

PS-AMBRISENTAN RISK EVALUATION AND MITIGATION STRATEGY (REMS)

Please visit www.PSAmbrisentanREMS.com or call 1-888-301-0333 9am to 5pm ET, Monday - Friday

Pharmacy Guide for the PS-Ambrisentan REMS

PS-Ambrisentan
— REMS —

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PS-Ambrisentan REMS

Indication

Ambrisentan is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):

- To improve exercise ability and delay clinical worsening.

Studies establishing effectiveness included trials predominantly in patients with WHO Functional Class II–III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%).

Risk of embryo-fetal toxicity

Ambrisentan may cause fetal harm when administered to a pregnant female and is contraindicated during pregnancy. There are limited data on ambrisentan use in pregnant females; the possibility of serious birth defects in humans cannot be excluded.

Pregnancy must be excluded prior to the initiation of ambrisentan treatment, monthly thereafter, and for one month after stopping treatment.

PS-Ambrisentan REMS

Because of the risk of serious birth defects, ambrisentan is only available to females through a restricted distribution program under an FDA-required REMS. The PS-Ambrisentan REMS helps ensure the benefits of ambrisentan outweigh the risk of embryo-fetal toxicity. The goal of the PS-Ambrisentan REMS is to mitigate the risk of embryo-fetal toxicity associated with ambrisentan by:

1. Ensuring prescribers are educated on the following:
 - the risk of embryo-fetal toxicity
2. Ensuring prescribers are educated on and adhere to the following:
 - counseling patients about the risk and the need for monthly monitoring
 - enrolling patients in the PS-Ambrisentan REMS
 - monitoring patients at baseline and monthly
3. Ensuring that pharmacies are educated on the following:

- the risk of embryo-fetal toxicity
4. Ensuring that pharmacies are educated on and adhere to the following:
- confirming that the appropriate patient monitoring and counseling has occurred before dispensing ambrisentan
5. Ensuring that patients are informed about:
- the risk of embryo-fetal toxicity
 - appropriate baseline and monthly patient monitoring
 - appropriate contraception

Outpatient Pharmacy Overview of the PS-Ambrisentan REMS

Outpatient pharmacies must be specially certified in the PS-Ambrisentan REMS to dispense ambrisentan, even if the pharmacy has previously enrolled in the Letairis REMS.

To become certified to dispense, an outpatient pharmacy must:

- Designate an authorized representative to carry out the certification process and oversee

implementation of and compliance with the REMS on behalf of the pharmacy.

- Have the authorized representative review the **Pharmacy Guide**.
- Have the authorized representative enroll in the REMS by completing the **Outpatient Pharmacy Enrollment Form** and submitting it to the REMS. Outpatient pharmacies must enroll as one of the following pharmacy types:
 1. A retail pharmacy that agrees to order ambrisentan on a per patient per prescription basis
 2. A central fill pharmacy
 3. A specialty pharmacy

Each of these pharmacy types have specific requirements that must be followed to dispense an ambrisentan prescription.

- Train all relevant staff involved in dispensing ambrisentan on the REMS requirements using the **Pharmacy Guide**.
- Establish processes and procedures to verify if the female of reproductive potential is counseled and the authorization number is valid.

Before dispensing ambrisentan, an outpatient pharmacy must:

- Obtain authorization to dispense each prescription from the REMS to verify female patients are enrolled, the reproductive status has not changed, the prescriber is certified, and pregnancy test is completed for females of reproductive potential or the prescriber authorizes the refill through the processes and procedures established as a requirement of the REMS.
- For patients who provide the authorization number: Verify the authorization number is valid through the processes and procedures established as a requirement of the REMS.
- For Females of Reproductive Potential: Verify that the patient is counseled through the processes and procedures established as a requirement of the REMS.
- For females of reproductive potential: Dispense no more than a 30 days' supply.

At all times, an outpatient pharmacy must:

- Report pregnancies to the REMS.
- Report a change or misclassification in reproductive status to the REMS.

- Not distribute, transfer, loan, or sell ambrisentan, except to certified dispensers.
- For pharmacies authorized to receive bulk shipments: Maintain and submit records of daily product dispensing data.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.

