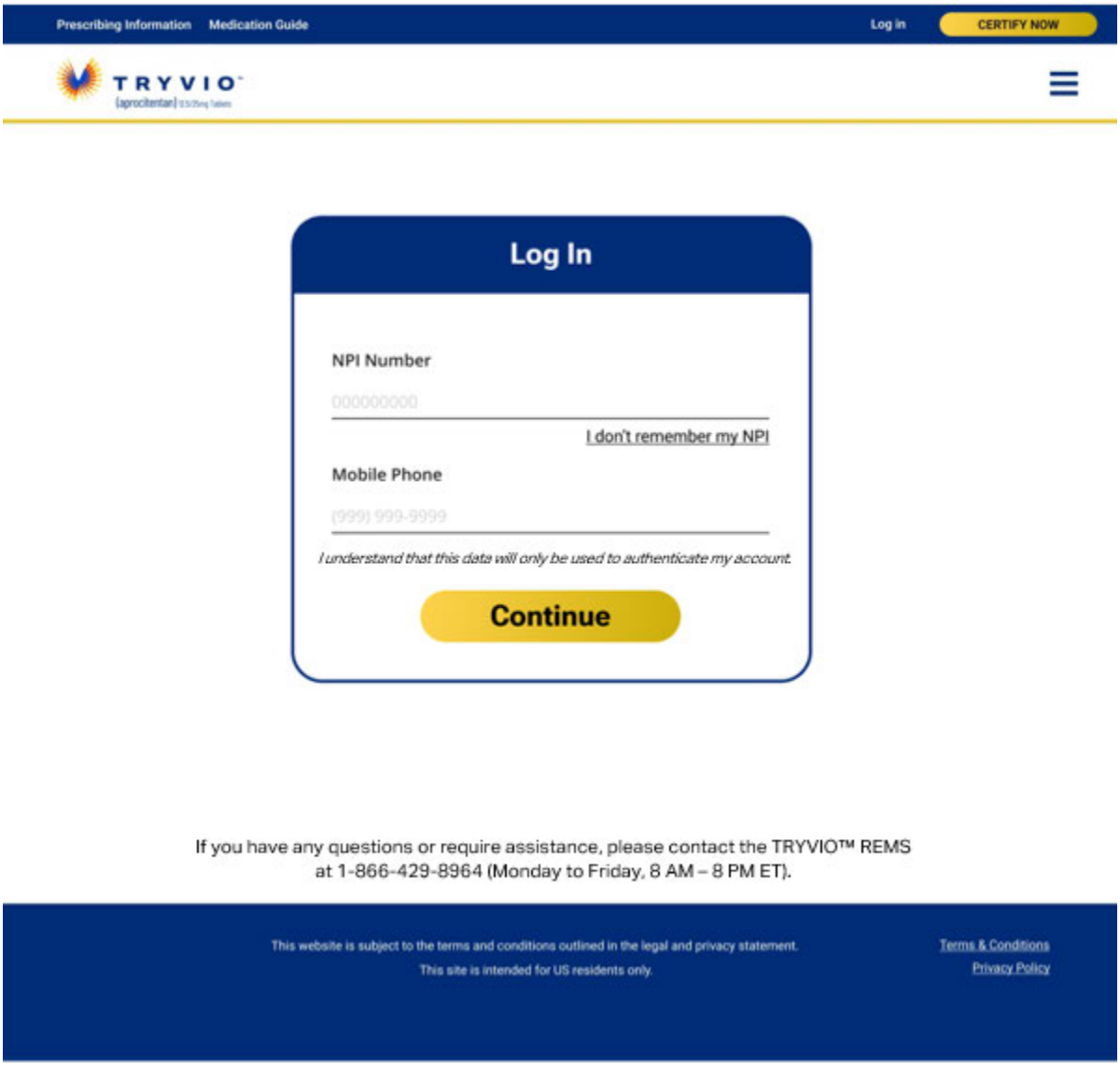


Home (Menu Open)

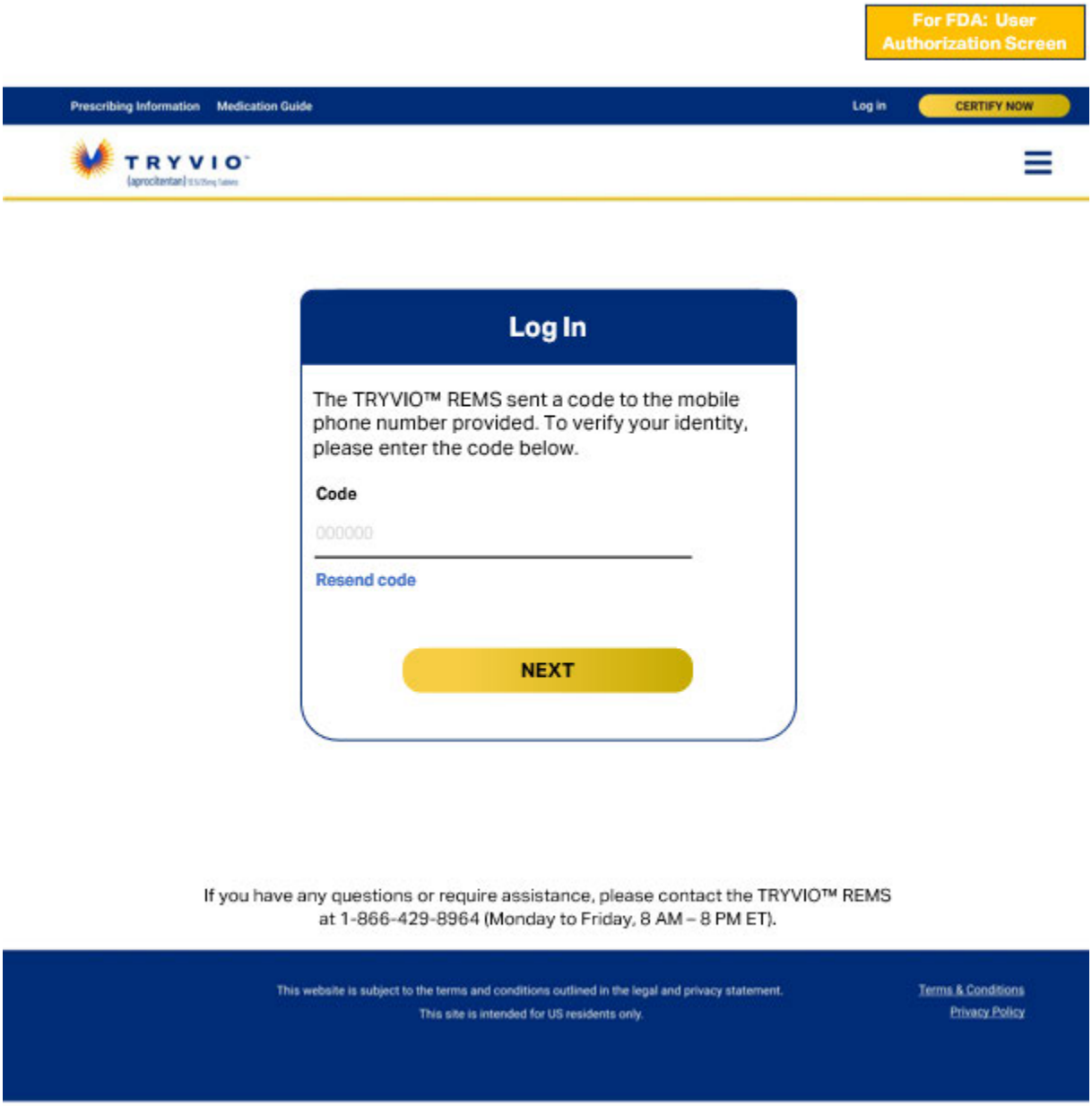


Log In

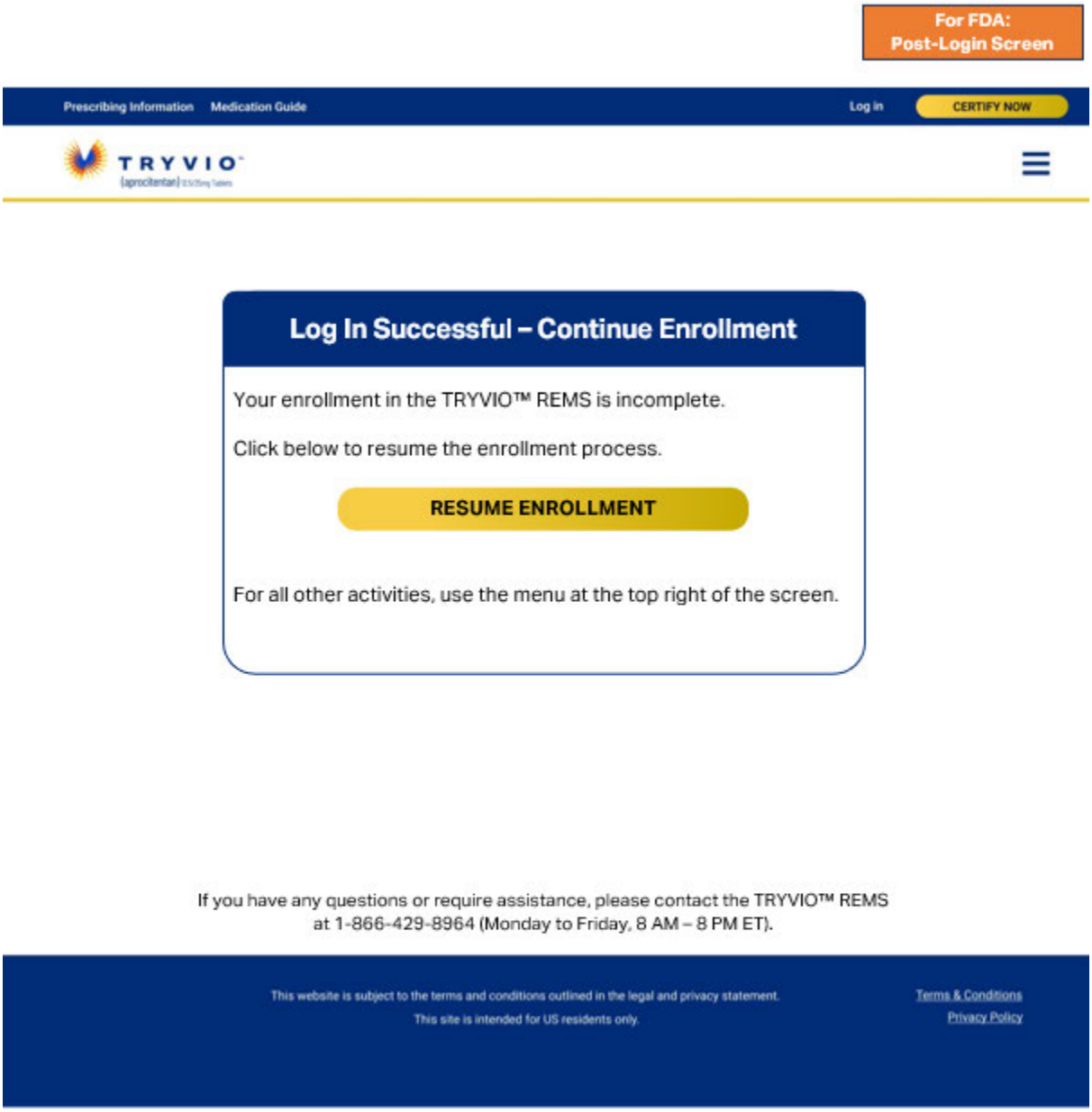
For FDA: User Authorization Screen



Log In (Identity Verification)

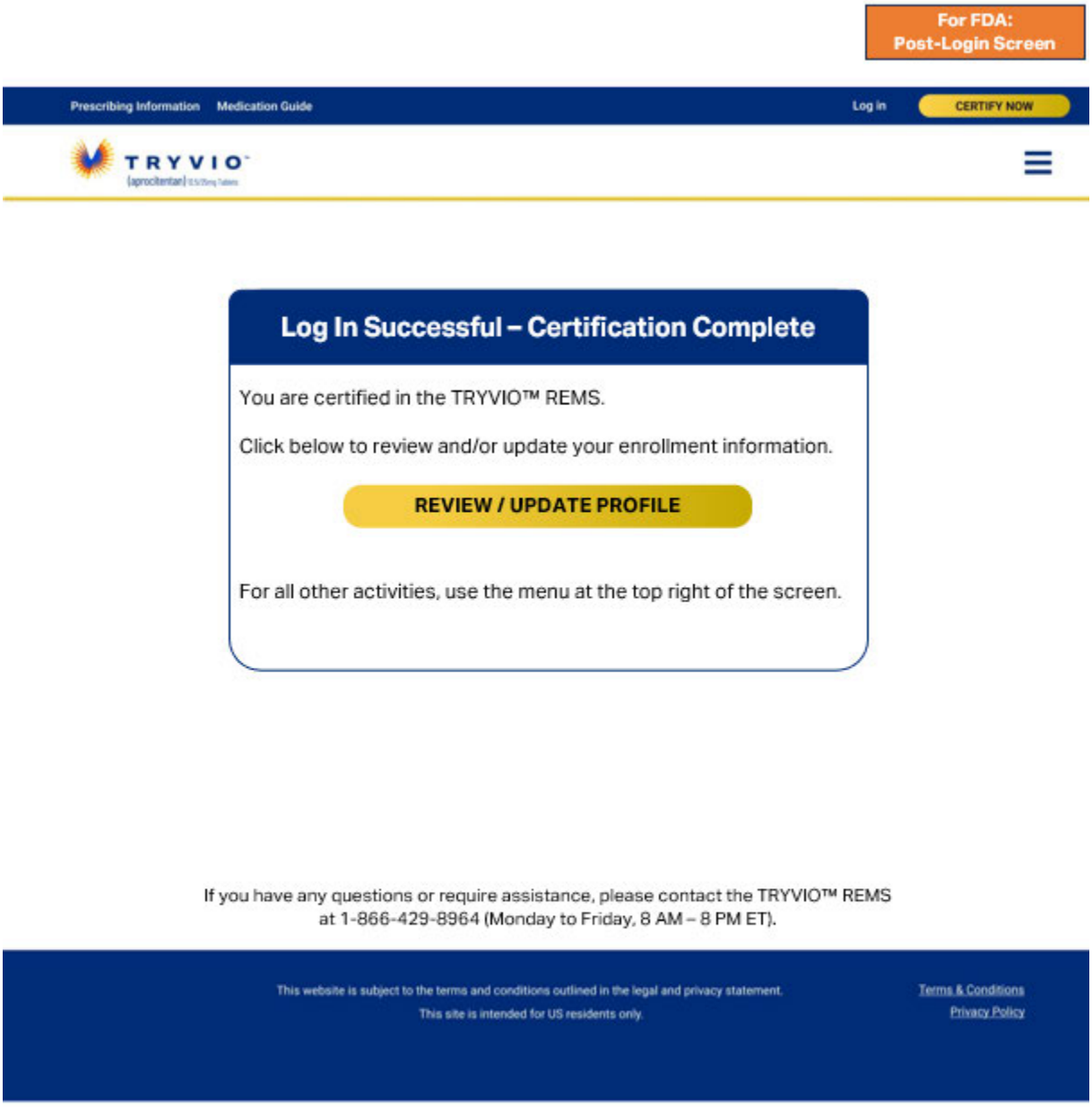


Log In (Successful, User Incomplete Certification)



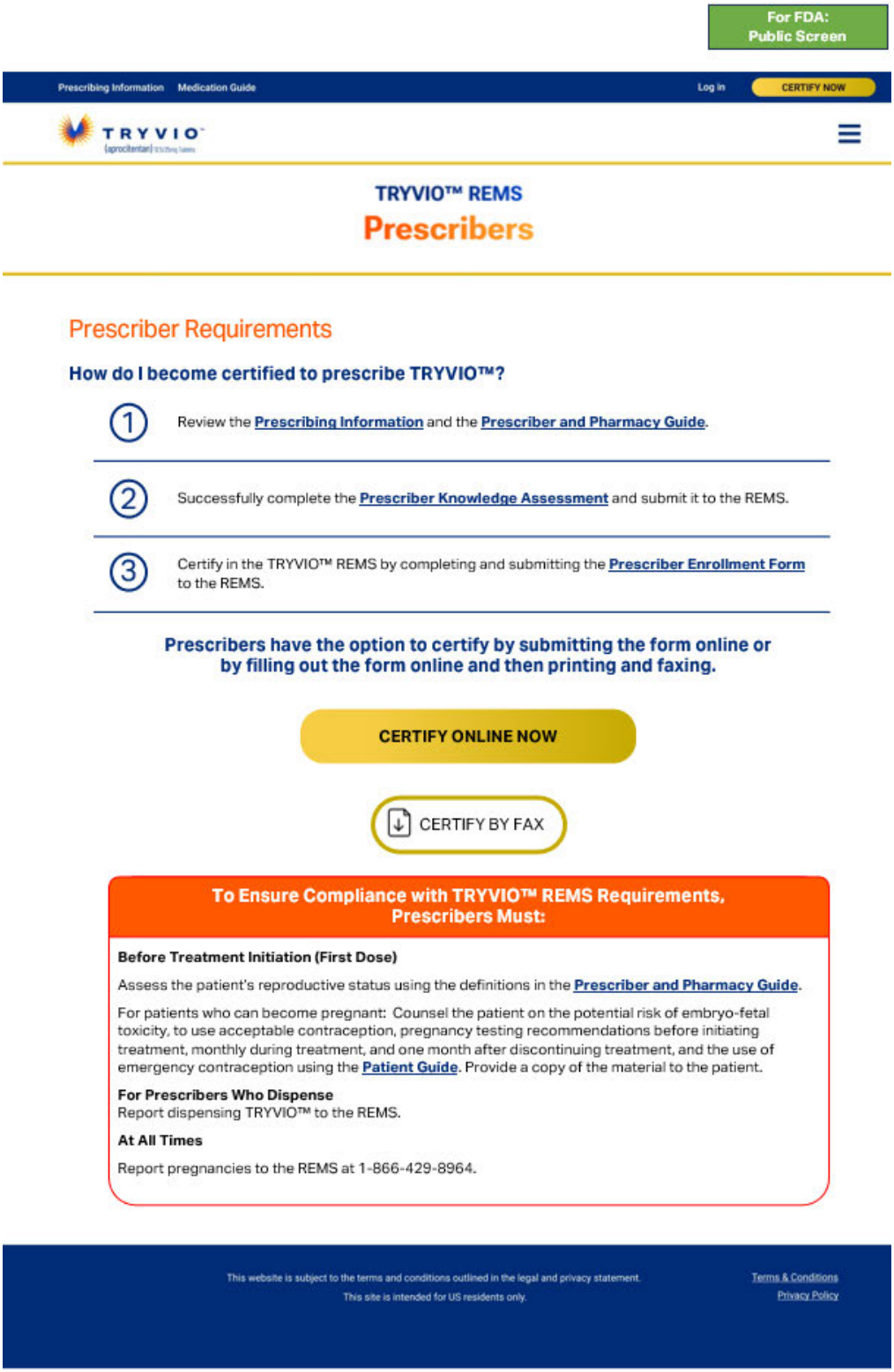
Note for FDA: User would be taken to the point at which they left the enrollment process (e.g., knowledge assessment for prescribers, outpatient pharmacy enrollment form authorized representative information) and have the option to continue the process.

