

Initial REMS Approval: 10/2013

Most Recent Modification: 02/2016

NDA 204410

OPSUMIT[®] (macitentan) Endothelin Receptor Antagonist

Sponsor: Actelion Pharmaceuticals Ltd
Contact: Actelion Clinical Research Inc
1820 Chapel Avenue West
Cherry Hill, NJ 08002
[856-773-4300]

Risk Evaluation and Mitigation Strategy (REMS)

I. GOALS:

The goals of the REMS are:

1. To inform prescribers, patients, and pharmacists about the serious risk of teratogenicity and safe-use conditions for Opsumit
2. To minimize the risk of fetal exposure and adverse fetal outcomes in females of reproductive potential (FRP) prescribed Opsumit:
 - a) Females who are pregnant must not be prescribed Opsumit
 - b) Females taking Opsumit must not become pregnant

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with each Opsumit prescription in accordance with 21 CFR 208.24.

The Opsumit Medication Guide is part of the REMS and is appended.

B. Elements to Assure Safe Use

1. **Healthcare providers (HCPs) who prescribe Opsumit will be specially certified.**
 - a. Actelion will ensure that HCPs who prescribe Opsumit are specially certified. Actelion will ensure that to become certified, each healthcare provider who prescribes Opsumit agrees on the *Opsumit REMS Prescriber Enrollment and Agreement Form* to:

- i. Read the Opsumit Prescribing Information (PI), the Opsumit Medication Guide, and the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
- ii. Enroll all females in the Opsumit REMS Program by completing the *Opsumit Patient Enrollment and Consent Form*
- iii. Advise all females that Opsumit is only available through a restricted distribution program called the Opsumit REMS Program
- iv. Determine whether each female is of reproductive potential as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
- v. For FRP (as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*) patients:
 - 1) Review the Opsumit Medication Guide and the *Opsumit REMS Guide for Females Who Can Get Pregnant* with the patient prior to initiating treatment
 - 2) Counsel patients about the risk of teratogenicity and the need to use reliable contraception as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program* during Opsumit treatment and for one month following treatment discontinuation, and her medical options in the event of unprotected sexual intercourse or known or suspected contraception failure
 - 3) Order and review pregnancy tests prior to initiation of Opsumit treatment, monthly during treatment, and for one month following treatment discontinuation
 - 4) Counsel the patient if the patient fails to comply with required testing or if she is not using reliable contraception
 - 5) Counsel the patient to immediately contact her healthcare provider if she misses a menstrual period or suspects that she is pregnant
 - 6) Report a change or misclassification in reproductive status by completing the Opsumit REMS *Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within ten (10) business days of becoming aware of the change
- vi. For females of non-reproductive potential (FNRP) (as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*) patients:
 - 1) Pre-pubertal patients:
 - a) Review the Medication Guide with the patient and/or a parent/guardian
 - b) Counsel the patient and/or a parent/guardian about the risk of teratogenicity.

- c) Counsel the patient and/or a parent/guardian to immediately contact her healthcare provider if the patient begins to menstruate
 - d) Evaluate patients age 8 and older at least annually for any change in reproductive status and complete the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* verifying their reproductive potential status
 - e) Report a change or misclassification in reproductive status by completing the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within ten (10) business days of becoming aware of the change
- 2) Post-menopausal patients:
- a) Report a change or misclassification in reproductive status by completing the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within ten (10) business days of becoming aware of the change
- 3) Females with other medical reasons for permanent, irreversible infertility (as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*):
- a) Report any change or misclassification in reproductive status by completing the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change
- vii. Report any pregnancy during Opsumit treatment to Actelion with all available information
- b. Actelion will:
- i. Ensure prescribers' certification information is linked to their enrolled patients' information in a validated secure database.
 - ii. For all females, ensure that patient information from a new prescriber is linked in a validated secure database with certification information from the prior prescriber.
 - iii. Maintain a validated secure database of all certified prescribers in the Opsumit REMS program. Actelion will ensure that the prescribers' certification requirements are met and may de-certify non-compliant prescribers until the requirements are met.
 - iv. Ensure all materials listed in or appended to the Opsumit REMS Program will be available through the Opsumit REMS Program Website (www.OpsumitREMS.com) or by calling *Actelion Pathways*[®] at 1-866-228-3546 within 60 days of modification approval.
- c. The following are part of the REMS and are appended:
- i. *Opsumit Patient Enrollment and Consent Form*

