Macitentan REMS
(Risk Evaluation and Mitigation Strategy)

Guide for Female Patients

Information to help you throughout your treatment with macitentan
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### What is macitentan?

Macitentan is a prescription medicine used to treat pulmonary arterial hypertension (PAH), which is high blood pressure in the arteries of your lungs.

Macitentan can improve your ability to exercise, improve some of your symptoms, and help slow down the progression of your disease. Macitentan can also lower your chance of being hospitalized for PAH.

It is not known if macitentan is safe and effective in children.

### What are the serious risks of macitentan?

Macitentan can cause serious birth defects if taken during pregnancy. Women must not be pregnant:

- When they start taking macitentan,
- While taking macitentan, or
- Within one month of stopping macitentan

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### What is the Macitentan REMS (Risk Evaluation and Mitigation Strategy)?

Because of the risk of serious birth defects when taking macitentan, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS). The purpose of the Macitentan REMS is to make sure the benefits of macitentan outweigh the risks. All females must enroll in the Macitentan REMS to receive macitentan.

### How do I enroll in the Macitentan REMS?

Your healthcare provider will complete your enrollment online at MacitentanREMSProgram.com OR by faxing a completed enrollment form to the REMS Coordinating Center. **Patients with the Veterans Affairs (VA) may only enroll by FAX.**

There are several steps you must take:

1. Read this *Guide for Female Patients*. Ask your healthcare provider any questions you have about taking macitentan and the Macitentan REMS.
2. Make sure you understand:
   - The benefits and risks of macitentan
   - How to enroll and take part in the Macitentan REMS
3. Complete and sign the *Patient Enrollment Form* with your healthcare provider. Your healthcare provider will fill out most of the enrollment form for you. For additional information, please see the next section titled *What are the Macitentan REMS requirements for me?*

### Can I be pre-enrolled in the Macitentan REMS?

Your prescriber may ask you to pre-enroll into the Macitentan REMS. Pre-enrolling will save time in your prescriber’s office when your prescriber completes your enrollment. To pre-enroll, your prescriber will send you an email with a link to complete the patient pre-enrollment online.

Clicking on the link will take you to the pre-enrollment screens on the Macitentan REMS website.

You will enter information such as your name, address, phone number, date of birth, and email address. This allows you to look at and agree to the REMS requirements for a female patient. You will also create your login account, which allows you to login to the Macitentan REMS website. When you are done, you will receive a “Patient Pre-Enrollment Confirmation Number.” Give this number to your prescriber to complete your enrollment. Your prescriber will then complete your enrollment.

### How do I change prescribers in the Macitentan REMS?

You can change prescribers in the Macitentan REMS either online at MacitentanREMSProgram.com or by calling the REMS Coordinating Center.

To change prescribers online, login at MacitentanREMSProgram.com and select the “My Prescriber” option. On the next screen, select the “Transfer Prescriber” button. You will be asked to confirm that you want to transfer to another prescriber. A Transfer Prescriber Confirmation Number will be given to you on the screen. You can have this number emailed or texted to you.
Give this number to your new prescriber. The new prescriber will use the number to complete the change.

To change prescribers by phone, call the REMS Coordinating Center. A REMS Coordinating Center associate will give you a Transfer Prescriber Confirmation Number over the phone. Give this number to your new prescriber. The new prescriber will use the number to complete the change.

What are the Macitentan REMS requirements for me?

Females Who **Cannot** Get Pregnant

You are considered a female who **is not** able to get pregnant if you:

- Have not yet entered puberty, or
- Do not have a uterus, or
- Have gone through menopause. (Menopause means that you have not had a menstrual period for at least 12 months for natural reasons, or that you have had your ovaries removed.), or
- Are infertile for other medical reasons and this infertility is permanent and cannot be reversed.

To receive macitentan, you must:

- Enroll in the Macitentan REMS by completing the **Patient Enrollment Form**
  - Your prescriber will help you complete this form
  - You must understand your requirements in the Macitentan REMS and provide your signature:
    - electronically (if enrolling online), or
    - on the form itself (if enrolling by paper)
- Tell your prescriber if you become pregnant or your ability to become pregnant changes
- Receive counseling from your prescriber on the risk of serious birth defects (only if you are premenopausal)
- Be monitored every year to see if your ability to become pregnant changes and tell your prescriber if your ability to become pregnant changes (only if you are over the age of 8)

**Note:**
- Enrollment by phone and online enrollment are not available for VA patients
- If you are a parent or caregiver of a female child who started taking macitentan before reaching puberty, you should check your child regularly to see if she is developing signs of puberty. Tell your prescriber right away if you notice that she is developing breast buds or pubic hair. Your prescriber should decide if your child has reached puberty. Your child may reach puberty before having her first menstrual period.