Log In (Successful, Certified User Options)

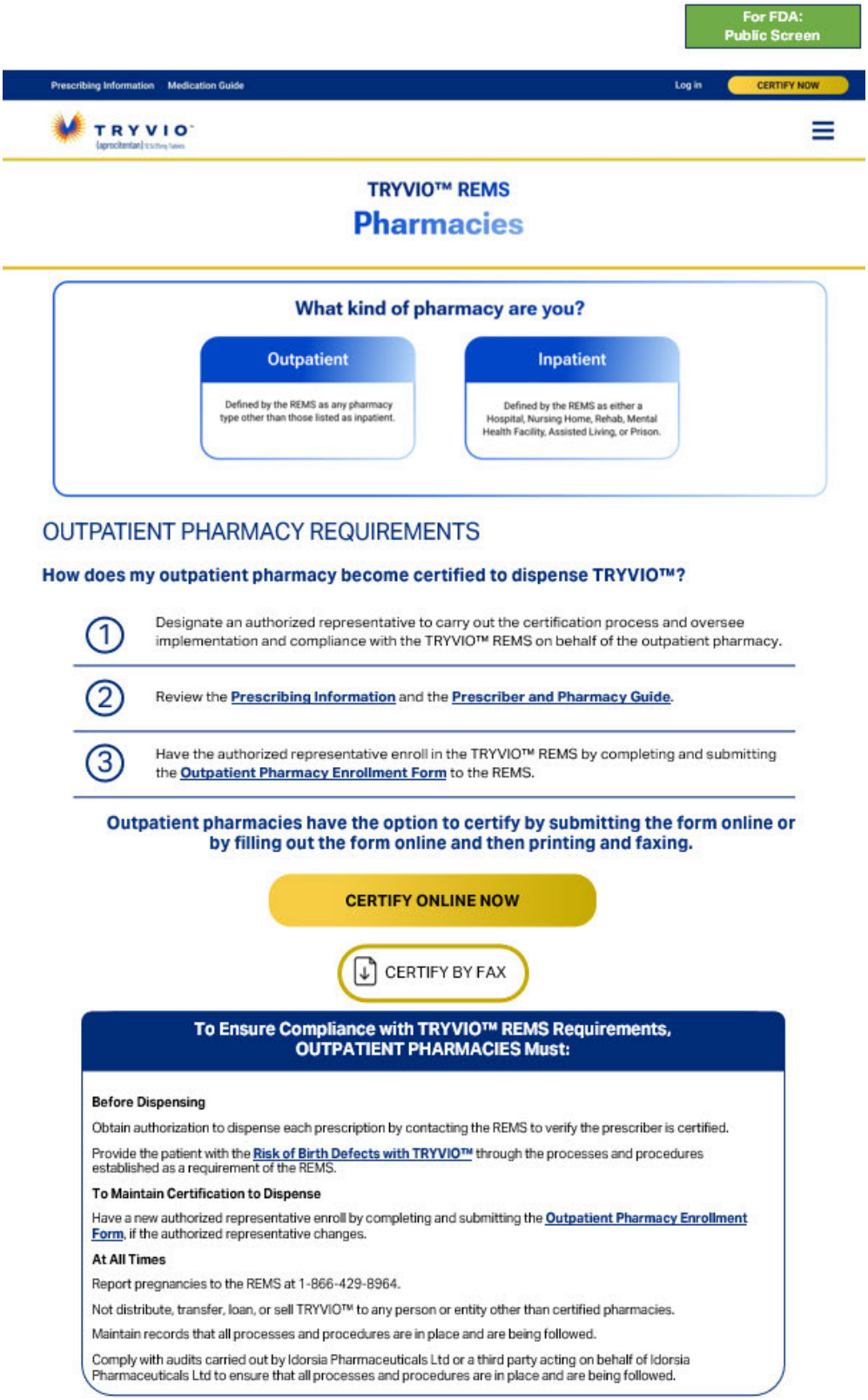


Note for FDA: User would be taken to their completed certification form and have the option to update administrative information (e.g., address, phone number)

Prescribers



Pharmacies


For FDA:
Public Screen
Prescribing Information
Medication Guide
Log in
CERTIFY NOW
TRYVIO
TRYVIO™ REMS
Pharmacies
What kind of pharmacy are you?
Outpatient
Defined by the REMS as any pharmacy type other than those listed as inpatient.
Inpatient
Defined by the REMS as either a Hospital, Nursing Home, Rehab, Mental Health Facility, Assisted Living, or Prison.
OUTPATIENT PHARMACY REQUIREMENTS
How does my outpatient pharmacy become certified to dispense TRYVIO™?
1
Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the TRYVIO™ REMS on behalf of the outpatient pharmacy.
2
Review the Prescribing Information and the Prescriber and Pharmacy Guide.
3
Have the authorized representative enroll in the TRYVIO™ REMS by completing and submitting the Outpatient Pharmacy Enrollment Form to the REMS.
Outpatient pharmacies have the option to certify by submitting the form online or by filling out the form online and then printing and faxing.
CERTIFY ONLINE NOW
CERTIFY BY FAX
To Ensure Compliance with TRYVIO™ REMS Requirements, OUTPATIENT PHARMACIES Must:
Before Dispensing
Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.
Provide the patient with the Risk of Birth Defects with TRYVIO™ through the processes and procedures established as a requirement of the REMS.
To Maintain Certification to Dispense
Have a new authorized representative enroll by completing and submitting the Outpatient Pharmacy Enrollment Form, if the authorized representative changes.
At All Times
Report pregnancies to the REMS at 1-866-429-8964.
Not distribute, transfer, loan, or sell TRYVIO™ to any person or entity other than certified pharmacies.
Maintain records that all processes and procedures are in place and are being followed.
Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

INPATIENT PHARMACY REQUIREMENTS

How does my inpatient pharmacy become certified to dispense TRYVIO™?

1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the TRYVIO™ REMS on behalf of the pharmacy.
2. Have the authorized representative review the **Prescribing Information** and the **Prescriber and Pharmacy Guide**.
3. Have the authorized representative enroll in the TRYVIO™ REMS by completing and submitting the **Inpatient Pharmacy Enrollment Form** to the REMS.

Inpatient pharmacies have the option to certify by submitting the form online or by filling out the form online and then printing and faxing.

CERTIFY ONLINE NOW

CERTIFY BY FAX

To Ensure Compliance with TRYVIO™ REMS Requirements, INPATIENT PHARMACIES Must:

Before Dispensing

Verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber through the processes and procedures established as a requirement of the REMS.

To Maintain Certification to Dispense

Have a new authorized representative enroll by completing and submitting the **Inpatient Pharmacy Enrollment Form** if the authorized representative changes.

At Discharge

Provide the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

At All Times

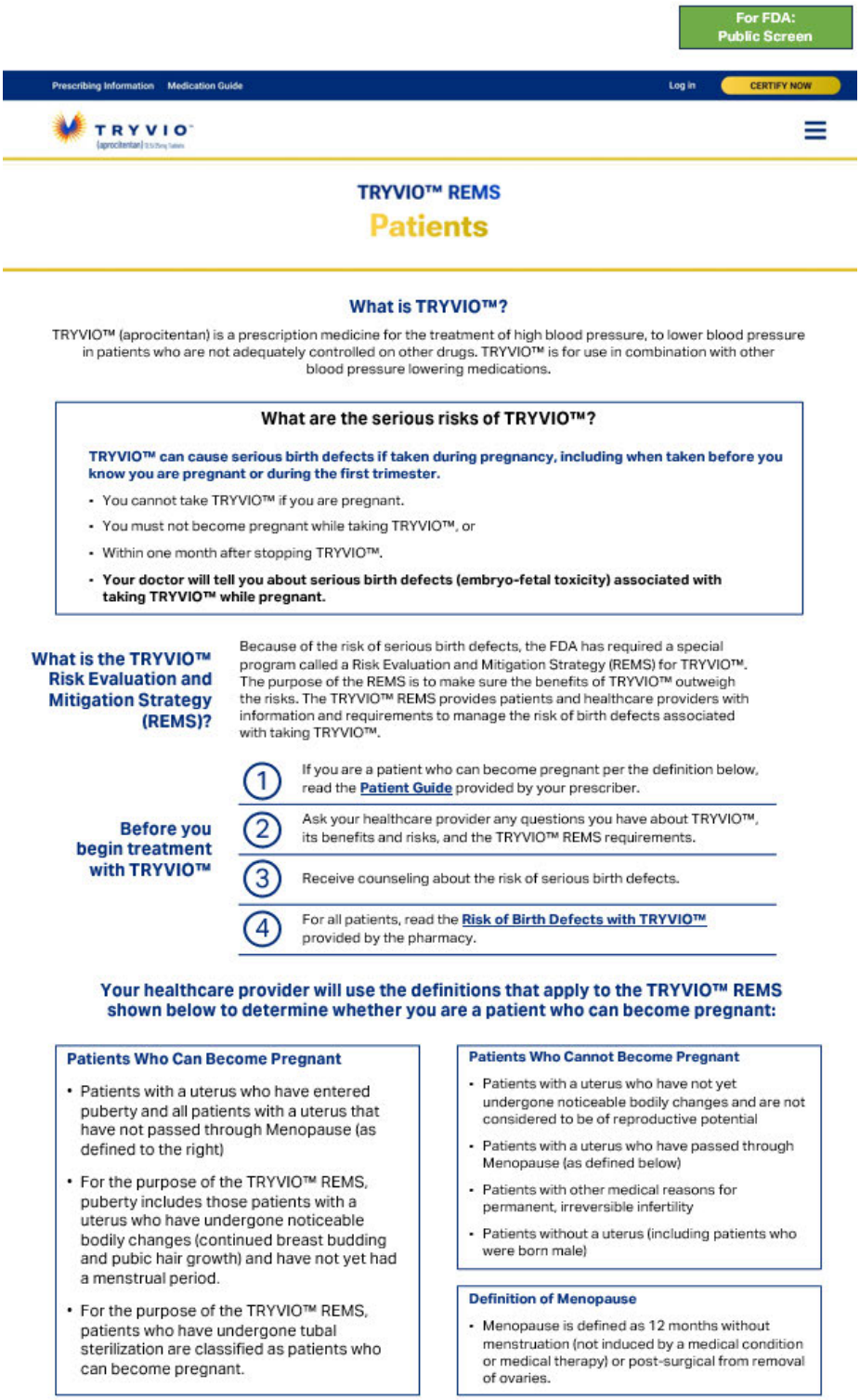
Report pregnancies to the REMS at 1-866-429-8964.

Not distribute, transfer, loan, or sell TRYVIO™ to any person or entity other than certified pharmacies.

Maintain records that all processes and procedures are in place and are being followed.

Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

Patients


For FDA:
Public Screen
Prescribing Information
Medication Guide
Log in
CERTIFY NOW
TRYVIO
(aprocitentan)
TRYVIO™ REMS
Patients
What is TRYVIO™?
TRYVIO™ (aprocitentan) is a prescription medicine for the treatment of high blood pressure, to lower blood pressure in patients who are not adequately controlled on other drugs. TRYVIO™ is for use in combination with other blood pressure lowering medications.
What are the serious risks of TRYVIO™?
TRYVIO™ can cause serious birth defects if taken during pregnancy, including when taken before you know you are pregnant or during the first trimester.
• You cannot take TRYVIO™ if you are pregnant.
• You must not become pregnant while taking TRYVIO™, or
• Within one month after stopping TRYVIO™.
• Your doctor will tell you about serious birth defects (embryo-fetal toxicity) associated with taking TRYVIO™ while pregnant.
What is the TRYVIO™ Risk Evaluation and Mitigation Strategy (REMS)?
Because of the risk of serious birth defects, the FDA has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for TRYVIO™. The purpose of the REMS is to make sure the benefits of TRYVIO™ outweigh the risks. The TRYVIO™ REMS provides patients and healthcare providers with information and requirements to manage the risk of birth defects associated with taking TRYVIO™.
Before you begin treatment with TRYVIO™
1 If you are a patient who can become pregnant per the definition below, read the Patient Guide provided by your prescriber.
2 Ask your healthcare provider any questions you have about TRYVIO™, its benefits and risks, and the TRYVIO™ REMS requirements.
3 Receive counseling about the risk of serious birth defects.
4 For all patients, read the Risk of Birth Defects with TRYVIO™ provided by the pharmacy.
Your healthcare provider will use the definitions that apply to the TRYVIO™ REMS shown below to determine whether you are a patient who can become pregnant:
Patients Who Can Become Pregnant
• Patients with a uterus who have entered puberty and all patients with a uterus that have not passed through Menopause (as defined to the right)
• For the purpose of the TRYVIO™ REMS, puberty includes those patients with a uterus who have undergone noticeable bodily changes (continued breast budding and pubic hair growth) and have not yet had a menstrual period.
• For the purpose of the TRYVIO™ REMS, patients who have undergone tubal sterilization are classified as patients who can become pregnant.
Patients Who Cannot Become Pregnant
• Patients with a uterus who have not yet undergone noticeable bodily changes and are not considered to be of reproductive potential
• Patients with a uterus who have passed through Menopause (as defined below)
• Patients with other medical reasons for permanent, irreversible infertility
• Patients without a uterus (including patients who were born male)
Definition of Menopause
• Menopause is defined as 12 months without menstruation (not induced by a medical condition or medical therapy) or post-surgical from removal of ovaries.

If you are a patient who can become pregnant, you should:

- ❑ Have a negative pregnancy test immediately before starting TRYVIO™.
- ❑ Have a negative pregnancy test each month while taking TRYVIO™ and for one month after discontinuing treatment.
- ❑ Use acceptable birth control at all times while taking TRYVIO™ and for one month after stopping TRYVIO™ using one of the four options in the chart below.
- ❑ **Report possible pregnancy immediately**.

Option 1	Option 2	Option 3	Option 4
One method from this list:	One method from this list:	One method from this list:	One method from this list:
Standard intrauterine device (Copper T 380A IUD)	Estrogen and progesterone oral contraceptives ("the pill")	Diaphragm with spermicide	Partner's vasectomy
Intrauterine system (LNG-20 IUS: progesterone IUS)	Estrogen and progesterone transdermal patch	Cervical cap with spermicide	PLUS One method from this list:
Progesterone implant	Vaginal ring	PLUS One method from this list:	Male condom
Tubal sterilization	Progesterone injection	Male condom	Diaphragm with spermicide
	PLUS One method from this list:		Cervical cap with spermicide
	Male condom		Estrogen and progesterone oral contraceptives ("the pill")
	Diaphragm with spermicide		Estrogen and progesterone transdermal patch
	Cervical cap with spermicide		Vaginal ring
			Progesterone injection

Talk to your healthcare provider right away if:

- You have a positive pregnancy test.
- You think your birth control has failed. Your healthcare provider may discuss medical options with you, such as emergency contraception.
- You missed your period.
- You think you are pregnant.

How will I receive TRYVIO™?

TRYVIO™ is only available at certified pharmacies. You must receive TRYVIO™ through a certified pharmacy and will receive a **Risk of Birth Defects with TRYVIO™** with your prescription.