- ii. *Opsumit Patient Enrollment and Consent Form - for VA use only*
- iii. *Opsumit REMS Guide for Females Who Can Get Pregnant*
- iv. *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
- v. *Opsumit REMS Prescriber Enrollment and Agreement Form*
- vi. *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*
- vii. *Opsumit REMS Website*

2. Pharmacies that dispense Opsumit will be specially certified

Outpatient Dispensing

- a. Actelion will ensure that pharmacies that dispense Opsumit are specially certified. Actelion will ensure that to be certified, pharmacies that dispense Opsumit have an authorized representative who is trained on the Opsumit REMS program and who attests that they will:
 - i. Train all dispensing staff on the Opsumit REMS Program procedures and REMS materials prior to dispensing Opsumit
 - ii. Put processes and procedures in place to ensure the following REMS requirements are met
 - a) Receive and accept the Opsumit Patient Enrollment and Consent Form only from *Actelion Pathways*
 - b) Dispense Opsumit only to patients who have a prescription written by a prescriber enrolled in the Opsumit REMS Program
 - c) Dispense Opsumit to females only if they are enrolled in the Opsumit REMS program
 - d) Dispense only up to a 30-day supply of Opsumit to FRP
 - e) Verify reproductive status of females with information provided by *Actelion Pathways* prior to each dispensing of Opsumit
 - f) Not transfer Opsumit to any pharmacy, practitioner or healthcare setting not certified by *Actelion Pathways*
 - g) For FRP patients:
 - 1) Counsel patients on the risk of serious birth defects and the need to use reliable contraception, as defined in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*, during Opsumit treatment and for one month after treatment discontinuation
 - 2) Inform patients of the need to complete a monthly pregnancy test and to inform their prescriber immediately if they suspect they are pregnant
 - 3) Dispense drug only upon completing the following process:
 - a) Obtain confirmation from the patient that pregnancy testing was completed
 - b) If unable to obtain confirmation that pregnancy testing was completed, or if the patient cannot be reached, obtain confirmation from the prescriber
 - c) If unable to obtain confirmation from the prescriber that pregnancy testing was completed, the certified pharmacy will:

- (i) Remind the prescriber of his/her obligation to order and review monthly pregnancy tests
 - (ii) Ask prescriber whether or not he/she authorizes the refill of Opsumit. The patient is eligible to receive a 30-day supply of Opsumit only if the prescriber authorizes the refill
- iii. Notify Actelion of any reports of pregnancy and provide all available information
- iv. Agree that the certified pharmacy may be audited by the FDA, Actelion, or a third party designated by Actelion
- b. Actelion will ensure that *Actelion Pathways* notifies certified pharmacies of a patient's change or misclassification in reproductive status within one business day of receipt of a completed *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*.

Inpatient Dispensing

- a. Actelion will ensure that only inpatient pharmacies (including, but not limited to, inpatient pharmacies in hospitals, long-term care facilities, prisons, and state psychiatric units) that are certified in the Opsumit REMS Program may stock Opsumit for patients being treated in the inpatient setting. In order for an inpatient pharmacy to become certified in the Opsumit REMS Program, an authorized representative must complete and submit an *Opsumit REMS Inpatient Pharmacy Enrollment Form*, agreeing to:
 - i. Complete training in the Opsumit REMS Program by reading the Opsumit Prescribing Information, Medication Guide and the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*.
 - ii. Train all dispensing staff on the Opsumit REMS Program requirements and Opsumit REMS materials before they dispense Opsumit
 - iii. Put processes and procedures in place to ensure the REMS requirements are met
 - a) Dispense Opsumit only to patients under the supervision and care of a healthcare provider who is enrolled in the Opsumit REMS program
 - b) Dispense Opsumit to a female only after she has been enrolled in the Opsumit REMS program or if she will be enrolled prior to discharge from the healthcare facility. A female who has not been enrolled by the certified prescriber will not have access to Opsumit in the outpatient setting until such time that registration has been completed
 - c) Dispense no more than a 15 day temporary supply of Opsumit, to any patient, upon discharge from the healthcare facility
 - d) Not transfer Opsumit to any pharmacy, practitioner or healthcare setting not certified by *Actelion Pathways*