The following sections explain the roles and requirements of the different pharmacy types in the PS-Ambrisentan REMS.

Central Fill Pharmacies in the PS-Ambrisentan REMS

A central fill pharmacy is a pharmacy that fills prescriptions on behalf of an originating pharmacy with which it has a contractual agreement to provide such services or with which it shares a common owner.

Note: A central fill pharmacy may provide a list of their participating originating pharmacies to the PS-Ambrisentan REMS. These pharmacies will be listed in the "Find a Pharmacy" search provided to patients and prescribers.

In the PS-Ambrisentan REMS, an authorized representative of the pharmacy must complete the following steps in the PS-Ambrisentan REMS:

- Carry out the certification process and oversee implementation of and compliance with the REMS on behalf of the pharmacy.
- Review the *Pharmacy Guide*.
- Enroll in the REMS by completing and submitting the *Outpatient Pharmacy Enrollment Form*.

- Train all relevant staff involved in dispensing ambrisentan on the REMS requirements using the *Pharmacy Guide*.
- Establish processes and procedures to verify if the female of reproductive potential is counseled and the authorization number is valid.

When a central fill pharmacy receives an ambrisentan prescription for a female patient from an originating pharmacy, the central fill pharmacy may fill the prescription only after validating or obtaining a REMS Dispense Authorization (RDA) from the PS-Ambrisentan REMS website (www.PSAmbrisentanREMS.com) or REMS Coordinating Center.

The RDA verifies female patients are enrolled, the reproductive status has not changed, the prescriber is certified, and pregnancy test is completed.

The central fill pharmacy shall not fill the prescription if an RDA cannot be obtained or verified for the patient. The central fill pharmacy must instruct the patient to call the REMS Coordinating Center to provide the missing information.

For females of reproductive potential: Verify that

the patient is counseled through the processes and procedures established as a requirement of the REMS. If monthly counseling has not been completed when an RDA is issued, the RDA will contain counseling guidelines and a message indicating to counsel the patient, OR call the REMS Coordinating Center to receive counseling guidelines and then counsel the patient, OR instruct the patient to call the REMS Coordinating Center to receive counseling.

The central fill pharmacy must record the NDC number and days' supply of the dispensed drug with the REMS once an RDA is validated or obtained.

For Females of Reproductive Potential, the central fill pharmacy must dispense no more than a 30 days' supply of ambrisentan.

Once the RDA is obtained, the central fill pharmacy may ship the prescription directly to the patient or back to the originating pharmacy for dispensing to the patient.

A central fill pharmacy must maintain and submit records of daily product dispensing data for Females of Reproductive potential.

Originating Pharmacies using a Central Fill Pharmacy in the PS-Ambrisentan REMS

An originating pharmacy is a retail pharmacy that fills ambrisentan prescriptions through an associated central fill pharmacy. In the PS-Ambrisentan REMS, originating pharmacies are not required to be certified or enrolled. However, originating pharmacies must not stock ambrisentan and must fill ambrisentan prescriptions through a central fill pharmacy certified in the REMS.

When the originating pharmacy receives an ambrisentan prescription, the prescription must be sent to a certified central fill pharmacy to be filled.

Please see page 6 for the requirements on the filling of an ambrisentan prescription by a Central Fill Pharmacy.

Pharmacies Ordering on a Just-in-Time Basis in the PS-Ambrisentan REMS

Pharmacies that do not use a central fill pharmacy may still certify and enroll in the PS-Ambrisentan REMS. To do so, these pharmacies must agree to not stock ambrisentan and to only order ambrisentan on a Just-in-Time, per patient per prescription basis from a wholesale distributor registered in the PS-Ambrisentan REMS.

In the PS-Ambrisentan REMS, an authorized representative of the pharmacy must complete the following steps in the PS - Ambrisentan REMS:

- Carry out the certification process and oversee implementation of and compliance with the REMS on behalf of the pharmacy.
- Review the *Pharmacy Guide*.
- Enroll in the REMS by completing and submitting the *Outpatient Pharmacy Enrollment Form*.
- Train all relevant staff involved in dispensing ambrisentan on the REMS requirements using the *Pharmacy Guide*.