FIND A PRESCRIBER OR PHARMACY CERTIFIED IN THE TRYVIO™ REMS

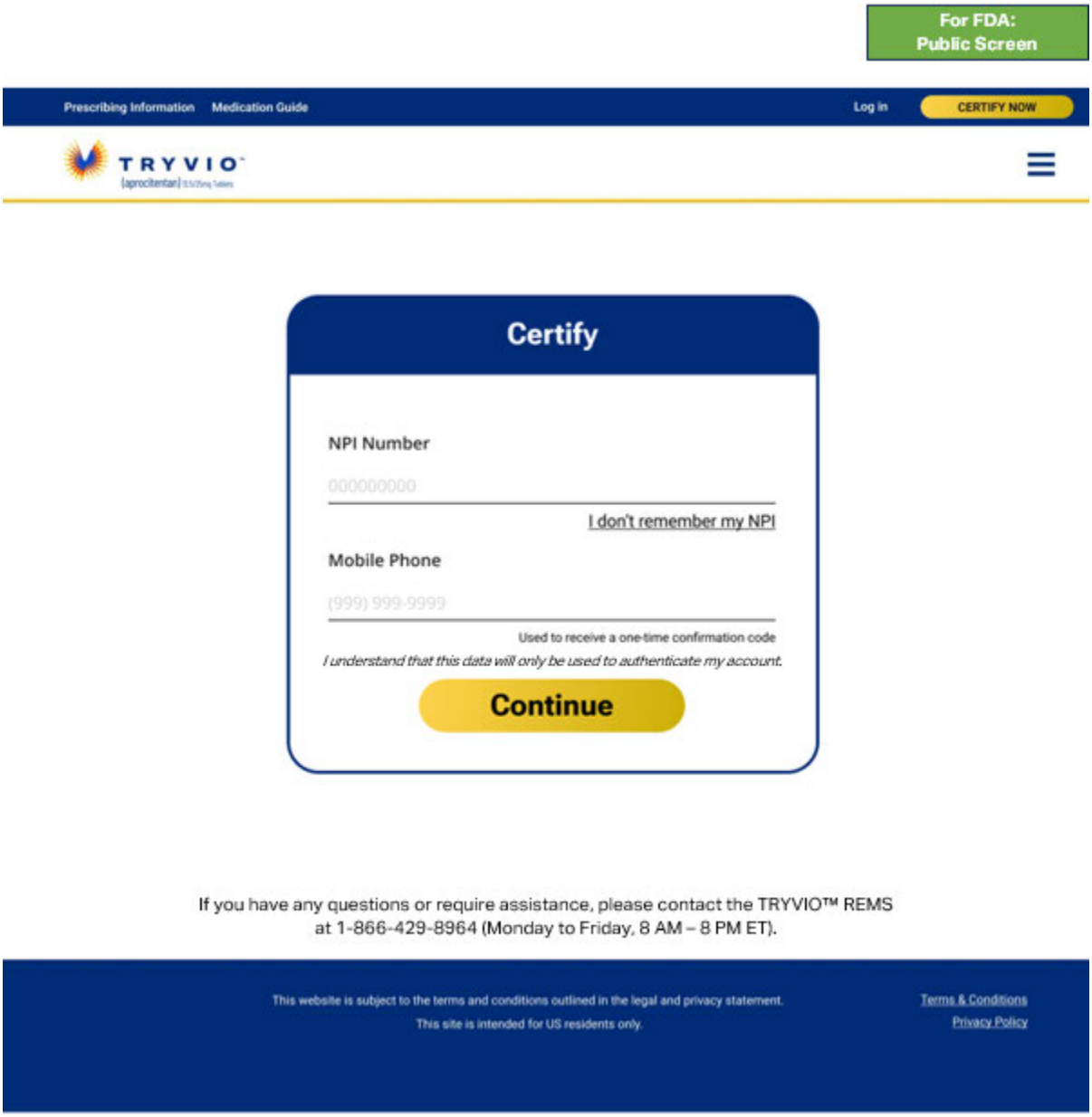
Where can I find more information about the REMS?

If you have any questions or require additional information, please contact the TRYVIO™ REMS at 1-866-429-8964 (Monday to Friday, 8 AM – 8 PM ET).

Live chat
Chat now

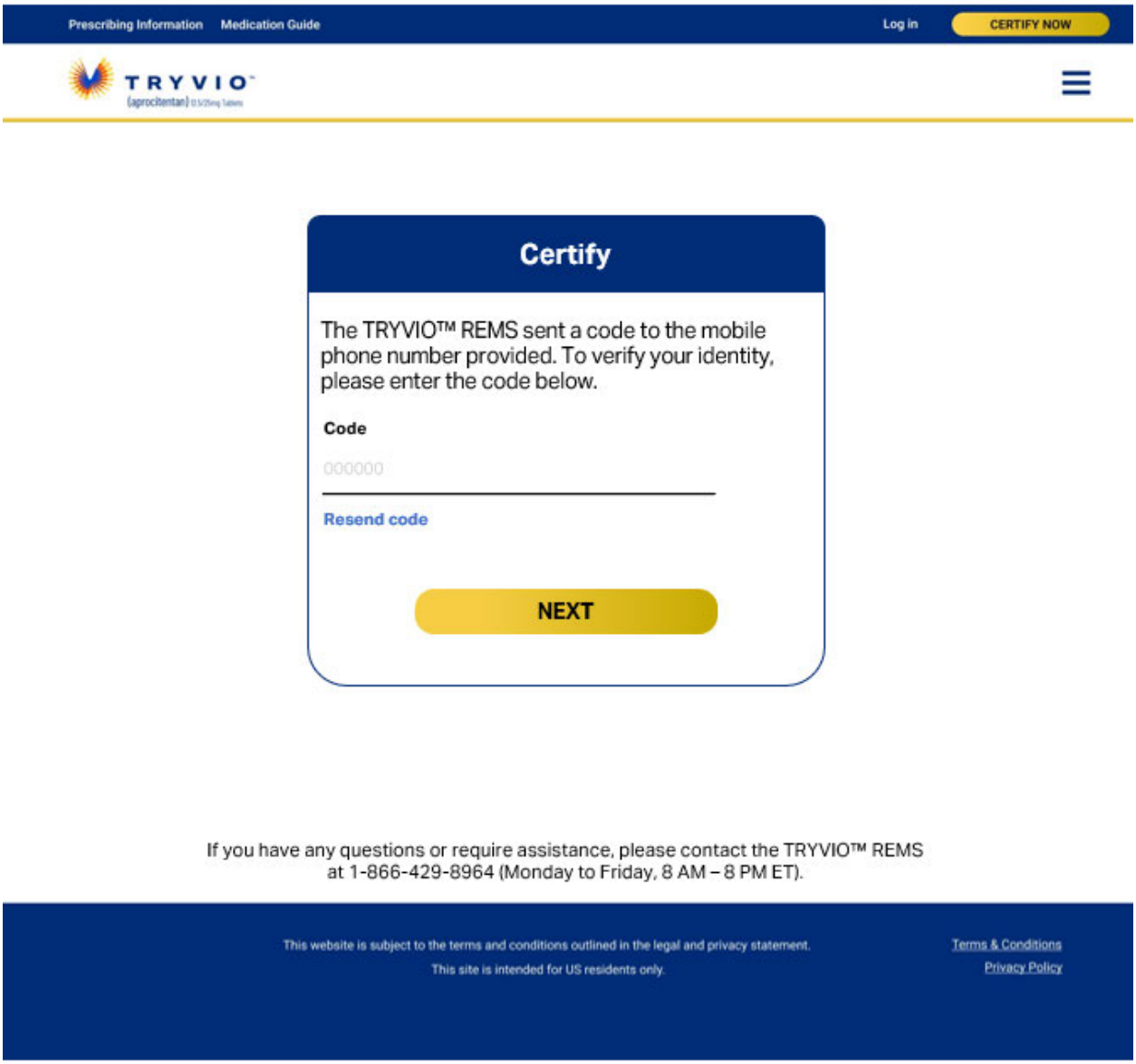
Email us
TryvioREMS@idorsia.com

Certify



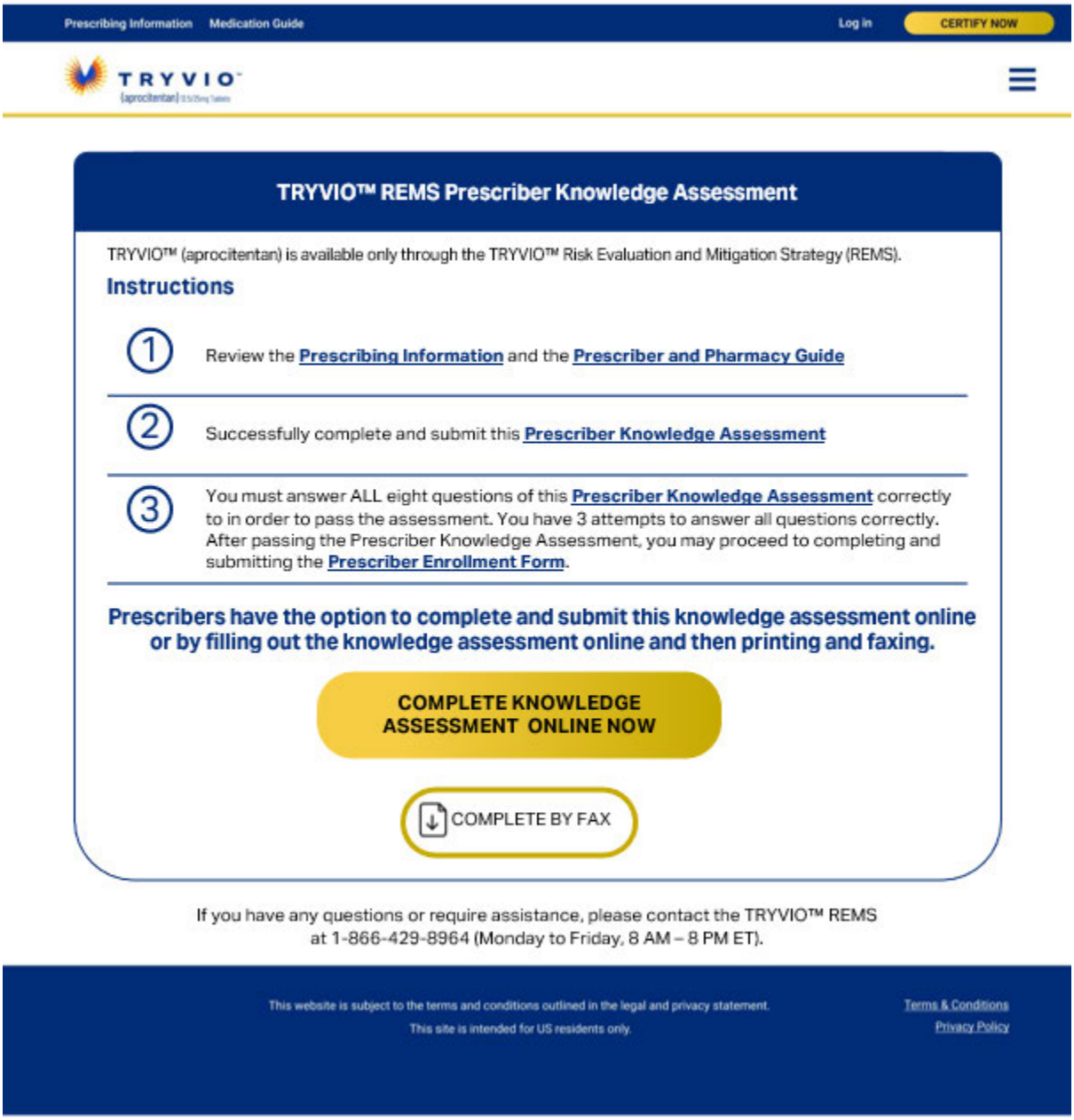
Certify (Identity Verification)

For FDA: User Authorization Screen



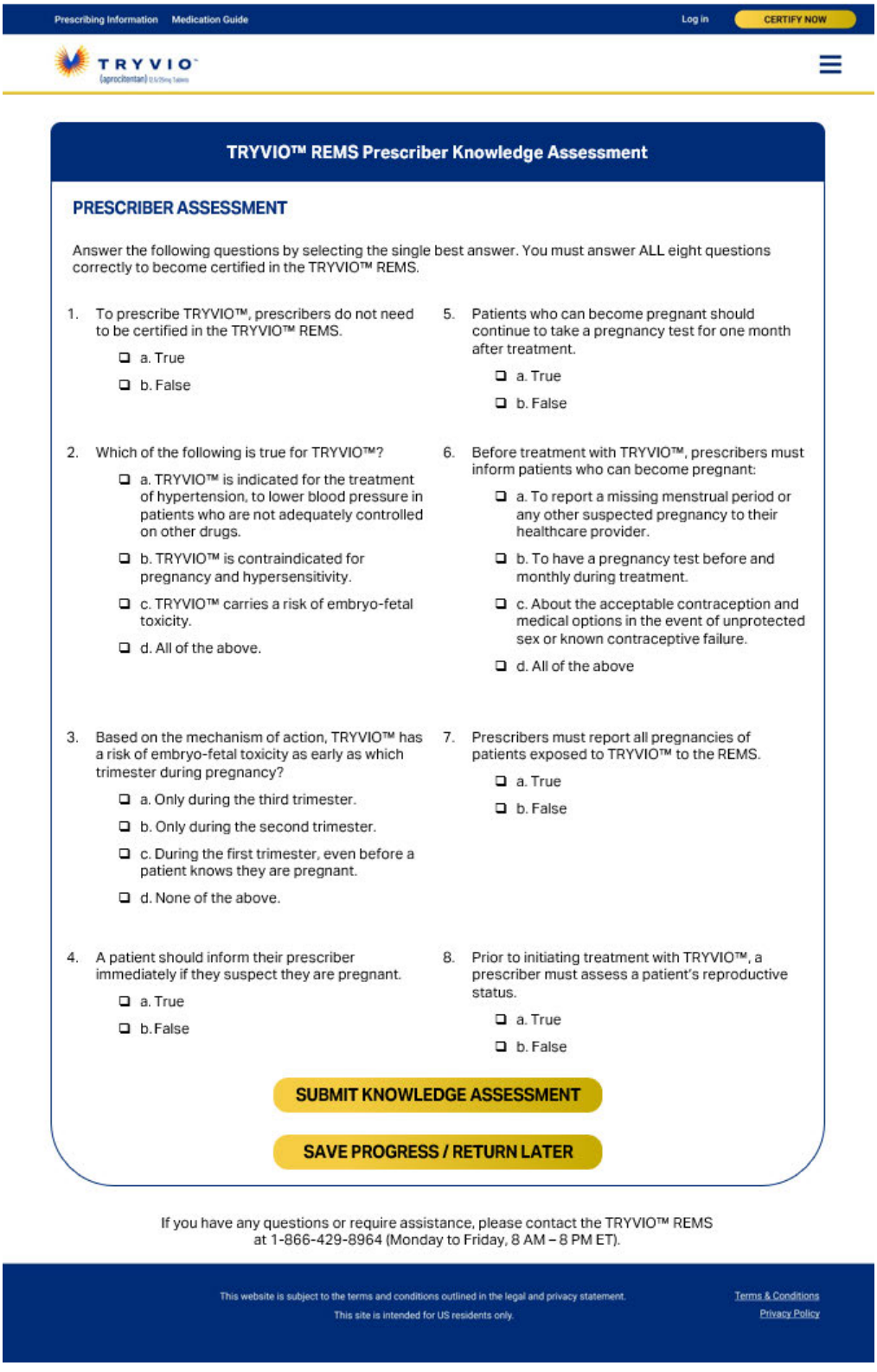
Prescriber Knowledge Assessment (Landing Page)