- iv. Audits by the FDA, Actelion or third party designated by Actelion
 - v. Notify Actelion of any reports of pregnancy during Opsumit treatment and provide all available treatment information
 - vi. Develop a process to track compliance with the conditions above and provide information about compliance to Actelion upon request
- b. Actelion will ensure that if an inpatient pharmacy needs Opsumit for a specific inpatient and is not enrolled in the Opsumit REMS Program, the inpatient pharmacy can contact *Actelion Pathways* for assistance in obtaining up to a 15 day supply of Opsumit for a specific inpatient while initiating enrollment.
- c. The following materials are part of the REMS and are appended:
- i. *Opsumit REMS Inpatient Pharmacy Enrollment Form*
 - ii. *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
- 3. Opsumit will be dispensed to females with evidence or other documentation of safe use conditions**
- a. Actelion will ensure that to become enrolled, or when changing prescribers, each female signs the *Opsumit Patient Enrollment and Consent Form*.
 - b. In order to become enrolled by completing the *Opsumit Patient Enrollment and Consent Form*, FRPs must agree:
 - i. To read the Opsumit Medication Guide and the *Opsumit REMS Guide for Females Who Can Get Pregnant*
 - ii. To have a pregnancy test prior to initiation of treatment with Opsumit, monthly during Opsumit treatment, and for one month after stopping Opsumit
 - iii. To be counseled each month by the pharmacy on the need to use reliable contraception during Opsumit treatment and for one month after stopping Opsumit treatment
 - iv. To be contacted prior to each dispensing of Opsumit to obtain confirmation that pregnancy testing was completed
 - v. To be counseled on the requirements of the Opsumit REMS program and the risk of serious birth defects
 - vi. To immediately notify her healthcare provider if she misses a menstrual period or suspects that she is pregnant
 - vii. To be contacted by Actelion if she becomes pregnant while on Opsumit or within one month after treatment discontinuation

C. Implementation System

The Implementation System will include the following:

1. Actelion will maintain a validated secure database of certified dispensers and patients enrolled in the Opsumit REMS Program to monitor and evaluate implementation of the elements under Section B.2. and B.3. above.
2. Actelion will monitor the distribution of Opsumit to ensure that the drug is only shipped to certified dispensers.
3. Actelion will track Opsumit dispensing and review the amount of medication dispensed to individual patients enrolled in the Opsumit REMS Program.
4. Actelion will audit all certified outpatient pharmacies and distributors within 180 days after they are certified in the Opsumit REMS Program to ensure the Opsumit REMS Program is implemented as directed. *Actelion Pathways* will also be audited. Thereafter, Actelion will include the certified outpatient pharmacies, all distributors and *Actelion Pathways* in the company's annual audit plan. At least 10% of certified inpatient pharmacies that have ordered Opsumit will be audited each year. Corrective actions will be instituted if noncompliance is found.
5. Actelion will maintain *Actelion Pathways* to support patients, prescribers, certified pharmacies, and distributors in interfacing with the Opsumit REMS Program.
6. Actelion will ensure that all materials listed in or appended to the Opsumit REMS Program will be available through the Opsumit REMS Program Website (www.OpsumitREMS.com) or by calling *Actelion Pathways* at 1-866-228-3546.
7. Actelion will monitor and evaluate implementation of elements provided under Section B.2. and B.3. above and if needed, take steps to improve implementation of these elements.
8. Actelion will monitor certified inpatient and outpatient dispensers to ensure compliance with the Opsumit REMS Program and institute corrective actions if they are non-compliant.

D. Timetable for Submission of Assessments

Actelion will submit REMS Assessments for Opsumit to the FDA at 6 months and 1 year from the date of the initial REMS approval, and then annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Actelion will submit each assessment so that it will be received by the FDA on or before the due date.

Opsumit® Patient Enrollment and Consent Form

Complete this form for ALL patients.

Fax this completed form and copies of all insurance cards (front and back) to 1-866-279-0669.

Contact Actelion Pathways® at 1-866-228-3546 for questions.