- Establish processes and procedures to verify if the female of reproductive potential is counseled and the authorization number is valid.
- Agree to not stock ambrisentan
- Order ambrisentan just-in-time on a per patient per prescription basis from a wholesale distributor registered in the REMS and provide with the order an indication that the patient is male or the RDA for a female patient.
- Order and dispense no more than a 30-day supply to Females of Reproductive Potential.

When a pharmacy receives an ambrisentan prescription, the pharmacy must order ambrisentan for this patient and this prescription from a wholesaler/distributor registered in the PS-Ambrisentan REMS.

Before ordering ambrisentan for a female patient, the pharmacy must validate or obtain an RDA from the PS-Ambrisentan REMS website (www.PSAmbrisentanREMS.com) or the REMS Coordinating Center. The RDA verifies female patients are enrolled, the reproductive status has

not changed, the prescriber is certified, and pregnancy test is completed.

For females of reproductive potential: Verify that the patient is counseled through the processes and procedures established as a requirement of the REMS. If monthly counseling has not been completed when an RDA is issued, the RDA will contain counseling guidelines and a message indicating to counsel the patient, OR call the REMS Coordinating Center to receive counseling guidelines and then counsel the patient, OR instruct the patient to call the REMS Coordinating Center to receive counseling.

The pharmacy must not order ambrisentan for the prescription if an RDA cannot be obtained or verified for the patient. The pharmacy must instruct the patient to call the REMS Coordinating Center to provide the missing information.

When the ambrisentan is received from the wholesaler/distributor, the pharmacy may dispense to the patient.

Specialty Pharmacies in the PS-Ambrisentan REMS

In the PS-Ambrisentan REMS, an authorized representative of the specialty pharmacy must complete the following steps in the PS-Ambrisentan REMS:

- Carry out the certification process and oversee implementation of and compliance with the REMS on behalf of the pharmacy.
- Review the *Pharmacy Guide*.
- Enroll in the REMS by completing and submitting the *Outpatient Pharmacy Enrollment Form*.
- Train all relevant staff involved in dispensing ambrisentan on the REMS requirements using the *Pharmacy Guide*.
- Establish processes and procedures to verify if the female of reproductive potential is counseled and the authorization number is valid.

When a specialty pharmacy receives an ambrisentan prescription for a female patient, the pharmacy may fill the prescription only after validating or obtaining an RDA from the PS-

Ambrisentan REMS website (www.PSAmbrisentanREMS.com) or REMS Coordinating Center.

The RDA verifies female patients are enrolled, the reproductive status has not changed, the prescriber is certified, and pregnancy test is completed.

The pharmacy shall not fill the prescription if an RDA cannot be obtained or verified for the patient. The pharmacy must instruct the patient to call the REMS Coordinating Center to provide the missing information.

For females of reproductive potential: Verify that the patient is counseled through the processes and procedures established as a requirement of the REMS. If monthly counseling has not been completed when an RDA is issued, the RDA will contain counseling guidelines and a message indicating to counsel the patient, OR call the REMS Coordinating Center to receive counseling guidelines and then counsel the patient, OR instruct the patient to call the REMS Coordinating Center to receive counseling.

The pharmacy must record the NDC number and days' supply of the dispensed drug with the REMS once an RDA is validated or obtained.

For Females of Reproductive Potential, the pharmacy must dispense no more than a 30 days' supply of ambrisentan.

A specialty pharmacy must maintain and submit records of daily product dispensing data for females of reproductive potential.

Once the RDA is obtained, the specialty pharmacy may ship the prescription to the patient.

Validating or Obtaining a REMS Dispense Authorization

Outpatient pharmacies may fill ambrisentan prescriptions for female patients only after validating an RDA provided by the patient or by obtaining an RDA from the REMS website or the REMS Coordinating Center. A new RDA will be issued for each prescription/refill.