For FDA:
Public Screen

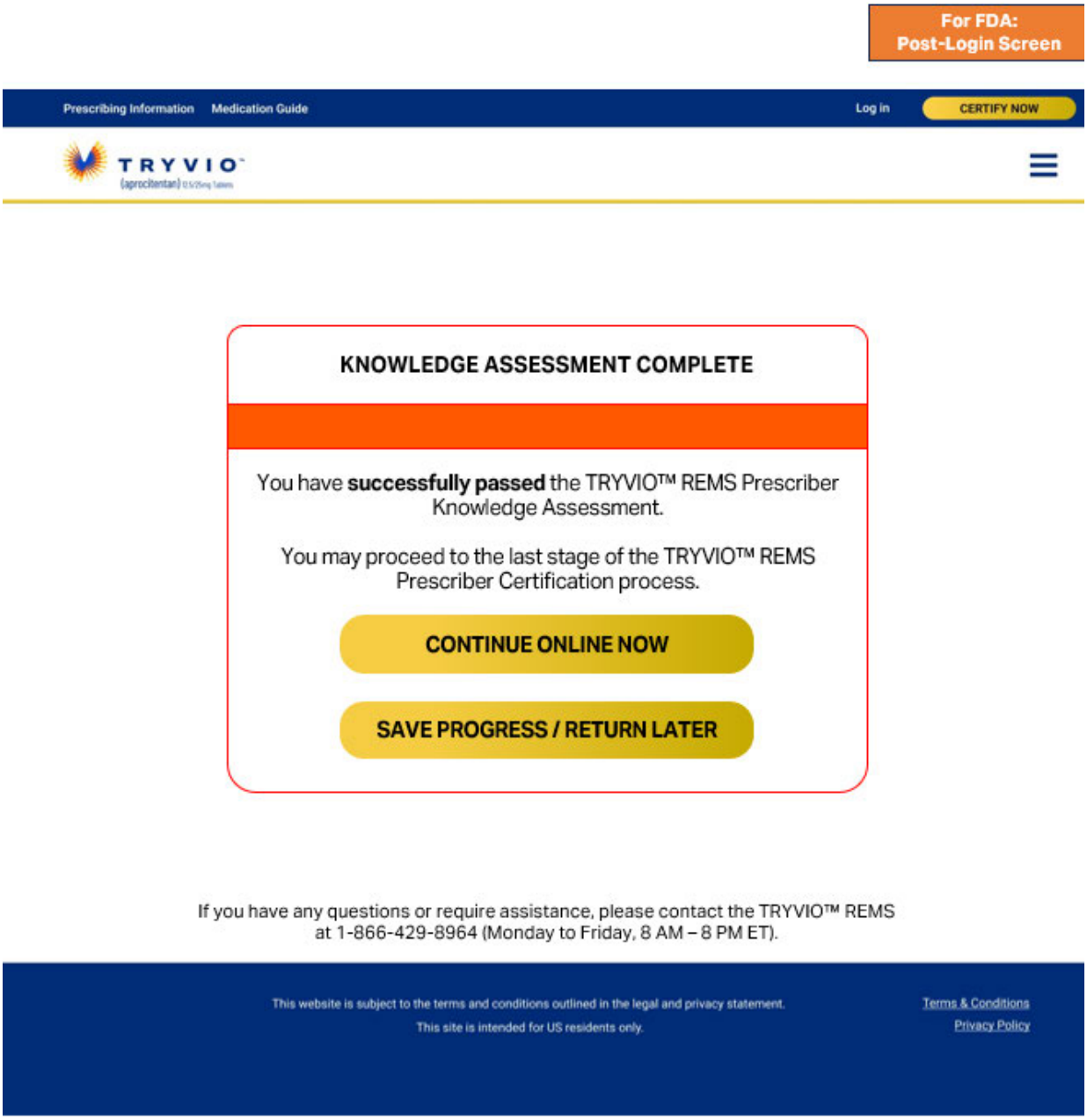


Prescriber Knowledge Assessment (Online Assessment)

For FDA:
Post-Login Screen

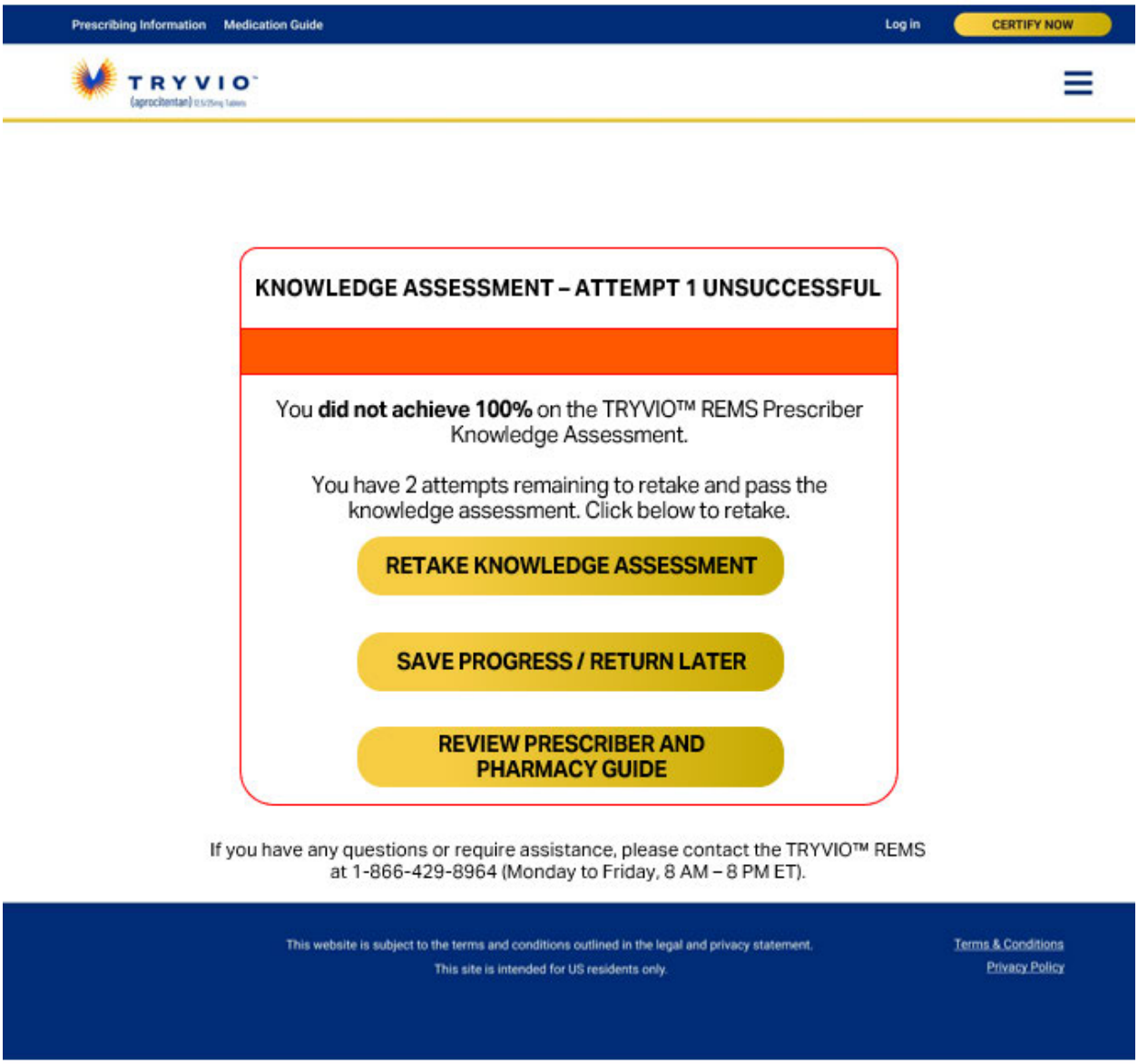


Prescriber Knowledge Assessment (Passed Notification)

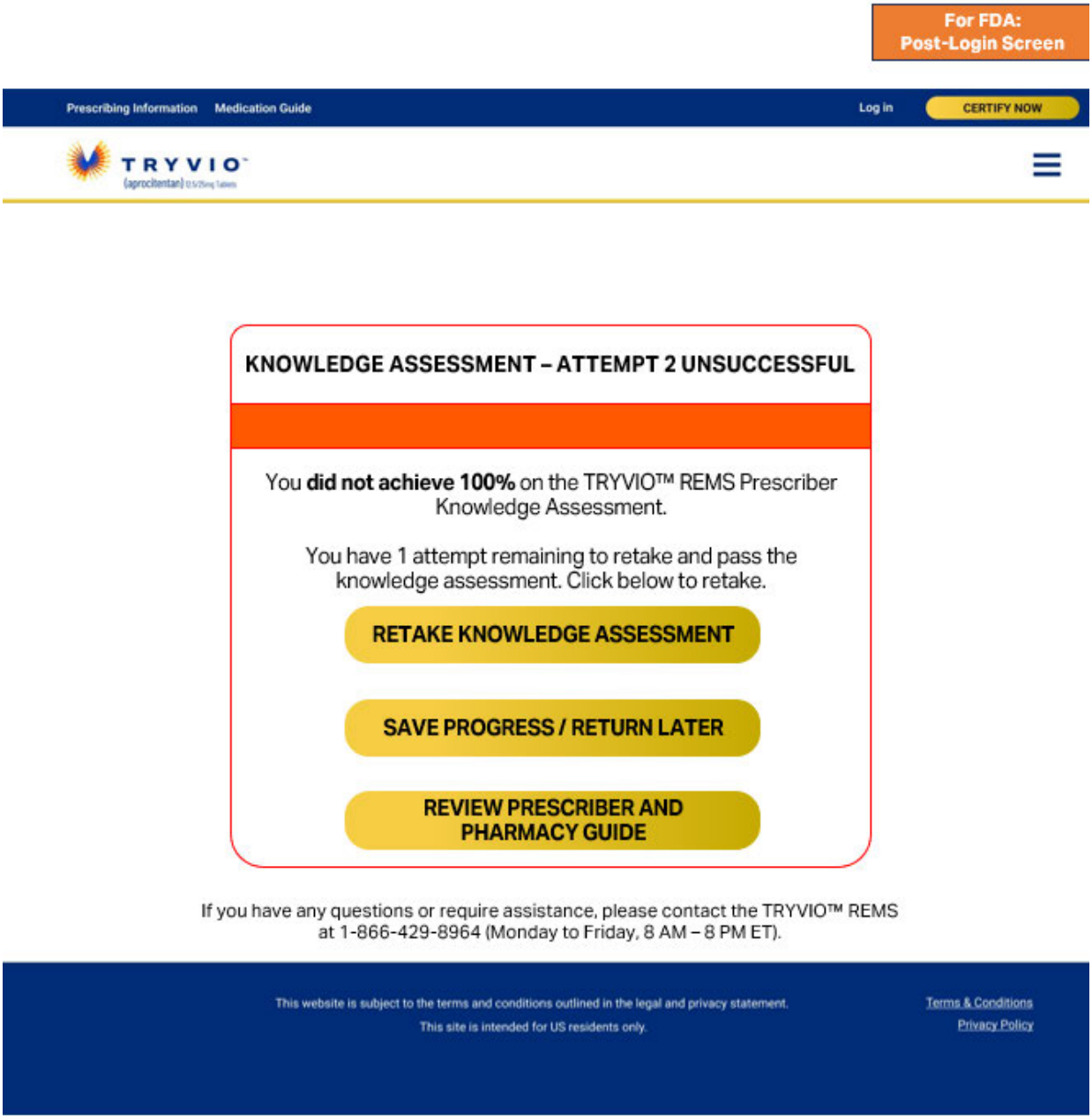


Prescriber Knowledge Assessment (Attempt 1 Failed Notification)

For FDA:
Post-Login Screen



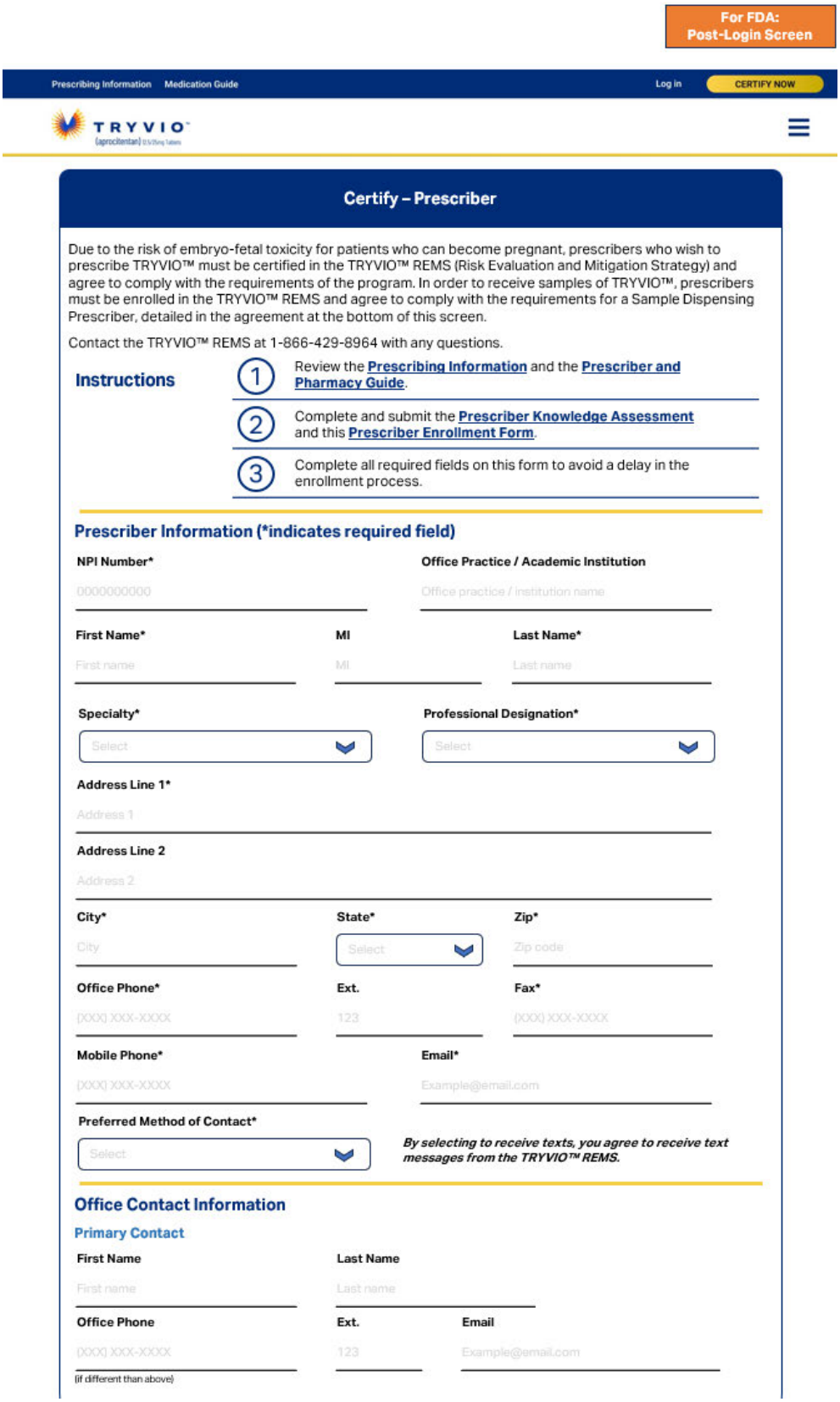
Prescriber Knowledge Assessment (Attempt 2 Failed Notification)

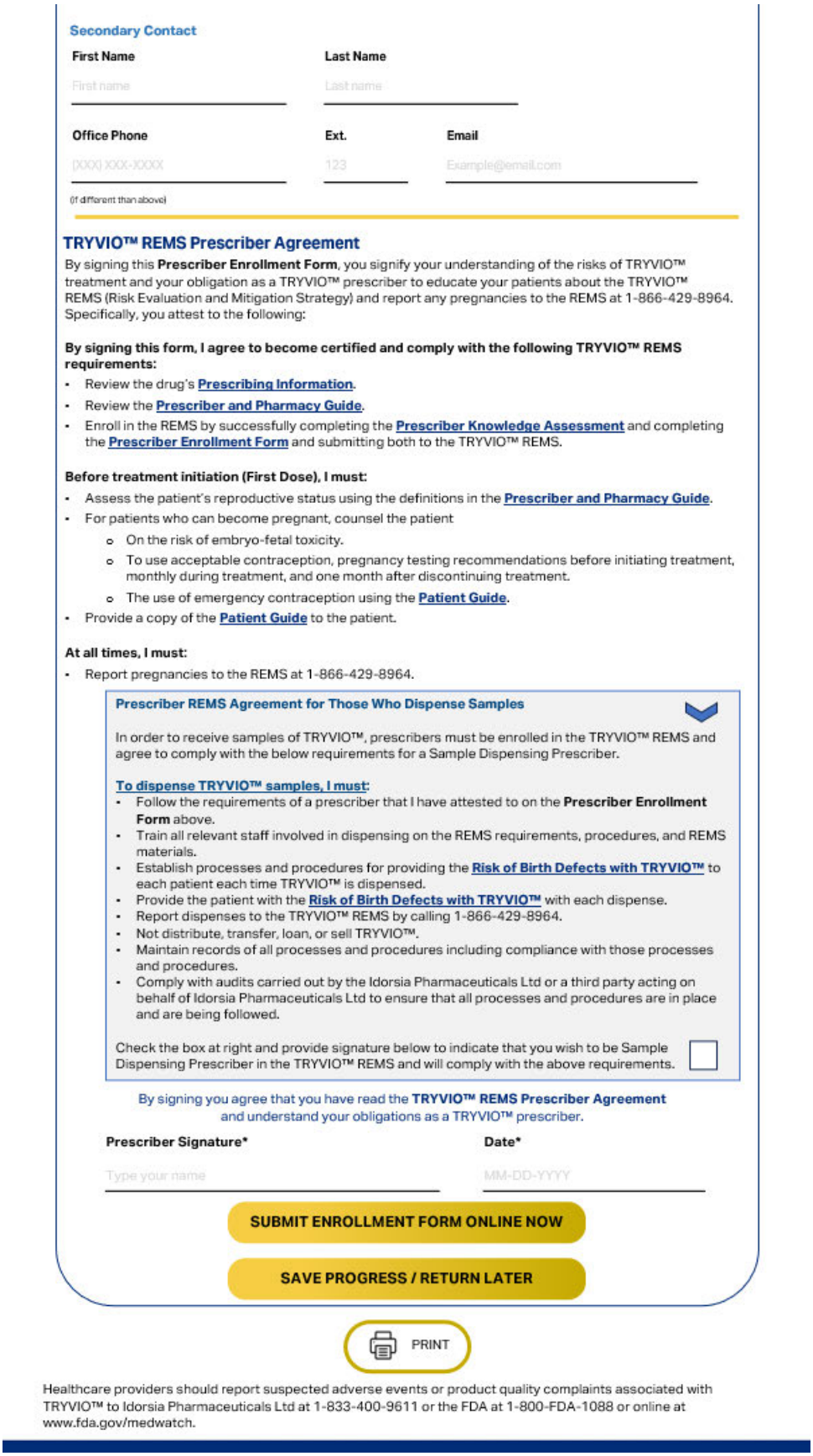


Prescriber Knowledge Assessment (Attempt 3 Failed Notification)

For FDA:
Post-Login Screen

Certify – Prescriber





Secondary Contact

First Name | Last Name

Office Phone | Ext. | Email

(if different than above)

TRYVIO™ REMS Prescriber Agreement

By signing this **Prescriber Enrollment Form**, you signify your understanding of the risks of TRYVIO™ treatment and your obligation as a TRYVIO™ prescriber to educate your patients about the TRYVIO™ REMS (Risk Evaluation and Mitigation Strategy) and report any pregnancies to the REMS at 1-866-429-8964. Specifically, you attest to the following:

By signing this form, I agree to become certified and comply with the following TRYVIO™ REMS requirements:

- Review the drug's **Prescribing Information**.
- Review the **Prescriber and Pharmacy Guide**.
- Enroll in the REMS by successfully completing the **Prescriber Knowledge Assessment** and completing the **Prescriber Enrollment Form** and submitting both to the TRYVIO™ REMS.