E02201512

1 Patient Information (please print)

First name _____ MI _____ Last name _____ Gender Male Female

Birth date _____ Primary language _____ Email address _____

Primary phone # _____ Alternate phone # _____ Best time to call _____

Address _____ City _____ State _____ ZIP _____

Legal guardian _____ Relationship _____ Phone # _____

Emergency contact _____ Relationship _____ Phone # _____

Certified pharmacy preference (If left blank, this referral will be sent to the appropriate certified pharmacy based on the patient's existing benefits.)

2 Actelion Pathways Services Authorization

I authorize my healthcare providers, pharmacies, health plans or payers ("my health care organizations") to share personal and health information about me related to my Actelion PAH therapies ("my information") with Actelion Pharmaceuticals US, Inc., its affiliates, agents and contractors (collectively, "Actelion"). I understand that once my information is shared with Actelion, my information may be protected by certain state privacy laws but not by federal health privacy laws, and may be redisclosed by Actelion. Actelion agrees to protect my information and to use and share it only for the reasons listed below. I understand that my pharmacy may receive compensation in connection with sharing my information with Actelion as allowed under this Authorization.

I authorize my health care organizations to share my information with Actelion, in order for Actelion to: (1) contact me or my healthcare organizations, or others I have identified, about my disease or treatment; (2) confirm my health plan eligibility and benefits, identify other payers for my therapy, or determine whether I may be eligible for assistance programs; (3) enroll me in Actelion PAH therapies-related programs and provide therapy access support services; (4) perform analyses or improve or develop products, services, programs, or treatment, related to my disease; (5) provide me by any means of communication, including by e-mail, mail, or telephone (including voicemail), with information to educate or inform me about Actelion PAH therapies and ways to help me maintain my prescribed treatment; and (6) use and disclose my information for safety reasons or as required by law. I understand that if I do not sign this form, I will still be eligible for health plan benefits and my treatment and payment for my treatment by my healthcare providers and pharmacy will not be affected, but I will not have access to the Actelion services and support described above.

This Authorization will expire 10 years from the date signed below unless a shorter period is required by the law of my state of residence. I may discuss the scope of my Authorization at any time by calling 1-866-875-0277 and may cancel it by writing a letter saying I cancel my Authorization, and mailing it to Actelion Pharmaceuticals US, Inc.: PO Box 826, South San Francisco, CA 94083. My cancellation will not be effective until after Actelion receives it and my health care organizations are notified of it by Actelion, and it will not apply to prior actions taken by Actelion and my health care organizations based on this Authorization. I have a right to request and receive a copy of this Authorization in the same ways described above for cancellation.

3 Female Patient Agreement

For All Females: I acknowledge that I understand that Opsumit is only available through a restricted distribution program under an FDA-required Risk Evaluation and Mitigation Strategy (REMS).

For Females Who Can Get Pregnant: I acknowledge that I have been counseled on the risks of Opsumit, including the risk of serious birth defects. I have read the *Opsumit Medication Guide* and the *Opsumit REMS Guide for Females Who Can Get Pregnant*. I understand that I will be contacted by Actelion and/or its agents and contractors to receive counseling on the risk of serious birth defects, the need to use reliable contraception during Opsumit treatment and for one month after stopping Opsumit treatment, the importance of not becoming pregnant, and to ensure that I have completed pregnancy testing before I start Opsumit, monthly before each refill, and for one month after stopping Opsumit. I agree to be counseled each month by the certified pharmacy on the need to use reliable contraception during Opsumit treatment and for one month after stopping Opsumit. I understand that I must immediately contact my healthcare provider if I miss a menstrual period or suspect that I am pregnant; and that I may be contacted by Actelion and/or its agents and contractors to obtain information about my pregnancy, if I become pregnant.

For Pre-pubertal Females: I acknowledge that I have been counseled on the risks of Opsumit, including the risk of serious birth defects, and that I have read the *Opsumit Medication Guide*. I understand that I must immediately contact my healthcare provider if I get my menstrual period.

For Post-menopausal Females: I acknowledge that I have received and read the *Opsumit Medication Guide*.

For Females with other medical reasons for permanent, irreversible infertility: I acknowledge that I have received and read the *Opsumit Medication Guide*.