The female patient may present the RDA to the pharmacist in either a paper or electronic format. The pharmacist must confirm that the RDA presented by the patient is valid. The validity can be confirmed on the PS-Ambrisentan REMS system website

(www.PSAmbrisentanREMS.com) or by contacting the REMS Coordinating Center at 1-888-301-0333 and providing the RDA number, and the patient's date of birth from the RDA as well as the pharmacy's NPI number.

If the patient does not provide the RDA, the pharmacist may obtain the RDA on the PS-Ambrisentan REMS website or by contacting the

PS-Ambrisentan REMS Coordinating Center and providing the patient's name, the patient's date of birth and the pharmacy's NPI number.

If an RDA cannot be obtained for the patient, the pharmacy should direct the patient to call the PS-Ambrisentan REMS Coordinating Center.

Once the RDA is obtained, the pharmacist must record the NDC number and days supply of the dispensed product in the PS-Ambrisentan REMS website or through the REMS Coordinating Center. To record the NDC number and days supply, the pharmacy will be required to confirm the patient's name and date of birth and provide the pharmacy's NPI number, and the RDA number.

If monthly counseling has not been completed for the patient when the RDA is issued, the RDA will contain counseling guidelines and a message indicating that the pharmacist must do one of the following:

1. Counsel the patient using the counseling guidelines on the RDA
2. Call the REMS Coordinating Center to receive counseling guidelines and then

- counsel the patient
3. Instruct the patient to call the REMS Coordinating Center to receive the counseling

Inpatient Pharmacy Overview of the PS-Ambrisentan REMS

Inpatient pharmacies must be specially certified and enrolled in the PS-Ambrisentan REMS and comply with the following PS-Ambrisentan REMS requirements to dispense ambrisentan, even if the pharmacy has previously enrolled in the Letairis REMS.

An authorized representative of the inpatient pharmacy must:

- Carry out the certification process and oversee implementation of and compliance with the REMS on behalf of the pharmacy.
- Review the *Pharmacy Guide*.
- Enroll in the REMS by completing and submitting the *Inpatient Pharmacy Enrollment Form*.

- Train all relevant staff involved in dispensing on REMS procedures and materials using the *Pharmacy Guide*.
- Establish processes and procedures to verify the female patient is enrolled or will be enrolled in the REMS prior to discharge, her reproductive status, and the female patient is under the supervision and care of a certified prescriber.
- For Females of Reproductive Potential: establish processes and procedures to verify the pregnancy testing is complete, and the patient is counseled on the risk of embryo-fetal toxicity, the need to use highly reliable contraception during treatment and for one month after stopping treatment, to get monthly pregnancy tests, and to inform the prescriber of a pregnancy immediately.

Prior to dispensing, the inpatient pharmacy must:

- Verify the female inpatient is under the supervision and care of a certified prescriber, her reproductive status, and she is enrolled or will be enrolled in the REMS prior to discharge through the processes and

procedures established as a requirement of the REMS.

- For Females of Reproductive Potential: Verify the pregnancy testing is complete, the patient is counseled on the risk of embryo-fetal toxicity, the need to use highly reliable contraception during treatment and for one month after stopping treatment, to get monthly pregnancy tests, and to inform the prescriber of a pregnancy immediately through the processes and procedures established as a requirement of the REMS.

At discharge of a patient, the inpatient pharmacy must:

- Dispense no more than a 15-days' supply of ambrisentan upon discharge.

At all times, the inpatient pharmacy must:

- Report pregnancies to the REMS.
- Report a change or misclassification in reproductive status to the REMS.
- Not distribute, transfer, loan, or sell ambrisentan, except to certified dispensers.

- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.

Options for Enrolling in the PS-Ambrisentan REMS

Pharmacies may enroll in the PS-Ambrisentan REMS online at www.PSAmbrisentanREMS.com or by completing a paper enrollment form and faxing it to the REMS Coordinating Center at 1-888-870-1819.

Additional questions

Please visit **www.PSAmbrisentanREMS.com** or call the PS-Ambrisentan REMS Coordinating Center at **1-888-301-0333** for more information about the PS-Ambrisentan REMS.