Before treatment initiation (First Dose), I must:

- Assess the patient's reproductive status using the definitions in the **Prescriber and Pharmacy Guide**.
- For patients who can become pregnant, counsel the patient
  - On the risk of embryo-fetal toxicity.
  - To use acceptable contraception, pregnancy testing recommendations before initiating treatment, monthly during treatment, and one month after discontinuing treatment.
  - The use of emergency contraception using the **Patient Guide**.
- Provide a copy of the **Patient Guide** to the patient.

At all times, I must:

- Report pregnancies to the REMS at 1-866-429-8964.

Prescriber REMS Agreement for Those Who Dispense Samples

In order to receive samples of TRYVIO™, prescribers must be enrolled in the TRYVIO™ REMS and agree to comply with the below requirements for a Sample Dispensing Prescriber.

To dispense TRYVIO™ samples, I must:

- Follow the requirements of a prescriber that I have attested to on the **Prescriber Enrollment Form** above.
- Train all relevant staff involved in dispensing on the REMS requirements, procedures, and REMS materials.
- Establish processes and procedures for providing the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed.
- Provide the patient with the **Risk of Birth Defects with TRYVIO™** with each dispense.
- Report dispenses to the TRYVIO™ REMS by calling 1-866-429-8964.
- Not distribute, transfer, loan, or sell TRYVIO™.
- Maintain records of all processes and procedures including compliance with those processes and procedures.
- Comply with audits carried out by the Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

Check the box at right and provide signature below to indicate that you wish to be Sample Dispensing Prescriber in the TRYVIO™ REMS and will comply with the above requirements. ☐

By signing you agree that you have read the **TRYVIO™ REMS Prescriber Agreement** and understand your obligations as a TRYVIO™ prescriber.

Prescriber Signature* | **Date***

Type your name | MM-DD-YYYY

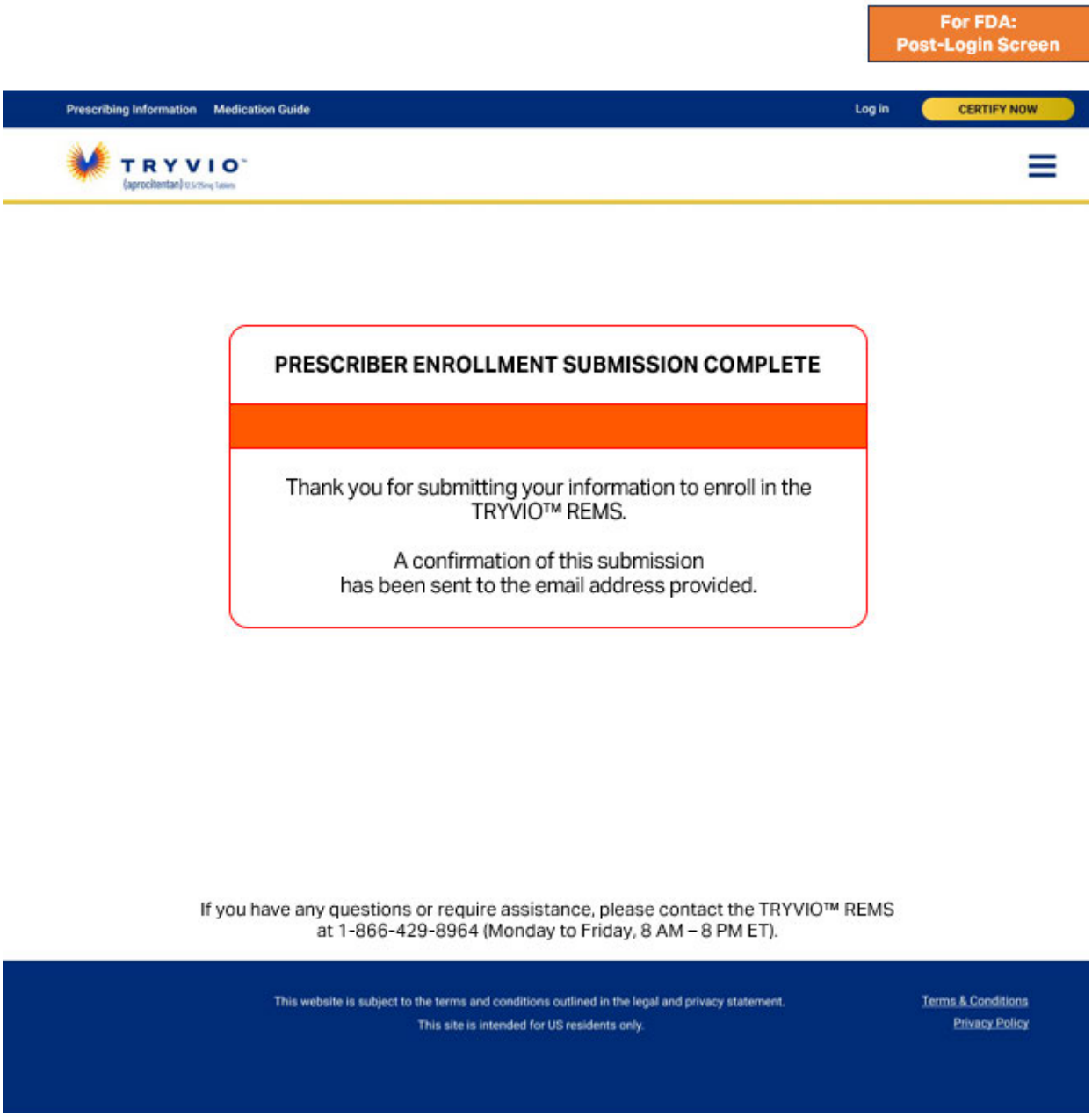
SUBMIT ENROLLMENT FORM ONLINE NOW

SAVE PROGRESS / RETURN LATER

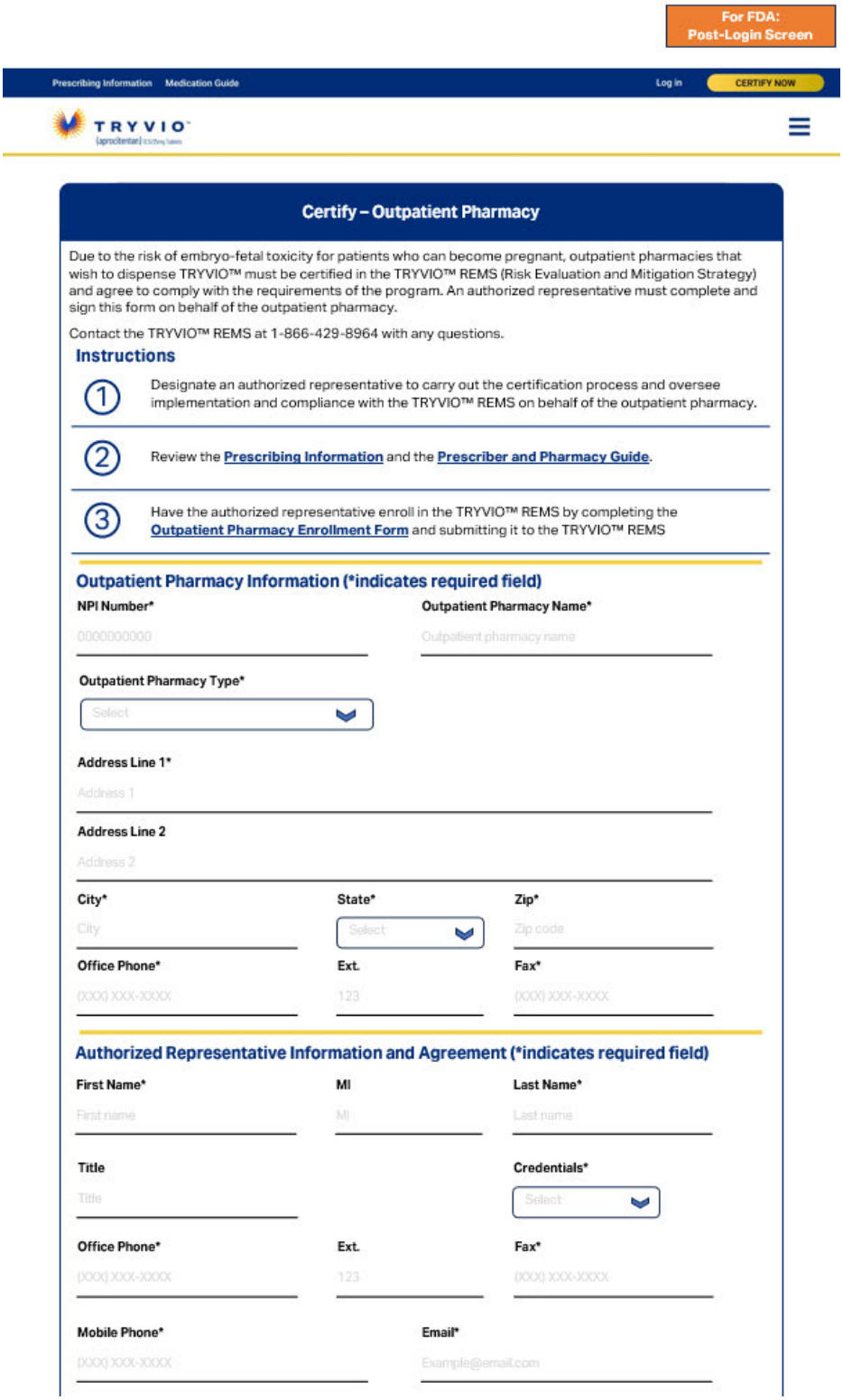
PRINT

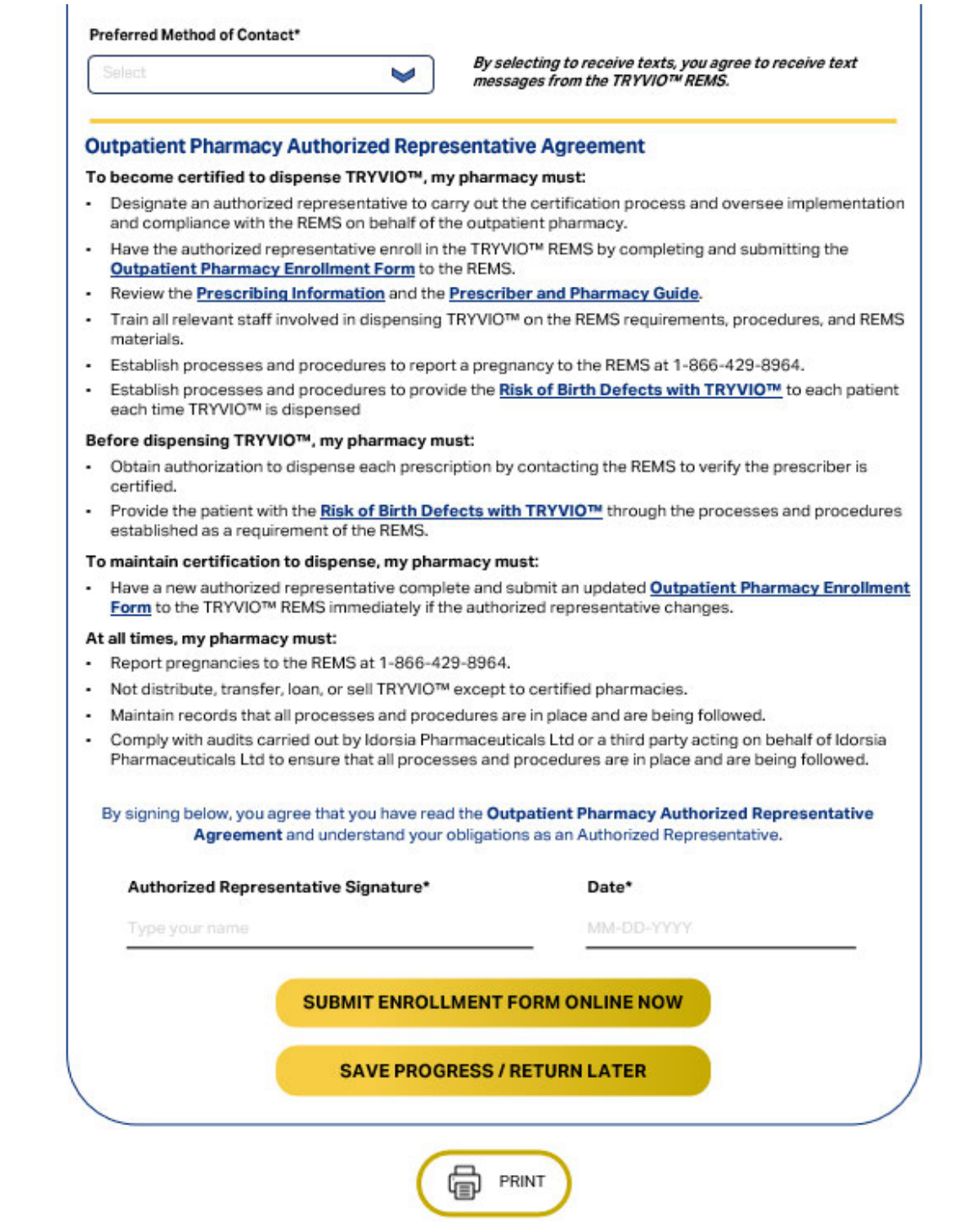
Healthcare providers should report suspected adverse events or product quality complaints associated with TRYVIO™ to Idorsia Pharmaceuticals Ltd at 1-833-400-9611 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Certify – Prescriber (Submission Received)



Certify – Outpatient Pharmacy





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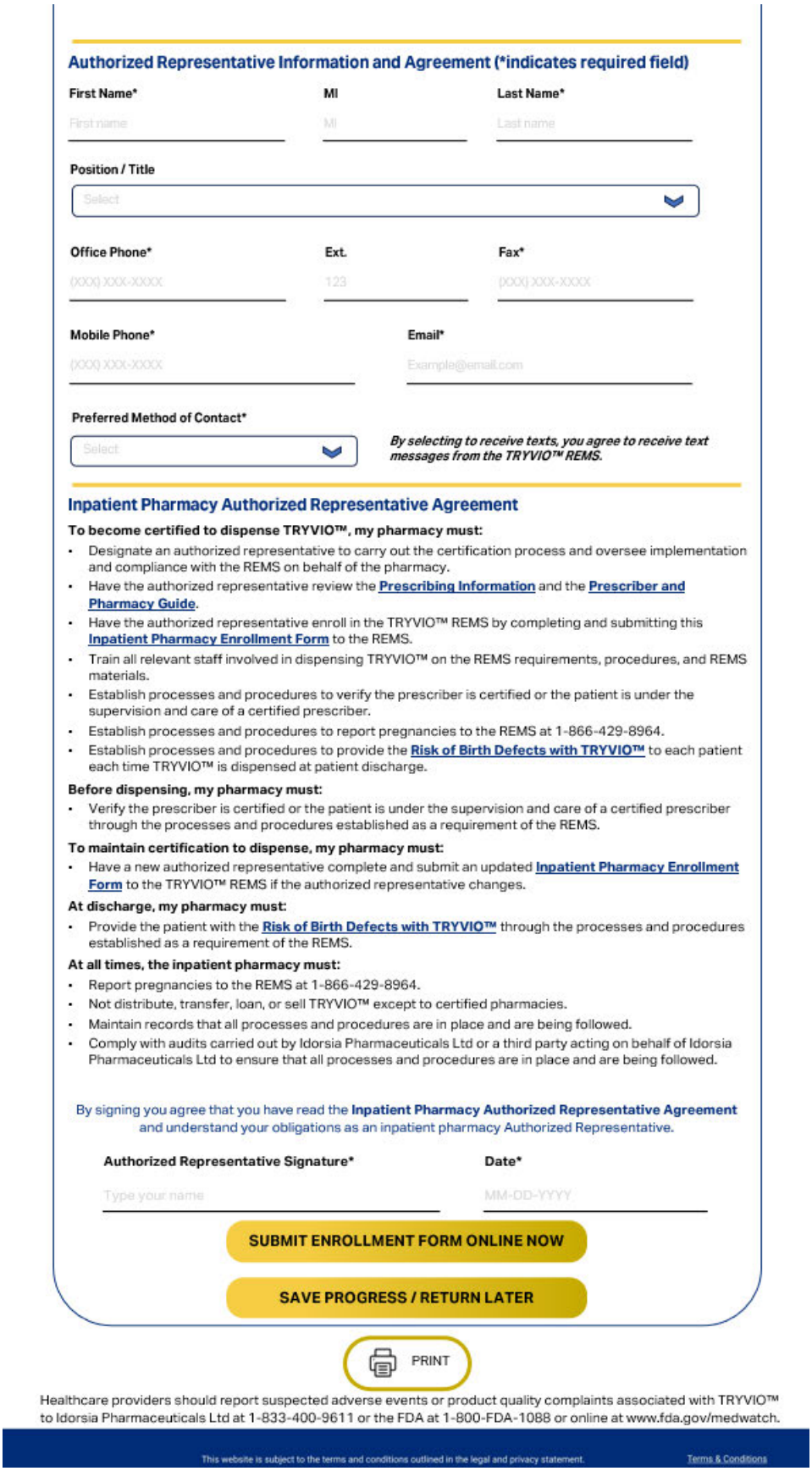
Certify – Outpatient Pharmacy (Submission Received)

For FDA:
Post-Login Screen

Certify – Inpatient Pharmacy



Authorized Representative Information and Agreement (*indicates required field)

First Name* | MI | Last Name*

First name | MI | Last name

Position / Title

Select

Office Phone* | Ext. | Fax*

(XXX) XXX-XXXX | 123 | (XXX) XXX-XXXX

Mobile Phone* | Email*

(XXX) XXX-XXXX | Example@email.com

Preferred Method of Contact*

Select

By selecting to receive texts, you agree to receive text messages from the TRYVIO™ REMS.

