Welcome to the Adempas REMS (Risk Evaluation and Mitigation Strategy)

The Adempas REMS is a program to help patients and healthcare providers about the serious risks of birth defects while taking Adempas. This program is required by the Food and Drug Administration (FDA). All females must enroll in the Adempas REMS to receive Adempas. REMS stands for Risk Evaluation and Mitigation Strategy.

Bayer Pharmaceuticals has worked with the FDA to develop the Adempas REMS to educate prescribers and patients about the risk of embryo-fetal toxicity. The REMS will require that females agree to follow the REMS requirements to be enrolled in the Adempas REMS in order to receive Adempas® (riociguat).

Adempas REMS Overview

- Females must not be pregnant when they start taking Adempas, become pregnant during treatment, or become pregnant for one month after stopping Adempas treatment.
- All healthcare providers must enroll in the Adempas REMS and agree to the REMS requirements to prescribe Adempas.
- All female patients must enroll in the Adempas REMS and agree to the REMS requirements to receive Adempas.
- A limited number of certified pharmacies will dispense Adempas for outpatients. They must enroll in the Adempas REMS and agree to the REMS requirements to provide Adempas for outpatient use.
- Inpatient pharmacies must enroll in the Adempas REMS and agree to the REMS requirements to stock Adempas for inpatient use.

Changes to the Adempas Risk Evaluation and Mitigation Strategy (REMS) December 2018

- Revised Form: Adempas REMS Patient Enrollment and Consent Form
- Revised Form: Adempas REMS Prescriber Enrollment and Agreement Form
- Revised Form: Adempas REMS Outpatient Pharmacy Enrollment Form
- Revised Guide: Adempas REMS Guide for Female Patients
- Revised Guide: Prescriber and Pharmacy Guide for the Adempas REMS

Click below to learn more about the Adempas REMS


INDICATIONS

- Adempas is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.
- Adempas is indicated for the treatment of adults with pulmonary arterial hypertension (PAH) (WHO Group 1), to improve exercise capacity, improve WHO functional class, and to delay clinical worsening.

Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominantly patients with WHO functional class II-III and etiologies of idiopathic or heritable PAH (81%) or PAH associated with connective tissue diseases (25%).
PRESCRIBER OVERVIEW

Due to the risk of embryo-fetal toxicity, Adempas is available only through the Adempas REMS (Risk Evaluation and Mitigation Strategy).

The goal of the Adempas REMS is to mitigate the risk of embryo-fetal toxicity associated with Adempas by:

1. Ensuring prescribers are educated on the following:
   - the risks of embryo-fetal toxicity

2. Ensuring-prescribers are educated on and adhere to the following:
   - counseling patients about these risks and the need for monthly monitoring
   - enrolling patients in the ADEMPAS REMS
   - monitoring patients at baseline and monthly

3. Ensuring that pharmacies are educated on the following:
   - the risks 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 Adempas

5. Ensuring that patients are informed about:
   - the risks of embryo-fetal toxicity
   - appropriate baseline and monthly patient monitoring
   - appropriate contraception

In order to prescribe and receive Adempas, prescribers and females must enroll in the Adempas REMS and agree to comply with the requirements of the program.

Only a limited number of certified pharmacies will dispense Adempas to outpatients.

To enroll in the Adempas REMS, prescribers must:

- Read the Adempas Prescribing Information (PI) and the Prescriber and Pharmacy Guide.
- Agree to follow the REMS requirements by completing and submitting a Prescriber Enrollment and Agreement Form.
- Complete and submit the Prescriber Enrollment and Agreement Form:
  - Online
  - By fax at 1-800-662-5200
  - By calling the Adempas REMS at 1-855-4ADEMPAS (1-855-423-6772)
- Receive an enrollment confirmation from the Adempas REMS verifying that enrollment has been completed.
1. Enroll in the Adepamas REMS

- Enroll all patients who are pregnant (or are a new patient), in the Adepamas REMS.