Females Who **Can** Get Pregnant

You are considered a female who can get pregnant if you:

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

To receive macitentan, you must:

- Enroll in the Macitentan REMS by completing the **Patient Enrollment Form**
  - Your prescriber will help you complete this form
  - You must understand your requirements in the Macitentan REMS and provide your signature:
    - electronically (if enrolling online), or
    - on the form itself (if enrolling by paper)
- Enrollment by phone and online enrollment are not available for VA patients
- Have a negative pregnancy test:
  - before starting macitentan,
  - each month for as long as you are being treated with macitentan, and
  - for one month after you stop taking macitentan
- Use reliable birth control at **all times** when taking macitentan and for one month after stopping macitentan. Your birth control options are listed on page 6.
- Do not have unprotected sex

Talk to your healthcare provider right away if you have unprotected sex, if you think your birth control has failed, or if you think you are pregnant. If so, your healthcare provider may discuss medical options with you (e.g., emergency contraception). Do not wait until your next appointment to tell your healthcare provider if you miss your menstrual period or if you think you are pregnant.

Macitentan is not available at your local pharmacy. You must receive macitentan through a certified outpatient pharmacy.

Your pharmacy will contact you every month to provide counseling and to ask if you have completed a pregnancy test before shipping your macitentan to your home or another shipping address you choose.
What are my birth control options?

If you are a female who can get pregnant, your healthcare provider will talk with you about your birth control options before starting macitentan. Ask your healthcare provider if you have any questions. Tell your healthcare provider if you want to change your birth control.

You must choose one of the 4 options listed below. More than one birth control method might be needed every time you have sex.

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<tr>
<th>Option 1</th>
<th>Option 2</th>
<th>Option 3</th>
<th>Option 4</th>
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<td>Standard intrauterine device (Copper T 380A IUD)</td>
<td>Estrogen and progesterone oral contraceptives (&quot;the pill&quot;)</td>
<td>Diaphragm with spermicide</td>
<td>Partner’s vasectomy</td>
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<td>Intrauterine system (LNg 20 IUS: progesterone IUS)</td>
<td>Estrogen and progesterone transdermal patch</td>
<td>Cervical cap with spermicide</td>
<td>PLUS One method from this list:</td>
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<td>Progesterone implant</td>
<td>Vaginal ring</td>
<td>Male condom</td>
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<tr>
<td>Tubal sterilization</td>
<td>Progesterone injection</td>
<td>Diaphragm with spermicide</td>
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How will I receive macitentan?

Macitentan is available only through certified outpatient pharmacies.

Before your first prescription is filled, the pharmacy you selected will call you to schedule a shipment of macitentan that will come right to your home or another shipping address you choose.

For females who can get pregnant, the pharmacy will contact you every month to ask if you have completed a pregnancy test before the pharmacy can ship your macitentan. It is important that you can be contacted to avoid delays in your refills.

A Medication Guide will be included with each macitentan shipment.

Read the Medication Guide each time you receive it. Important information may have been added or changed.

For a list of certified pharmacies, please call the REMS Coordinating Center at 1-888-572-2934.

Your steps to treatment with macitentan

Use this helpful checklist to get started with macitentan and to stay on track during your treatment.

FIRST:

☐ Review the Guide for Female Patients with your healthcare provider
☐ Make sure you understand the risks and benefits of taking macitentan
☐ For females who can get pregnant, go for your pregnancy test
☐ Enroll in the Macitentan REMS

NEXT:

☐ Expect a call from the pharmacy you selected to schedule your first shipment

EVERY MONTH:

☐ Read the Medication Guide that comes with every shipment
For females who can get pregnant:

☐ Use reliable birth control method(s) agreed upon with your healthcare provider—during treatment and for one month after you stop taking macitentan
☐ Complete the monthly pregnancy test ordered by your healthcare provider
☐ Expect your pharmacy to call you every month to ask if you had a pregnancy test in the last month before it reorders your macitentan. The refill may not be done on time if you’ve not had your pregnancy test
☐ Do not get pregnant. Tell your healthcare provider right away if you:
  – Have unprotected sex
  – Think that your birth control failed
  – Miss a menstrual period
  – Think you are pregnant
You can reach the Macitentan REMS by calling toll free at 1-888-572-2934.

Monday – Friday
8:00 AM to 8:00 PM ET

For more information about the Macitentan REMS, please visit MacitentanREMSProgram.com