Inpatient Pharmacy Authorized Representative Agreement

To become certified to dispense TRYVIO™, my pharmacy must:

- Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy.
- Have the authorized representative review the **Prescribing Information** and the **Prescriber and Pharmacy Guide**.
- Have the authorized representative enroll in the TRYVIO™ REMS by completing and submitting this **Inpatient Pharmacy Enrollment Form** to the REMS.
- Train all relevant staff involved in dispensing TRYVIO™ on the REMS requirements, procedures, and REMS materials.
- Establish processes and procedures to verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber.
- Establish processes and procedures to report pregnancies to the REMS at 1-866-429-8964.
- Establish processes and procedures to provide the **Risk of Birth Defects with TRYVIO™** to each patient each time TRYVIO™ is dispensed at patient discharge.

Before dispensing, my pharmacy must:

- Verify the prescriber is certified or the patient is under the supervision and care of a certified prescriber through the processes and procedures established as a requirement of the REMS.

To maintain certification to dispense, my pharmacy must:

- Have a new authorized representative complete and submit an updated **Inpatient Pharmacy Enrollment Form** to the TRYVIO™ REMS if the authorized representative changes.

At discharge, my pharmacy must:

- Provide the patient with the **Risk of Birth Defects with TRYVIO™** through the processes and procedures established as a requirement of the REMS.

At all times, the inpatient pharmacy must:

- Report pregnancies to the REMS at 1-866-429-8964.
- Not distribute, transfer, loan, or sell TRYVIO™ except to certified pharmacies.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by Idorsia Pharmaceuticals Ltd or a third party acting on behalf of Idorsia Pharmaceuticals Ltd to ensure that all processes and procedures are in place and are being followed.

By signing you agree that you have read the **Inpatient Pharmacy Authorized Representative Agreement** and understand your obligations as an inpatient pharmacy Authorized Representative.

Authorized Representative Signature* | **Date***

Type your name | MM-DD-YYYY

SUBMIT ENROLLMENT FORM ONLINE NOW

SAVE PROGRESS / RETURN LATER

PRINT

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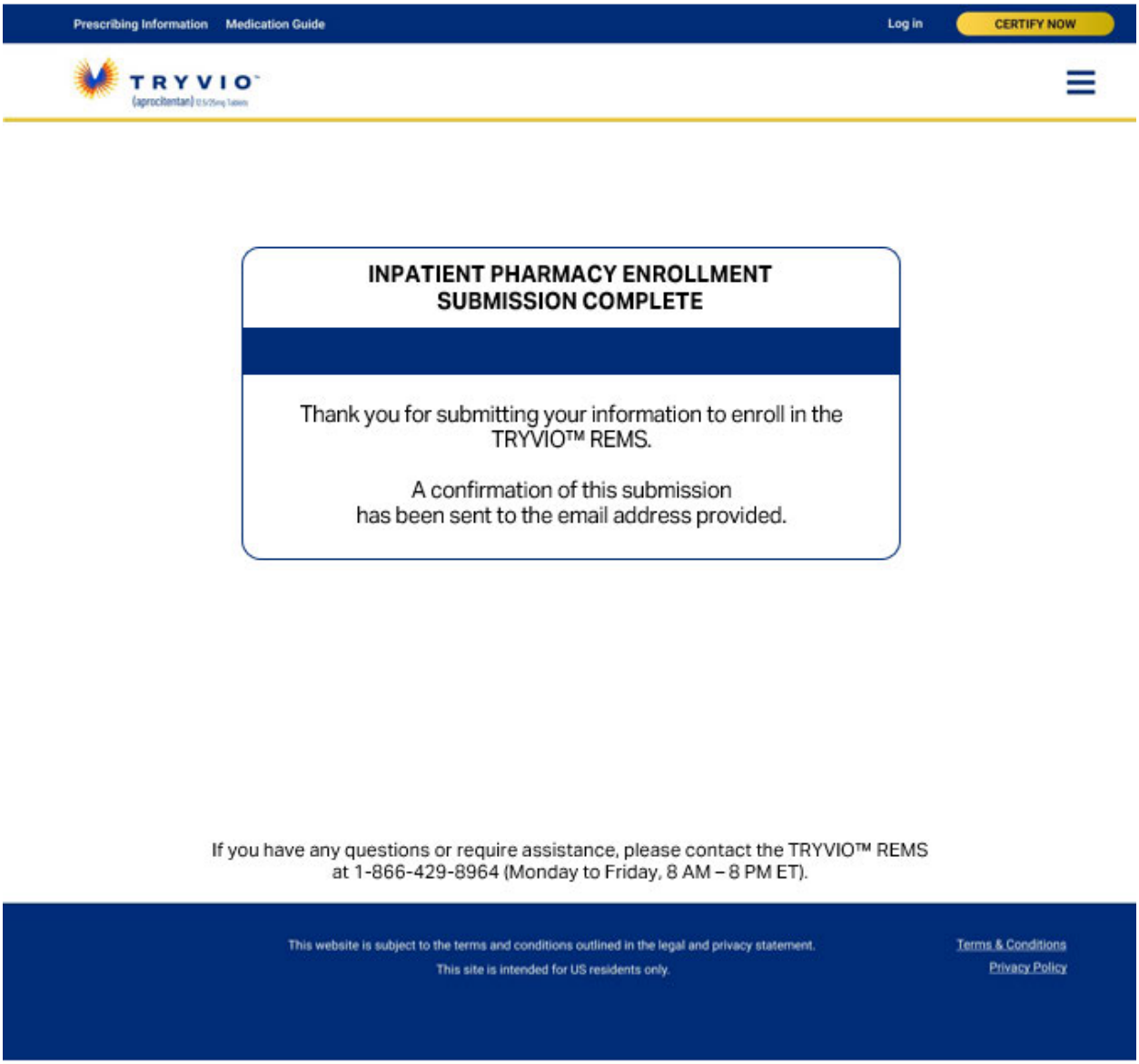
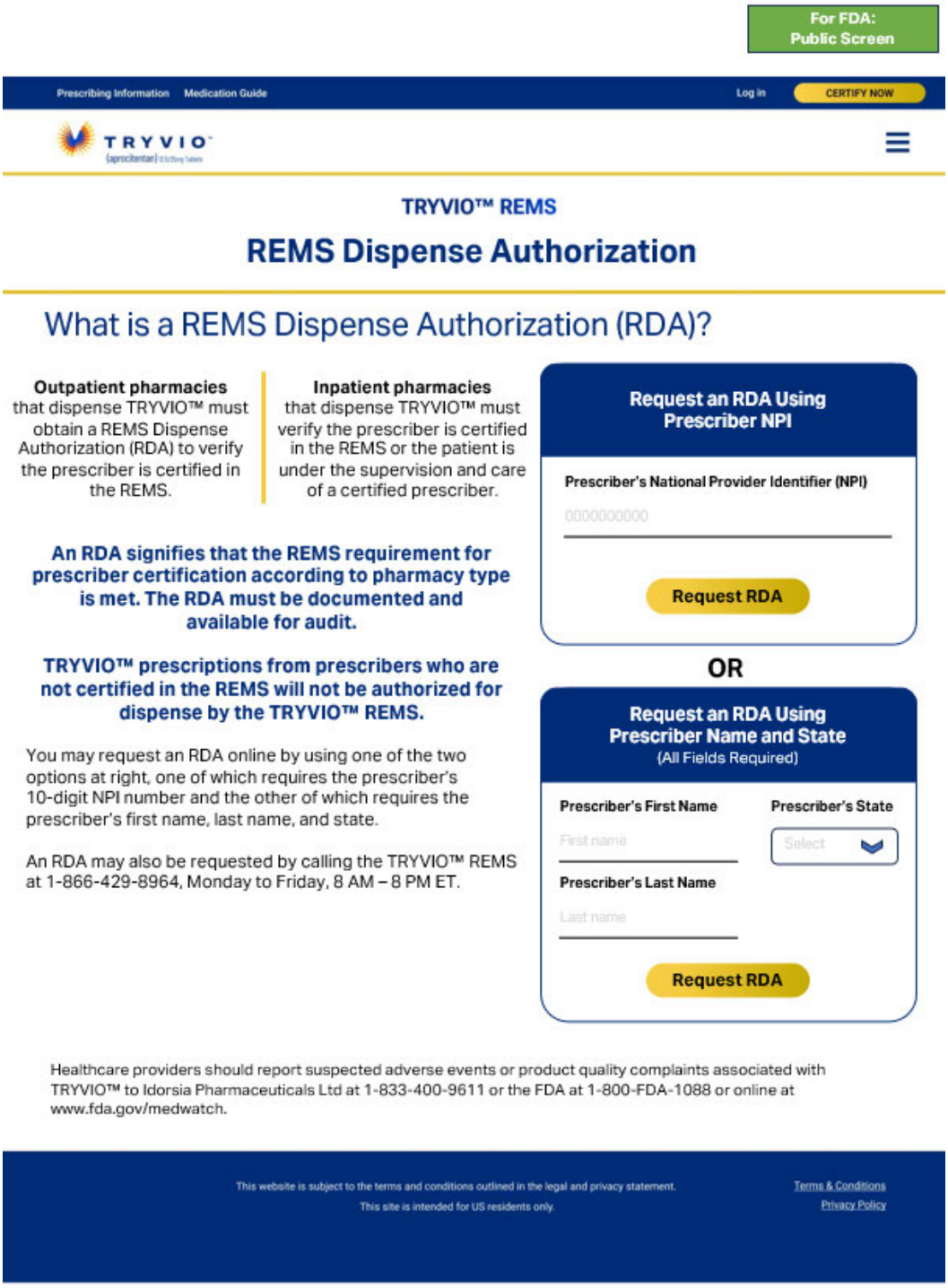
Certify – Inpatient Pharmacy (Submission Received)

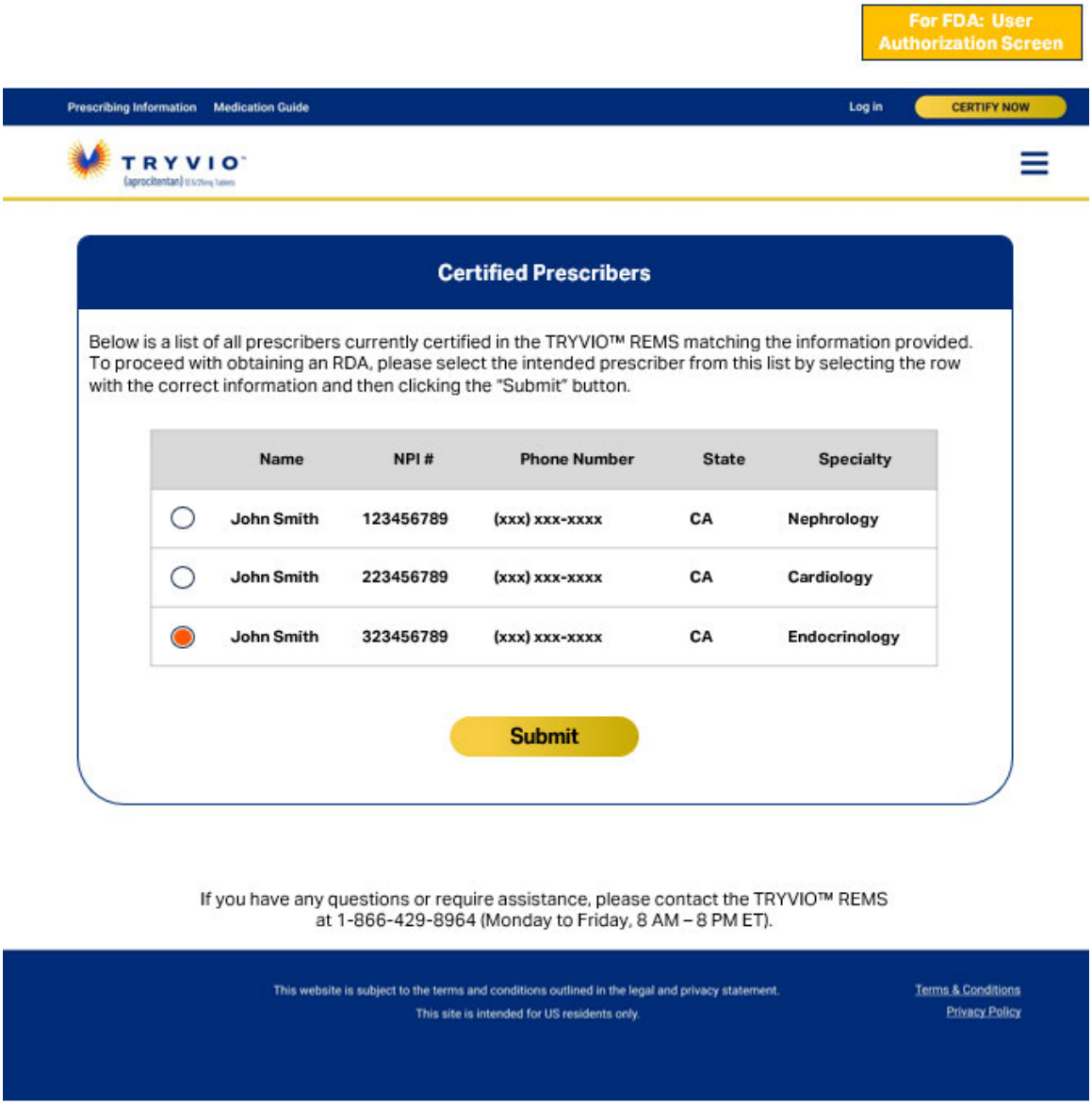
For FDA:
Post-Login Screen



REMS Dispense Authorization (Landing Page)



REMS Dispense Authorization (List of Matching Certified Prescribers)

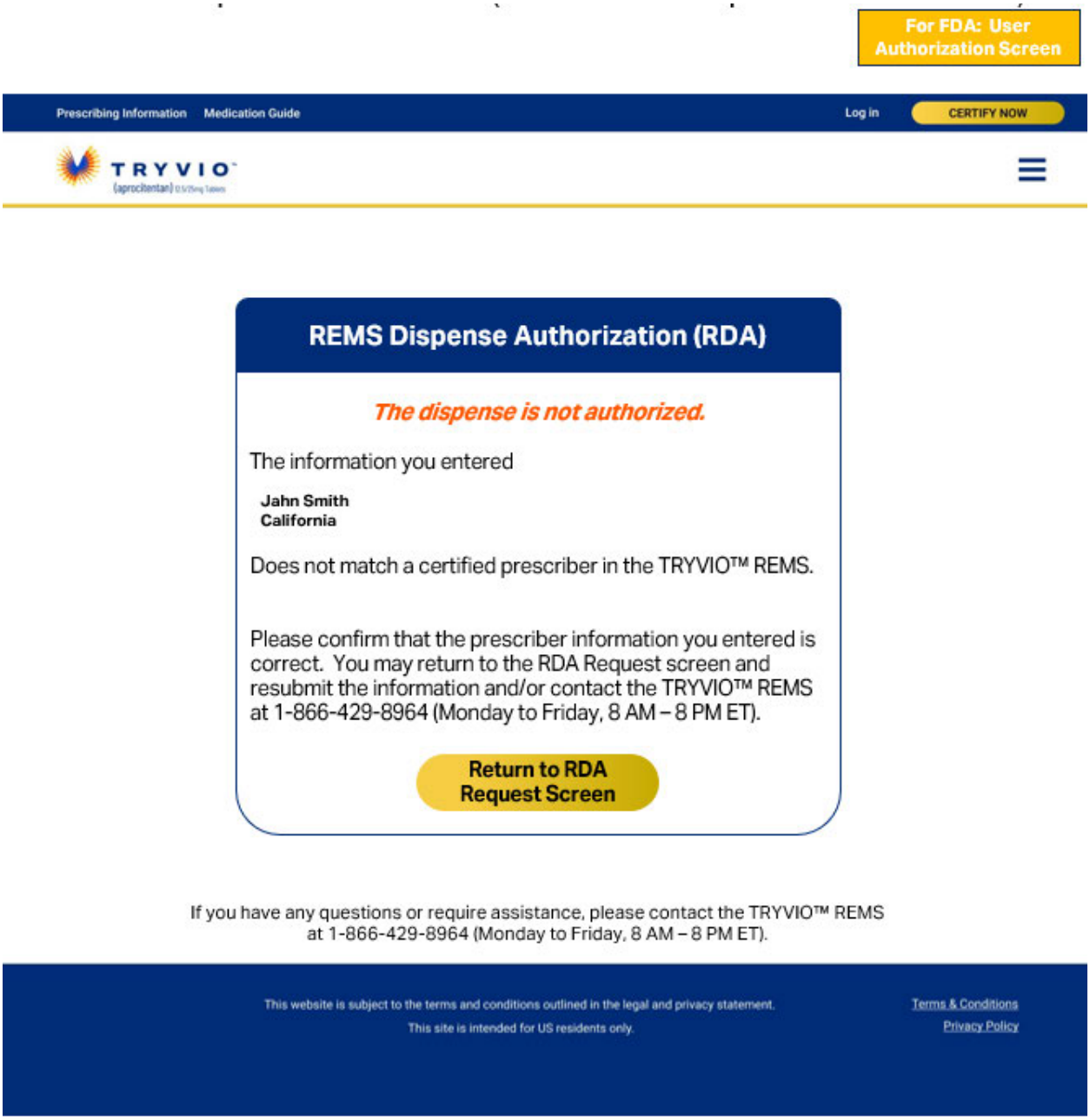


Note for FDA: From either of the "Request an RDA" options on REMS Dispense Authorization (Landing Page), users would be shown a list of certified prescriber(s) so that they can confirm that they have the correct prescriber. If they searched using the name and state, there is an opportunity to use phone and specialty to confirm the correct user; if they searched for NPI, there is an opportunity to confirm that the name, phone, state, and specialty match the correct prescriber.