2. Determine the reproductive potential status of female patients

a. Evaluate reproductive potential

- For female patients, evaluate if they are at risk for reproductive potential.
- For female patients, evaluate if they are at risk for reproductive potential due to their medical conditions.

b. For female patients, evaluate if they are at risk for reproductive potential.

- For female patients, evaluate if they are at risk for reproductive potential due to their medical conditions.
- For female patients, evaluate if they are at risk for reproductive potential due to their medical conditions.

3. Educate and Counsel Patients

- Educate the patient on the risks of pregnancy.
- Educate the patient on the benefits of pregnancy.
- Educate the patient on the importance of pregnancy.

4. Check Pregnancy Status (In Females of Reproductive Potential)

- Confirm pregnancy status.
- Confirm pregnancy status.

5. Enroll Female Patients in the Adepamas REMS

- Enroll all female patients who are at risk for reproductive potential.

6. Monitor Patients

- Monitor patients for signs and symptoms of pregnancy.
- Monitor patients for signs and symptoms of pregnancy.

7. Report Pregnancies

- Report pregnancies as soon as possible.
- Report pregnancies as soon as possible.
INFORMATION FOR FEMALE PATIENTS

Adempas® is a prescription medicine to treat adults with:

- chronic thromboembolic pulmonary hypertension (CTEPH)
  - treated with surgery but who continue to have high pulmonary blood pressure (persistent) or it comes back after surgery (recurrent), or
  - that cannot be treated with surgery

CTEPH is a type of high blood pressure in the arteries of your lungs caused by blood clots that narrow or block blood flow. Adempas can improve your ability to exercise and can help to improve some of your symptoms.

- pulmonary arterial hypertension (PAH)

PAH is a type of high blood pressure in the arteries of your lungs. Adempas can improve your ability to exercise, improve some of your symptoms, and help slow down the worsening of your physical condition.

It is unknown if Adempas is safe and effective in children.

Because of the serious risks of birth defects while taking Adempas, the FDA (Food and Drug Administration) requires a program called REMS. REMS stands for Risk Evaluation and Mitigation Strategy. The purpose of this program is to make sure that patients and prescribers understand the risks. All females must enroll in the Adempas REMS to receive Adempas.

Females Who Cannot Get Pregnant:

You are considered a female who cannot get pregnant if you have not yet entered puberty, or you do not have a uterus, or you have gone through menopause (have not had a period for at least 12 months for natural reasons or have had your ovaries removed).

To receive Adempas, you must:

- Enroll in the Adempas REMS by completing the Patient Enrollment and Consent Form.
- Receive counseling from your prescriber on the risks of serious birth defects (Pre-menopausal only)
- Tell your prescriber if you become pregnant or your ability to become pregnant changes
- If you are ever over the age of 18, Be monitored every year to see if your ability to become pregnant changes and tell your prescriber if your ability to become pregnant changes

If you are the parent or caregiver of a female child who started taking Adempas before reaching puberty, you should check your child regularly to see if she is developing signs of puberty. Tell your doctor right away if you notice that she is developing breast buds or pubic hair. Your doctor 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 is able to get pregnant if you have entered puberty, even if you have not started your period, and you have a uterus and have not gone through menopause (have not had a period for at least 12 months for natural reasons or you have had your ovaries removed).

If you are a female who can get pregnant, to receive Adempas you must:

- Talk to your healthcare provider about the risks and benefits of Adempas.
- Read:
  - The Guide for Female Patients, Special Guide for Female Patients
- Make sure you understand the risks and benefits of taking Adempas
- Have a pregnancy test before you start taking Adempas to be sure you are not pregnant
- Have a pregnancy test before you receive your refill each month
- Use effective forms of birth control during Adempas treatment and for one month after stopping treatment with Adempas
- Immediately notify your healthcare provider if you miss a menstrual period or suspect you are pregnant

For more information on Adempas, the Adempas REMS and effective forms of birth control, download the Guide for Female Patients, Special Guide for Female Patients.

To learn more about the serious risks associated with Adempas, please refer to the Prescribing Information including boxed Warning: Read Prescribing Information.
CERTIFIED OUTPATIENT PHARMACY OVERVIEW

Due to the risk of embryo-fetal toxicity, Adempas is available only through the Adempas REMS.