★ (REQUIRED FOR ALL PATIENTS) Patient or Parent/Guardian Signature _____ Date _____

4 Prescriber Information

First name _____ Middle initial _____

Last name _____

Address _____ City _____

State _____ ZIP _____ Phone # _____

Fax _____ NPI # _____

Opsumit ID _____

Office contact and email address _____

★ (REQUIRED FOR ALL FEMALES) Patient or Parent/Guardian Signature _____ Date _____

5 Diagnosis, Prescription, and Shipping Information (Check ONLY ONE Box for the Diagnosis Related to Opsumit Treatment)

Pulmonary Arterial Hypertension (PAH)

Idiopathic PAH Heritable PAH Connective Tissue Disorder Congenital Heart Disease

Other _____

Opsumit (macitentan) dosing: 10 mg tablet(s) NDC66215-501-30

_____ Time(s) daily Quantity: _____ Refills: _____

Instructions for use: _____

Ship to: Patient home Prescriber office Other _____

Address _____

City _____ State _____ ZIP _____

6 Prescriber Authorization: If your patient is FEMALE, check correct female patient category (please see definitions of these terms on the following page):

REQUIRED (Check one box)

Female of Reproductive Potential
If this patient is a Female of Reproductive Potential, has a negative pregnancy test been completed prior to prescribing Opsumit?

Female of Non-Reproductive Potential

Pre-pubertal Female

Post-menopausal Female

Female with other medical reasons for permanent, irreversible infertility

I certify that the above therapy ordered is medically necessary and agree to follow the "Prescriber Requirements" indicated on the second page of this form. Further, I hereby authorize Actelion and/or its designated representative(s), to act on my behalf for the limited purposes of providing this prescription to the certified specialty pharmacy for patient treatment purposes.

Reference ID: 3890030

★ (REQUIRED FOR ALL PRESCRIBERS) Prescriber Signature _____ Date _____

Definitions of Reproductive Potential Status

Females of Reproductive Potential

- Females of reproductive potential include girls who have entered puberty and all females who have a uterus and have not passed through menopause (as defined below)
- For the purposes of this REMS, puberty includes those girls who are at least Tanner Stage 3 and have not yet had a menses (premenarchal)

Females of Non-Reproductive Potential

- Pre-pubertal Females: Females who are at Tanner Stages 1 and 2 are not considered to be of reproductive potential
- Post-menopausal Females: Females who have passed through menopause. Menopause is defined as 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy) or post-surgical form bilateral oophorectomy
- Females with other medical reasons for permanent, irreversible infertility

Prescriber Requirements

For All Females

- I acknowledge that I have counseled the patient (and parent/guardian when appropriate) that Opsumit is only available through a restricted distribution program under an FDA-required REMS
- I will evaluate the patient and agree to document any change or misclassification in reproductive potential status by submitting an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change

For Females of Reproductive Potential

- I acknowledge that I have counseled the patient (and parent/guardian when appropriate) on the risks of Opsumit, including the risk of serious birth defects, and that I have reviewed the *Opsumit Medication Guide* and the *Opsumit REMS Guide for Females Who Can Get Pregnant* with the patient (and parent/guardian when appropriate)
- I will order and review pregnancy tests prior to initiation of Opsumit treatment, monthly during treatment, and for 1 month after stopping treatment in accordance with the Opsumit REMS Program

For Pre-pubertal Females

- I acknowledge that I have counseled the patient and parent/guardian on the risks of Opsumit, including the risk of serious birth defects, and that I have reviewed the *Opsumit Medication Guide* with the patient and parent/guardian
- I will evaluate the patient's reproductive potential status, verify reproductive potential status annually for Pre-pubertal Females who are at least 8 years of age and older, and agree to report any change or misclassification in reproductive potential status on an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change

7 Fax this form to 1-866-279-0669

Please visit www.OpsumitREMS.com or call 1-866-ACTELION (1-866-228-3546) for more information about the Opsumit REMS Program.

Opsumit® Patient Enrollment and Consent Form

FOR VA USE ONLY

Complete this form for ALL patients.

Fax this completed form and copies of all insurance cards (front and back) to 1-866-279-0669.

Contact Actelion Pathways® at 1-866-228-3546 for questions.