REMS Dispense Authorization (RDA Code Generated)

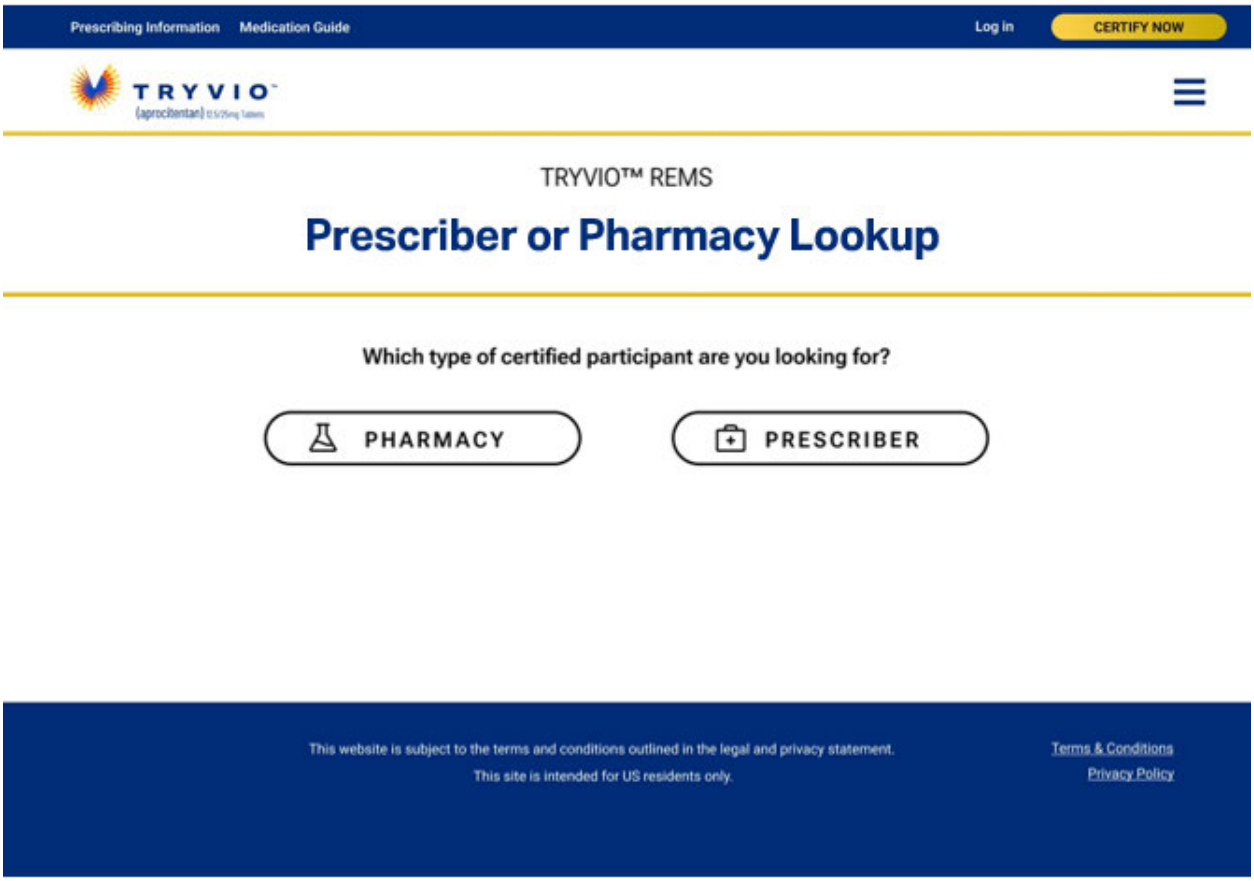
For FDA: User Authorization Screen

REMS Dispense Authorization (No Matches / Dispense Not Authorized)