Adempas will be dispensed to outpatients by a limited number of certified pharmacies. Prior to dispensing Adempas the pharmacy will confirm that the prescriber who wrote the prescription is enrolled, and if the patient is a female that she is enrolled in the Adempas REMS. If either the female or prescriber is not enrolled, Adempas will not be dispensed.

For all female patients, outpatient pharmacies will:

- Contact the Adempas REMS Coordinating Center to determine if the patient has received sample medication from the prescriber
- Verify the female patient is enrolled, the reproductive status has not changed, and the prescriber is certified through processes and procedures established as a requirement of the REMS.

For Females of Reproductive Potential, outpatient pharmacies will:

- Counsel her on the risk of embryo-fetal toxicity
- Contact her each month to arrange the dispensing of Adempas
- Ask the patient if she has had a pregnancy test within the last month or that the prescriber has authorized the refill through processes and procedures established as part of the REMS requirements
- Counsel her on the need to use effective contraception during Adempas treatment and for one month after stopping treatment
- Counsel her to get monthly pregnancy tests
- Counsel her to inform her prescriber immediately if she misses a menstrual period or suspects that she may be pregnant
- Dispense no more than 30-days’ supply

All outpatient pharmacies must report any pregnancies associated with the use of Adempas to Bayer at 1-888-842-2937 or send the information to DrugSafety.GPV.US@bayer.com

Females of Reproductive Potential will only be able to get a 30-day supply of Adempas at one time.

To learn more about the serious risks associated with Adempas, please refer to the Prescribing Information, including Boxed Warning, Spanish Prescribing Information, and the Prescriber and Pharmacy Guide.
CERTIFIED INPATIENT PHARMACY OVERVIEW

Due to the risk of embryolethal toxicity, Adempas is available only through the Adempas REMS. In order to stock Adempas, inpatient pharmacies must enroll and be certified in the Adempas REMS.

Inpatient pharmacies must agree to follow the REMS requirements, including:

- Establish processes and procedures to ensure the REMS requirements are met.
- Complete training in the Adempas REMS by reading the Prescriber and Pharmacy Guide.
- Assign an authorized representative to assume responsibility for the training of dispensing staff on the Adempas REMS requirements and Adempas REMS materials prior to dispensing Adempas.
- Assume responsibility for the training of all relevant staff in dispensing on the Adempas REMS requirements, procedures, and Adempas REMS materials prior to dispensing Adempas, using the Prescriber and Pharmacy Guide.
- Establish processes and procedures to verify the female patient is enrolled in the REMS or will be enrolled 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 pregnancy testing is complete and that the patient is counseled on the risk of embryolethal toxicity, the need to use effective contraception, to get monthly pregnancy tests, and to inform the prescriber of a pregnancy immediately.

Before dispensing:

- Verify the female patient is under the supervision and care of a certified prescriber, her reproductive status, and that she is enrolled or will be enrolled in the REMS. If she is already enrolled, discharge the process through the processes and procedures established as a requirement of the REMS.
- For females of reproductive potential: verify pregnancy testing is complete and that the patient is counseled on the risk of embryolethal toxicity, the need to use effective contraception, 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:

- Verify the female patient is enrolled in the REMS through the processes and procedures established as a requirement of the REMS.
- Dispose no more than a 15-day temporary supply of Adempas to any female patient upon discharge from the healthcare facility.

At all times:

- Never distribute, transfer, loan, or sell Adempas.
- Report any pregnancies associated with the use of Adempas to Bayer at 1-888-842-2937, or send the information to GetAlerts@Bayer.com.
- Comply with audits by the manufacturer or a third party acting on behalf of the manufacturer to ensure all processes and procedures are in place and being followed.
- Maintain records of all processes and procedures including compliance with these processes and procedures.

To be certified in the Adempas REMS, an authorized representative of the inpatient pharmacy must:

- Complete training in the Adempas REMS by reading the Adempas Prescriber Information (PI) and the Prescriber and Pharmacy Guide for the Adempas REMS to understand the risks of Adempas and the Adempas REMS requirements.
- Agree to follow the REMS requirements by completing and submitting an Inpatient Pharmacy Enrollment Form to the Adempas REMS.