EO2201512

1 Patient Information (please print)

First name		MI	Last name		<input type="checkbox"/> Male <input type="checkbox"/> Female
Gender					
Birth date	Primary language		Email address		
Primary phone #	Alternate phone #		Best time to call		
Address		City	State	ZIP	
Legal guardian	Relationship		Phone #		
Emergency contact	Relationship		Phone #		

2 Actelion Pathways Services Authorization

I allow the Veterans Healthcare Administration, my healthcare providers, pharmacy providers, and health plans to use and share personal and health information about me and my Actelion therapies ("my information") with Actelion Pharmaceuticals US, Inc. and its contractors (collectively, "Actelion") for the following purposes: 1) to establish my benefit eligibility, including benefit eligibility for laboratory services; 2) to communicate with my healthcare providers, health plans, other payers, and pharmacies about my medical care; and 3) to help provide any therapy access support services to me that will assist in my Actelion therapy. Actelion may leave messages for me on the telephone number(s) that I provide. These messages may state that I take an Actelion medication as well as provide me with additional information. I also allow the sharing of my information to specific people I have identified.

I understand that Actelion does not promise to find ways to pay for my medications. I know that I am responsible for the costs of my care. I understand that once my health information has been shared with Actelion, privacy laws may no longer protect it; however, Actelion agrees to protect my information and to use and share it only for reasons listed above or as required by law. I understand that my certified pharmacy may receive payment in connection with the use and disclosure of my information for purposes allowed under this permission. If I do not sign this form, my eligibility for health plan benefits and treatment by my healthcare provider will not change, but I will not have access to the Actelion support services. I may also cancel my permission at any time by writing a letter saying I cancel my written permission and mailing to Actelion Pharmaceuticals US, Inc.: PO Box 826, South San Francisco, CA 94083 or by faxing it to 1-866-279-0669 or by calling 1-866-228-3546. I am allowed a copy of this signed agreement. This written permission will expire 10 years after the date on which I sign it.

3 Female Patient Agreement

For All Females: I acknowledge that I understand that Opsumit is only available through a restricted distribution program under an FDA-required Risk Evaluation and Mitigation Strategy (REMS).

For Females Who Can Get Pregnant: I acknowledge that I have been counseled on the risks of Opsumit, including the risk of serious birth defects. I have read the *Opsumit Medication Guide* and the *Opsumit REMS Guide for Females Who Can Get Pregnant*. I understand that I will be contacted by Actelion and/or its agents and contractors to receive counseling on the risk of serious birth defects, the need to use reliable contraception during Opsumit treatment and for one month after stopping Opsumit treatment, the importance of not becoming pregnant, and to ensure that I have completed pregnancy testing before I start Opsumit, monthly before each refill, and for one month after stopping Opsumit. I agree to be counseled each month by the certified pharmacy on the need to use reliable contraception during Opsumit treatment and for one month after stopping Opsumit. I understand that I must immediately contact my healthcare provider if I miss a menstrual period or suspect that I am pregnant; and that I may be contacted by Actelion and/or its agents and contractors to obtain information about my pregnancy, if I become pregnant.

For Pre-pubertal Females: I acknowledge that I have been counseled on the risks of Opsumit, including the risk of serious birth defects, and that I have read the *Opsumit Medication Guide*. I understand that I must immediately contact my healthcare provider if I get my menstrual period.

For Post-menopausal Females: I acknowledge that I have received and read the *Opsumit Medication Guide*.

For Females with other medical reasons for permanent, irreversible infertility: I acknowledge that I have received and read the *Opsumit Medication Guide*.

★ (REQUIRED FOR ALL PATIENTS) Patient or Parent/Guardian Signature _____ Date _____

4 Prescriber Information

First name	Middle initial	Last name	
Address			
City	State	ZIP	
Phone #	Fax #		
NPI #	Opsumit ID		

Office contact and email address _____

6 Diagnosis, Prescription, and Shipping Information

(Check ONLY ONE box for the Diagnosis Related to Opsumit Treatment)

Pulmonary Arterial Hypertension (PAH)

- Idiopathic PAH Heritable PAH Connective Tissue Disorder Congenital Heart Disease
- Other _____

Opsumit (macitentan) dosing: 10 mg tablet(s) NDC66215-501-30

_____ Time(s) daily Quantity: _____ Refills: _____

Instructions for use: _____

Ship to: Patient home (use address in section 1) VA Pharmacy location (use address in section 5)

Reference ID: 3890030

★ (REQUIRED FOR ALL FEMALES) Patient or Parent/Guardian Signature _____ Date _____

5 VA Pharmacy Information

VA Pharmacy	
Address	
City	State ZIP
Contact	
Phone #	Fax#

7 Prescriber Authorization: If your patient is FEMALE, check correct female patient category (please see definitions of these terms on the following page):

REQUIRED (Check one box)

Female of Reproductive Potential

If this patient is a Female of Reproductive Potential, has a negative pregnancy test been completed prior to prescribing Opsumit?