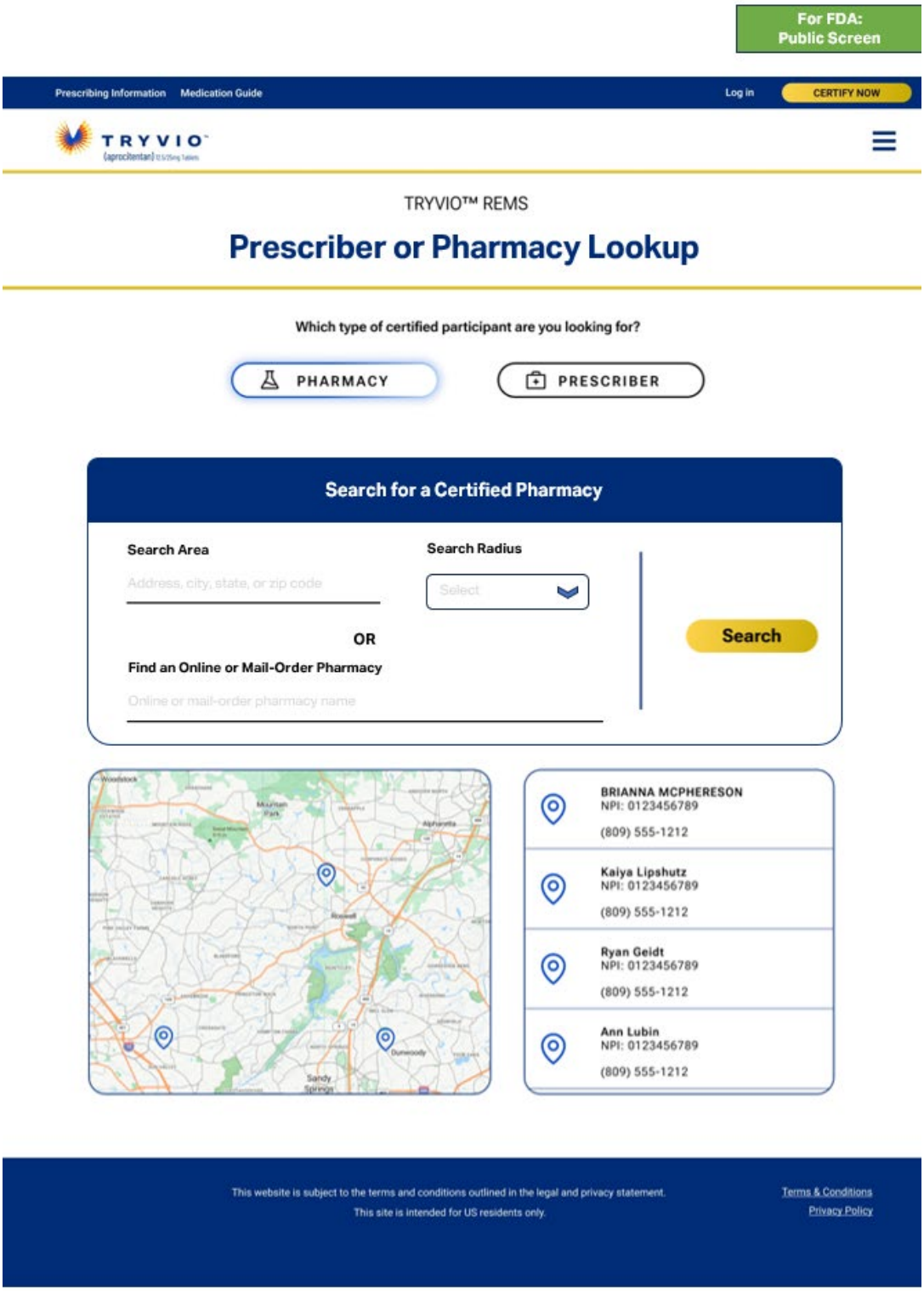


Lookup

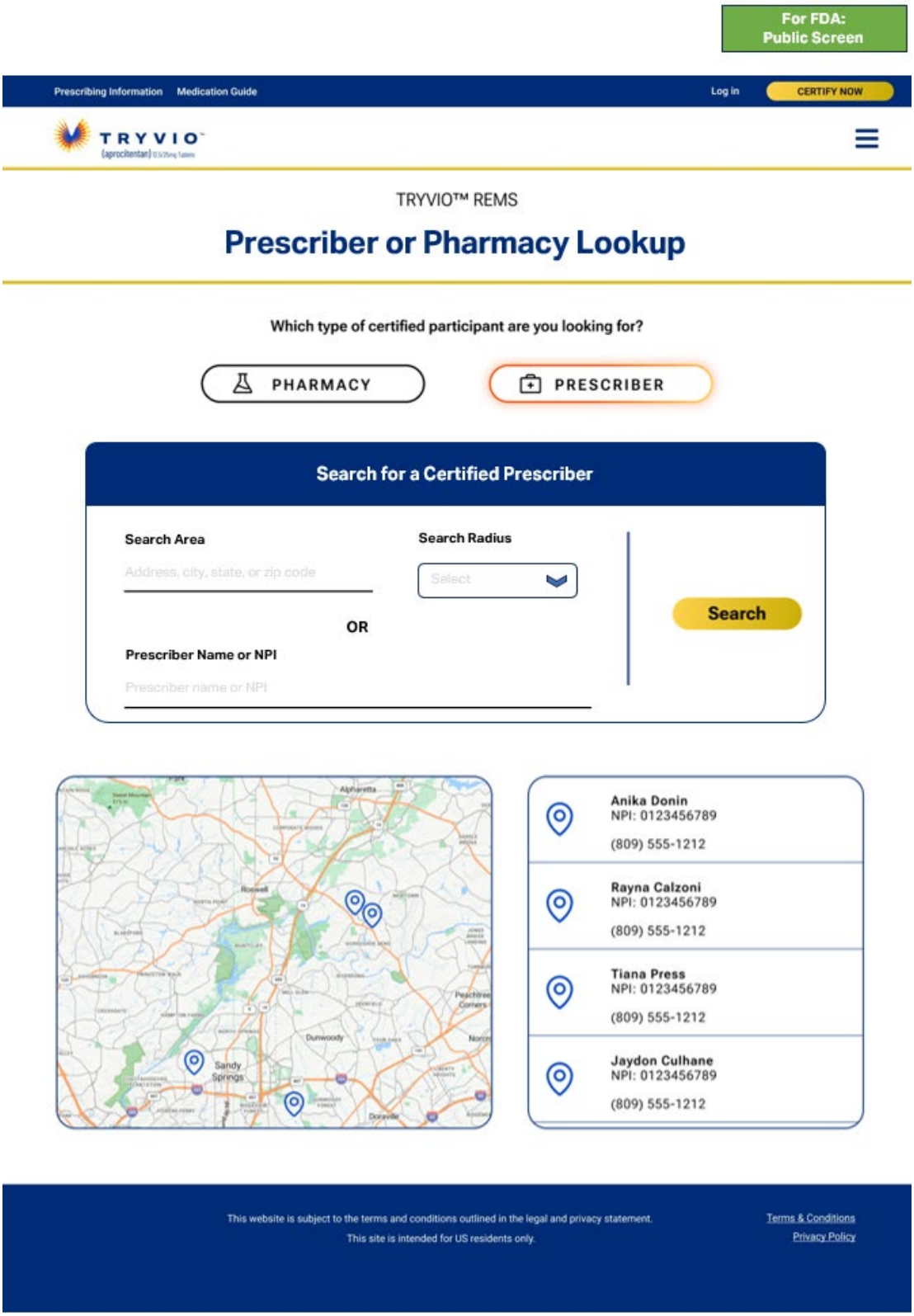
For FDA:
Public Screen



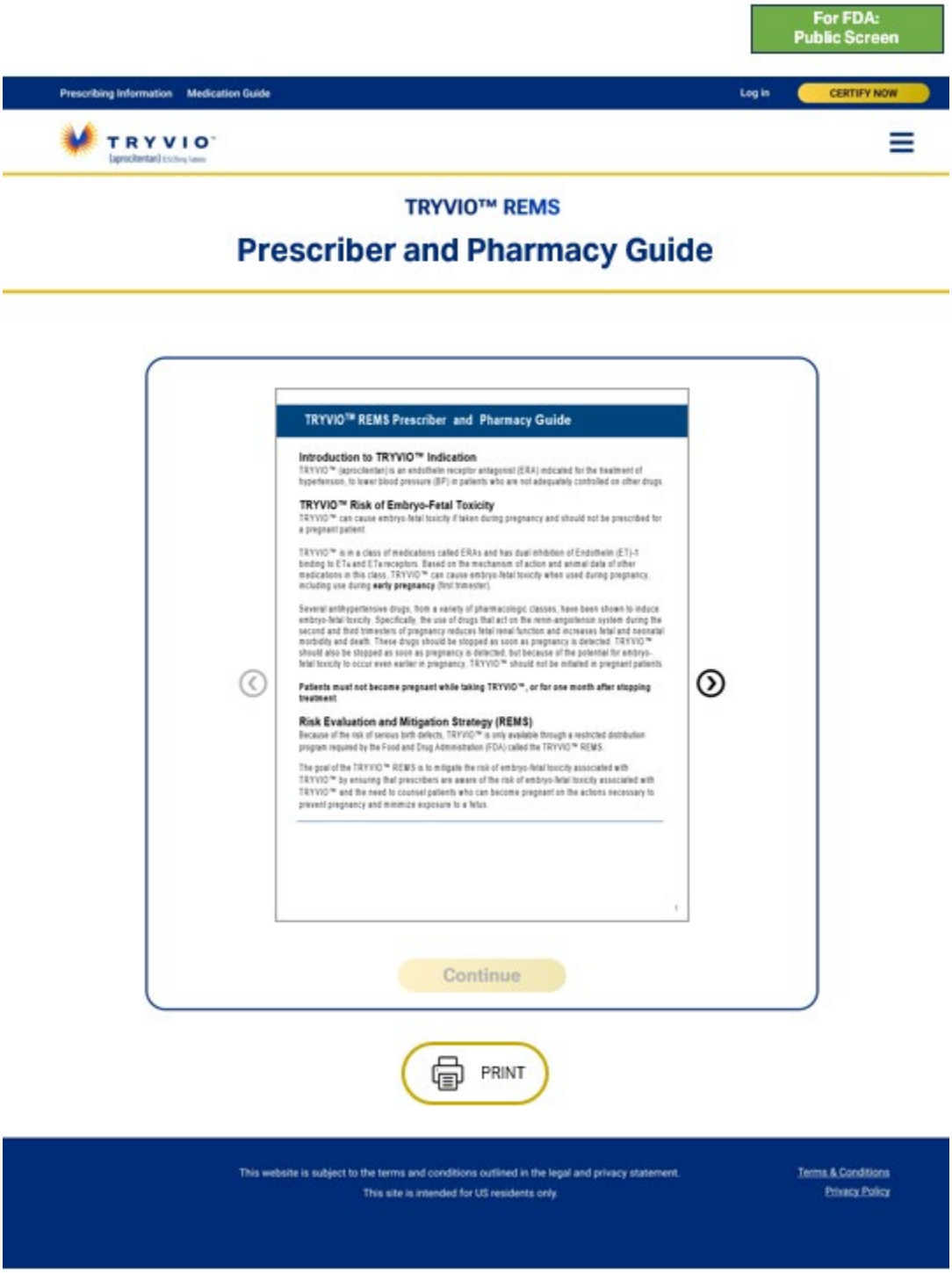
Lookup – Pharmacy



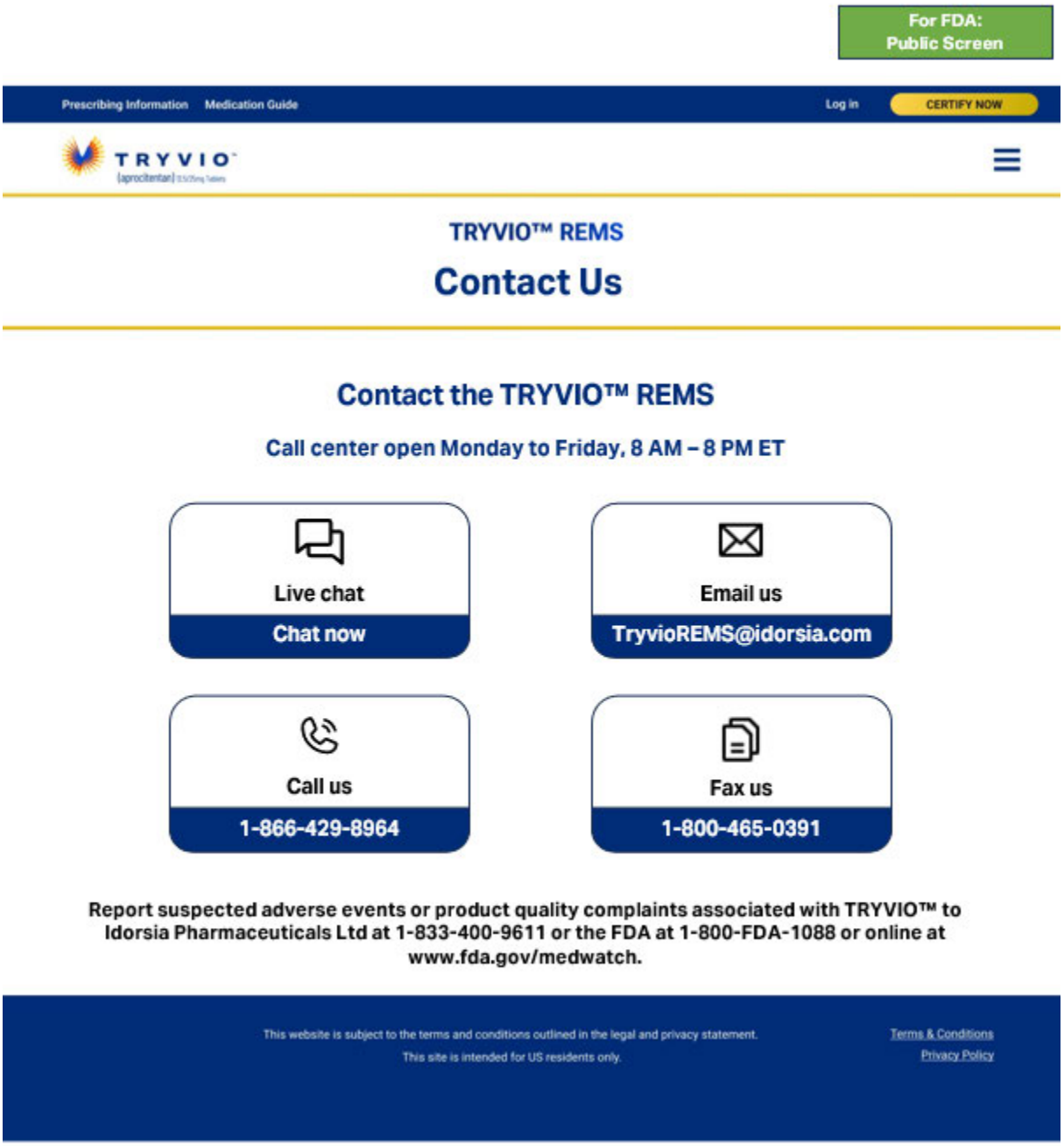
Lookup – Prescriber



Prescriber and Pharmacy Guide



Contact


For FDA:
Public Screen
Prescribing Information
Medication Guide
Log in
CERTIFY NOW
TRYVIO
(aprocitentan)
TRYVIO™ REMS
Contact Us
Contact the TRYVIO™ REMS
Call center open Monday to Friday, 8 AM – 8 PM ET
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Fax us
1-800-465-0391
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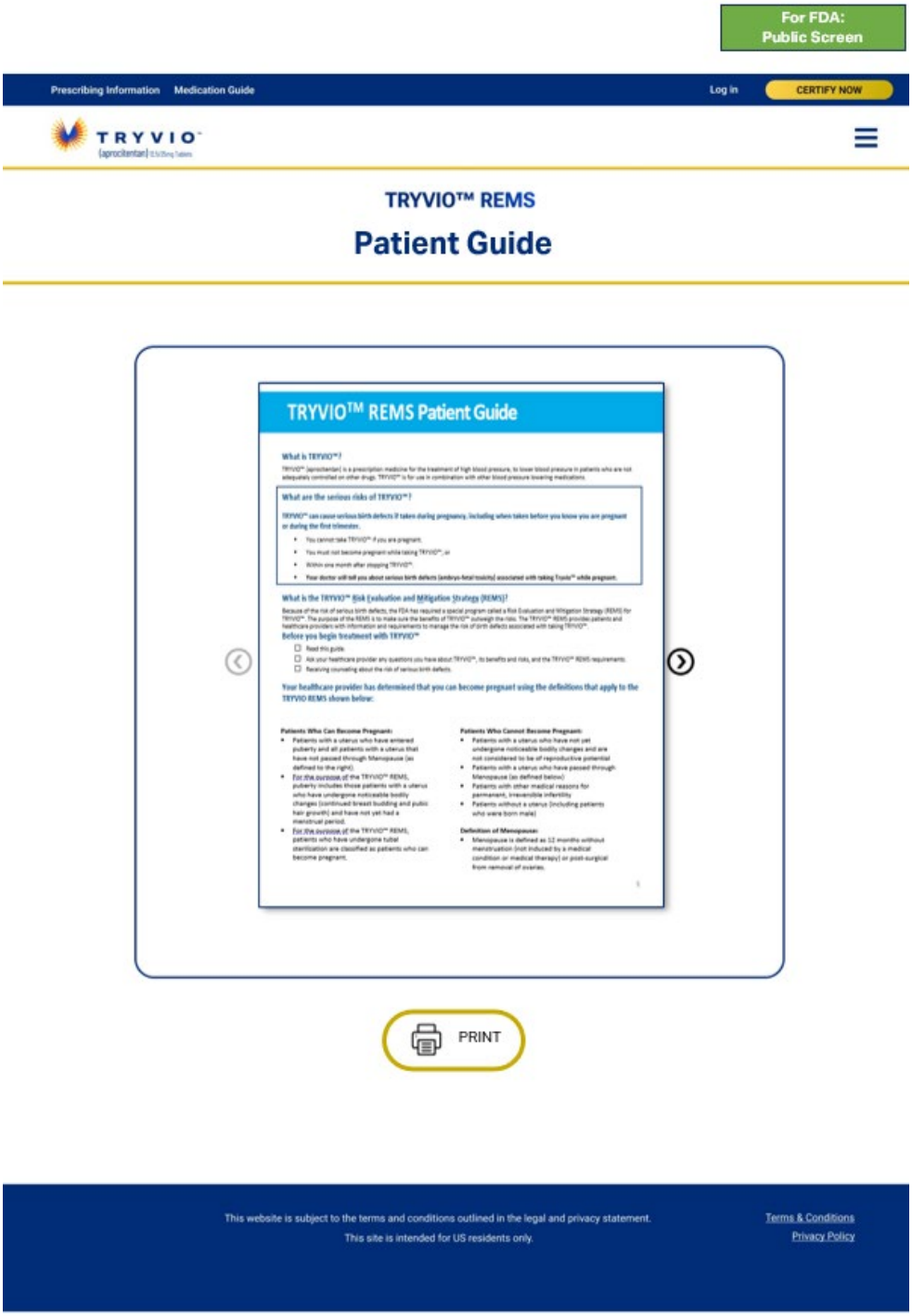
Privacy Policy

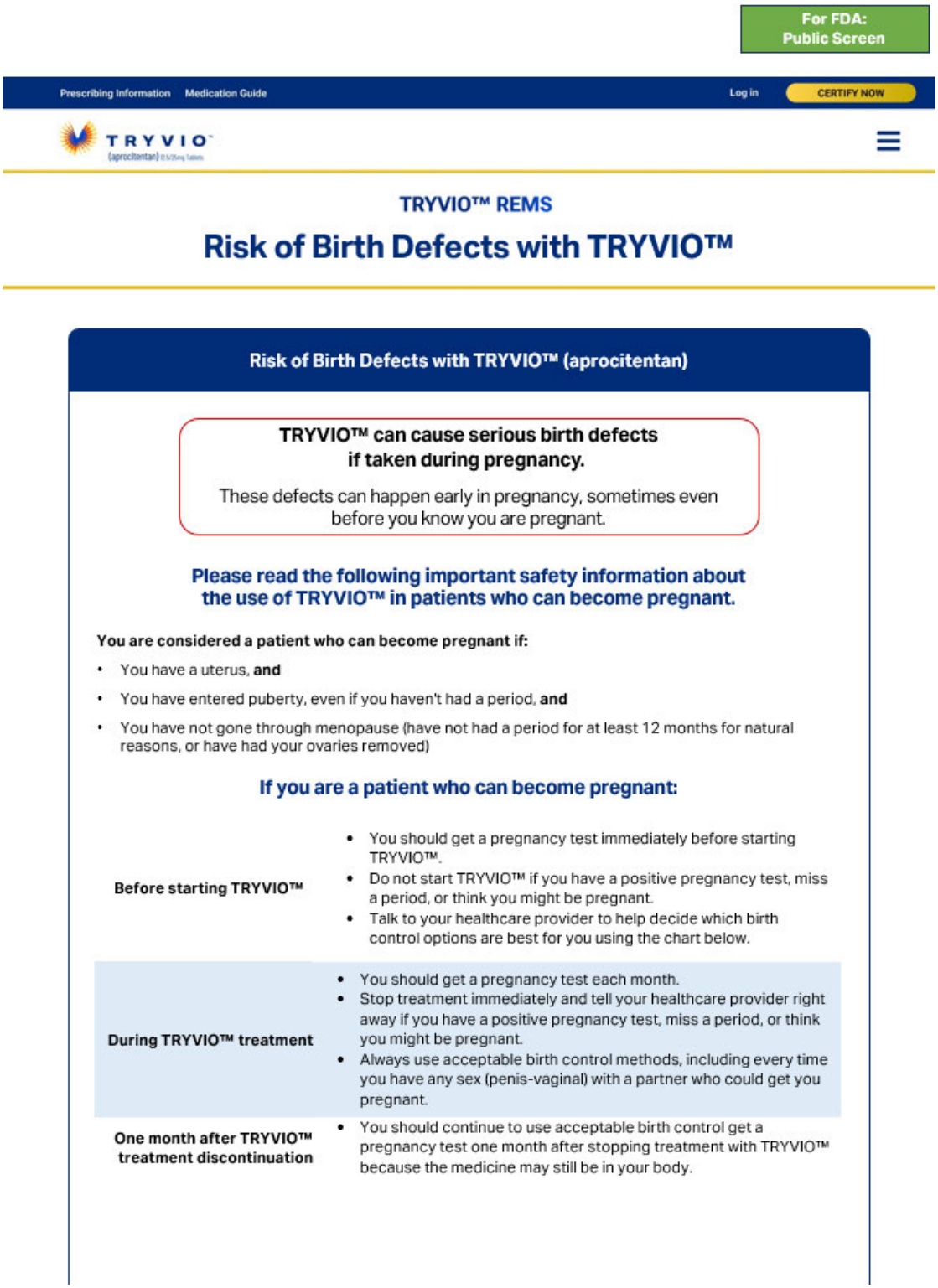
Resources

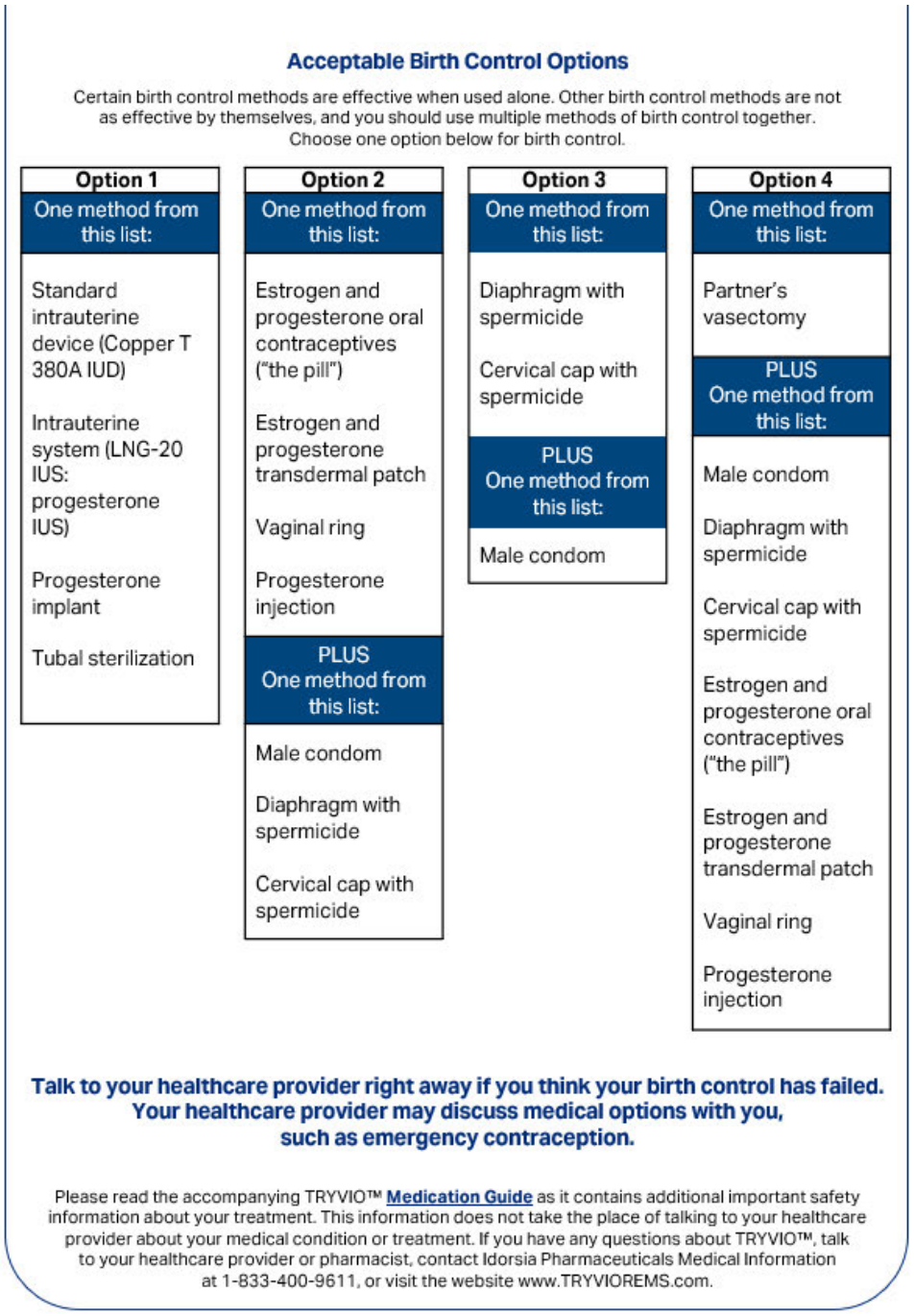
For FDA:
Public Screen

Patient Guide



Risk of Birth Defects with TRYVIO™





Acceptable Birth Control Options

Certain birth control methods are effective when used alone. Other birth control methods are not as effective by themselves, and you should use multiple methods of birth control together. Choose one option below for birth control.

Option 1	Option 2	Option 3	Option 4
One method from this list:	One method from this list:	One method from this list:	One method from this list:
Standard intrauterine device (Copper T 380A IUD)	Estrogen and progesterone oral contraceptives ("the pill")	Diaphragm with spermicide	Partner's vasectomy
Intrauterine system (LNG-20 IUS: progesterone IUS)	Estrogen and progesterone transdermal patch	Cervical cap with spermicide	PLUS One method from this list:
Progesterone implant	Vaginal ring	PLUS One method from this list:	Male condom
Tubal sterilization	Progesterone injection	Male condom	Diaphragm with spermicide
	PLUS One method from this list:		Cervical cap with spermicide
	Male condom		Estrogen and progesterone oral contraceptives ("the pill")
	Diaphragm with spermicide		Estrogen and progesterone transdermal patch
	Cervical cap with spermicide		Vaginal ring
			Progesterone injection

Talk to your healthcare provider right away if you think your birth control has failed. Your healthcare provider may discuss medical options with you, such as emergency contraception.

Please read the accompanying TRYVIO™ **Medication Guide** as it contains additional important safety information about your treatment. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about TRYVIO™, talk to your healthcare provider or pharmacist, contact Idorsia Pharmaceuticals Medical Information at 1-833-400-9611, or visit the website www.TRYVIOREMS.com.

PRINT

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LISA B YANOFF
03/22/2024 10:16:29 AM