- Authorized representatives can complete the Inpatient Pharmacy Enrollment Form:
  - Online
  - By fax at 1-855-462-5200
  - By calling the Adempas REMS at 1-855-44-DEMPAS (1-855-443-6783)

If an inpatient pharmacy needs Adempas and is not certified in the Adempas REMS, the inpatient pharmacy can contact the Adempas REMS Program Coordinating Center at 1-855-44-DEMPAS (1-855-443-6783) for assistance in obtaining up to a 15-day supply of Adempas for a specific patient while initiating enrollment.

To learn more about the serious risks associated with Adempas, please refer to the Prescriber Information including Boxed Warning, Spanish Prescriber Information, Prescriber and Pharmacy Guide and the Guide for Female Patients.
Login is available for enrolled prescribers and office contacts designated by prescribers only.

To learn more about the serious risks associated with Adempas, please refer to the Prescribing Information including Boxed Warning, Spanish Prescribing Information, and the Prescriber and Pharmacy Guide.
Phone: 1-855-4ADEMPAS (1-855-423-3672)
Fax: 1-855-662-5200

Hours of Operation: Monday- Friday 8:00 AM - 8:00 PM Eastern

To report any adverse events, product technical complaints, medication errors, or pregnancies associated with the use of Adempas, contact:

Bayer at 1-888-842-2937 or send the information to DrugSafety.GPV.US@bayer.com.

To learn more about the serious risks associated with Adempas, please refer to the Prescribing Information including Boxed Warning, Spanish Prescribing Information, and the Prescriber and Pharmacy Guide.
Adempas REMS Patient Enrollment and Consent Form

Access this form online at: www.adempasrems.com, or fax the form to the Adempas REMS at 1-800-462-5289.

For Patients: This is required for Receiving enrollment form.

1 Patient Information

- **First Name:**
- **Last Name:**
- **Address Line 1:**
- **Address Line 2:**
- **City:**
- **State:**
- **Zip Code:**
- **Telephone:**
- **Email:**
- **Preferred Phone:**
- **Preferred Time to Contact:**
- **Cell/Alternative Phone:**
- **Email:**
- **Alternate Contact Name:**
- **Phone:**
- **Relationship:**

2 Statement of Medical Necessity

The following does not support approved uses or indications.

- **Diagnoses:**
  - Chronic obstructive pulmonary disease (COPD)
  - Chronic obstructive pulmonary disease (COPD) treatment failure
  - Pulmonary hypertension status:
  - Primary pulmonary hypertension
  - Pulmonary arterial hypertension
  - Other

3 Female Patient Agreement

For all Females: I understand that Adempas is only available through a restricted distribution program under an FDA-recognized Risk Evaluation and Mitigation Strategy (REMS).

For Females Who Are Postpartum: I have been counseled on the risks of Adempas, including the following of Adempas, which are not intended as a replacement for informed consent. I understand that I will receive counseling from the prescriber on the risks of various birth defects, the need to use effective contraception during Adempas treatment and for one year after stopping Adempas treatment. My partner is an adult in the event of exposure to Adempas in pregnancy. In the event of unexpected pregnancy, I will consult with my prescriber to determine the best course of action.

For Post-Pregnancy Females: I have been counseled on the risks of Adempas, including the risks of various birth defects, and that I have read the Guide for Female Patients. I understand that I must immediately communicate with my healthcare provider if I get my pregnancy confirmed. For Post-Pregnancy Females: I have received and read the Guide for Female Patients. I understand that I must immediately communicate with my healthcare provider if I get my pregnancy confirmed.

4 Prescriber Information

- **First Name:**
- **Last Name:**
- **NPI Number:**

5 Prescriber Agreement

For female patients, please indicate the patient's current reproductive status below.

- **Reproductive Status:**
  - Female of Reproductive Potential
  - Female of Non- Reproductive Potential

I certify that the information provided is accurate to the best of my knowledge. I certify that I have provided the appropriate counseling and Adempas REMS materials, and will continue to fulfill my obligations under the Adempas REMS. I understand that I may not delegate signature authority.

For Female Patients: I certify that I have reviewed and understand the Guide for Female Patients. I understand that I must immediately communicate with my healthcare provider if I get my pregnancy confirmed.

For All Patients: I certify that I have reviewed and understand the Guide for All Patients. I understand that I must immediately communicate with my healthcare provider if I get my pregnancy confirmed.

To report any adverse events, product technical complaints, medication errors or progressive associated with the use of Adempas, contact Bayer at 1-888-462-5289, or send the information to DrugSafety@JPR1.LG.com.

For Patients: Required field for submitting enrollment form.
5 Prescriber Authorization

For female patients, please indicate the patient's current reproductive status below.

- Reproductive Status:
  - Female of Reproductive Potential
  - Female of Non-Reproductive Potential

  If this patient is a Female of Reproductive Potential has a pregnancy test been completed prior to prescribing Adempas?:
  - Yes
  - No

I certify that the information provided is accurate to the best of my knowledge. I certify that for female patients, I have provided the appropriate counseling and Adempas REMS materials, and I will continue to fulfill my obligations under the Adempas REMS. I understand that I may not delegate signature authority.

Definitions:
5 Prescriber Authorization

For female patients, please indicate the patient’s current reproductive status below.

- Reproductive Status:
  - Female of Reproductive Potential
  - Female of Non-Reproductive Potential

- Female of Non-Reproductive Potential:
  - Pre-Pubertal Female
  - Post-Menopausal Female
  - Female with other medical reasons for permanent, irreversible infertility

I certify that the information provided is accurate to the best of my knowledge. I certify that for female patients, I have provided the appropriate counseling and Adempas REMS materials, and I will continue to fulfill my obligations under the Adempas REMS. I understand that I may not delegate signature authority.
Adempas REMS (Risk Evaluation and Mitigation Strategy) Prescriber Enrollment and Agreement Form

In order to prescribe Adempas, prescribers must enroll in the Adempas REMS by completing this form in its entirety. Use this form to enroll in the Adempas REMS and agree to comply with the requirements for enrolling in the Adempas REMS. This form must be submitted with the RemS Enrollment Prescriber Document in the detail page on page 2. Access this form at repeatsignature.com, or via this form at 1-855-866-9260 or call the Adempas REMS hotline at 1-888-ADEMPAS (233-6727).

Prescriber Information (*indicates required field)

First Name: [redacted]
Middle Name: [redacted]
Last Name: [redacted]
NPI: [redacted]
State License #: [redacted]
Specialties: Cardiology, Gastroenterology, General Practice
Other

Facility Name:
Address:
City: [redacted]
State: [redacted]
Zip Code: [redacted]
Phone Number: [redacted]
Fax Number: [redacted]
Email: [redacted]

Preferred Method of Contact:
Phone Number: [redacted]
Fax Number: [redacted]
Email: [redacted]

Office Contact
First Name: [redacted]
Last Name: [redacted]
Email: [redacted]
Office (if applicable provided): [redacted]

Prescriber REMS Agreement

By signing below, you signify your understanding of the risks of Adempas treatment and your agreement on an Adempas prescriber to educate your female patients about the Adempas REMS, monitor them appropriately, and report any adverse experiences to the Adempas REMS. Specifically, you attest to the following:

I have read and understood the Adempas Prescriber Information, and the Prescriber and Pharmacy Agreement.

For all Feminizers:
I affirm that I am the responsible pharmacist on at least one Adempas product using the information provided in the Prescriber and Pharmacy Agreement.

For all Adempas prescribers, I affirm that Adempas is only available through a network distribution program called the Adempas REMS.

I am aware of all current contact information of the Adempas REMS and submitting this form.

For Patients:
I certify that I will comply with the Patient Agreement.

For Patients of Reproductive Potential:
I certify that I am not a patient with reproductive potential (IP) for Adempas administration, including unconfirmed, ruled-out, and review for the Guideline for Female Patients with the patient.

I certify that I already contacted her contact her prescriber if she misses a menstrual period or a pregnancy test fails for the first time after starting treatment, monthly during treatment, and for one month after stopping treatment.

I certify that I will report any change or relapse of reproductive status by submitting a Change in a Reproductive Potential Status and Patient’s Annual Verification Form within 10 business days of becoming aware of the change.

I hereby attest to my agreement to the patient’s annual verification form.

I hereby certify that I have read, understood, and agreed to all terms and conditions of this agreement.

Date: [redacted]

Please indicate your Subscribers by the circling your preferred approach:

Phone: [redacted]
Fax: [redacted]
Email: [redacted]
Adempas Risk Evaluation and Mitigation Strategy (REMS) Inpatient Pharmacy Enrollment Form

Due to a risk of fetal exposure and adverse fetal outcomes in females of reproductive potential prescribed Adempas, Adempas is available only through the Adempas REMS. The Adempas REMS is comprised of a Patient Counseling and Mitigation Strategy (REMS). In order for inpatient pharmacies to receive Adempas, female as well as inpatient pharmacies that wish to stock this product, must enroll in the Adempas REMS and agree to comply with the requirements of the program.

Access this form online at www.adempasREMS.com, fax this form to 1-855-662-5200 or call the Adempas REMS at 1-855-44DEMAPS (1-855-443-6272).

Inpatient Pharmacy Information (* indicates required field)

- Type of Facility: [Select]
- Facility Name: [Enter]
- Address Line 1: [Enter]
- Address Line 2: [Enter]
- City: [Enter]
- State: [Select]
- Zip code: [Enter]
- Phone: [Enter]
- Fax: [Enter]

Ship To Information (* indicates required field)

- Ship to Address: [Select]
- Ship to Contact: [Enter]

Authorized Representative Information (* indicates required field)

- First Name: [Enter]
- Middle Initial: [Enter]
- Last Name: [Enter]
- Position/Title: [Select]
- Phone: [Enter]
- Email: [Enter]

Inpatient Pharmacy / Authorized Representative Acknowledgement

This inpatient pharmacy will:
- establish procedures and procedures to ensure the REMS requirements are met
- complete training in the Adempas REMS by reading the Prescriber and Pharmacy Guide
- assume responsibility for the training of all relevant staff on dispensing the Adempas REMS requirements, processes, and Adempas REMS materials prior to dispensing Adempas, using the Prescriber and Pharmacy Guide
- establish processes and procedures to verify the female patient is enrolled in the REMS or will be enrolled 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 pregnancy testing is complete and that the patient is counseled on the risk of embryonic/fetal toxicity, the need to use effective contraception, to get monthly pregnancy tests, and to inform the prescriber of a pregnancy immediately
- before dispensing, verify the patient is under the supervision and care of a certified prescriber, her reproductive status, and that 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 pregnancy testing is complete, and that the patient is counseled on the risk of embryonic/fetal toxicity, the need to use effective contraception, 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:
- verify the female patient is enrolled in the REMS through the processes and procedures established as a requirement of the REMS
- dispense no more than a 15-day temporary supply of Adempas to any female patient upon discharge from the healthcare facility
- at all times:
  - do not distribute, transfer, loan, or sell Adempas
  - report any pregnancies associated with the use of Adempas to Bayer at 1-888-440-2977 or send the information to DrugSafety@Bayer.com
  - comply with audits by the manufacturer or a third party on behalf of the manufacturer to ensure all processes and procedures are in place and being followed
  - maintain records of all processes and procedures including compliance with these processes and procedures

Note: If your inpatient pharmacy needs Adempas and is not certified in the Adempas REMS, contact the Adempas REMS Coordinating Center at 1-855-44DEMAPS (1-855-443-6272) for assistance in obtaining up to a 15-day supply of Adempas for a specific inpatient while enrolling in the program.

To report any adverse events, product technical complaints, medication errors or pregnancies associated with the use of Adempas, contact Bayer at 1-888-440-2977 or send the information to DrugSafety@Bayer.com.