Yes No

Female of Non-Reproductive Potential

Pre-pubertal Female

Post-menopausal Female

Female with other medical reasons for permanent, irreversible infertility

I certify that the above therapy ordered is medically necessary and agree to follow the "Prescriber Requirements" indicated on the second page of this form. Further, I hereby authorize Actelion and/or its designated representative(s), to act on my behalf for the limited purposes of providing this prescription to the certified specialty pharmacy for patient treatment purposes.

★ (REQUIRED FOR ALL PRESCRIBERS) Prescriber Signature _____ Date _____

Definitions of Reproductive Potential Status

Females of Reproductive Potential

- Females of reproductive potential include girls who have entered puberty and all females who have a uterus and have not passed through menopause (as defined below)
- For the purposes of this REMS, puberty includes those girls who are at least Tanner Stage 3 and have not yet had a menses (premenarchal)

Females of Non-Reproductive Potential

- Pre-pubertal Females: Females who are at Tanner Stages 1 and 2 are not considered to be of reproductive potential
- Post-menopausal Females: Females who have passed through menopause. Menopause is defined as 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy) or post-surgical form bilateral oophorectomy
- Females with other medical reasons for permanent, irreversible infertility

Prescriber Requirements

For All Females

- I acknowledge that I have counseled the patient (and parent/guardian when appropriate) that Opsumit is only available through a restricted distribution program under an FDA-required REMS
- I will evaluate the patient and agree to document any change or misclassification in reproductive potential status by submitting an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change

For Females of Reproductive Potential

- I acknowledge that I have counseled the patient (and parent/guardian when appropriate) on the risks of Opsumit, including the risk of serious birth defects, and that I have reviewed the *Opsumit Medication Guide* and the *Opsumit REMS Guide for Females Who Can Get Pregnant* with the patient (and parent/guardian when appropriate)
- I will order and review pregnancy tests prior to initiation of Opsumit treatment, monthly during treatment, and for 1 month after stopping treatment in accordance with the Opsumit REMS Program

For Pre-pubertal Females

- I acknowledge that I have counseled the patient and parent/guardian on the risks of Opsumit, including the risk of serious birth defects, and that I have reviewed the *Opsumit Medication Guide* with the patient and parent/guardian
- I will evaluate the patient's reproductive potential status, verify reproductive potential status annually for Pre-pubertal Females who are at least 8 years of age and older, and agree to report any change or misclassification in reproductive potential status on an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change

8 Fax this form to 1-866-279-0669

Please visit www.OpsumitREMS.com or call 1-866-ACTELION (1-866-228-3546) for more information about the Opsumit REMS Program.

Opsumit[®] REMS (Risk Evaluation and Mitigation Strategy) Guide for Females Who Can Get Pregnant

Information to help you throughout your treatment with Opsumit



*Please see accompanying full Prescribing Information, including **BOXED WARNING** for birth defects, and Medication Guide.*

ACTELION
Pathways[®]

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What is Opsumit?

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

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

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

What are the serious risks of Opsumit?

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

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

What is the Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program?

The Opsumit REMS is a program to tell patients and healthcare providers about the risk of serious birth defects when taking Opsumit. This program is required by the Food and Drug Administration (FDA). All females must enroll in the Opsumit REMS Program to receive Opsumit. REMS stands for **R**isk **E**valuation and **M**itigation **S**trategy.

How do I enroll in the Opsumit REMS Program?

There are several steps you must take:

1. Read this *Opsumit REMS Guide for Females Who Can Get Pregnant* and the *Opsumit Medication Guide* (which comes with your medicine)
2. Ask your healthcare provider any questions you have about taking Opsumit and the Opsumit REMS Program
3. Make sure you understand:
 - The benefits and risks of Opsumit
 - How to enroll and take part in the Opsumit REMS Program
4. Complete and sign the *Opsumit Patient Enrollment and Consent Form* with your healthcare provider. Your healthcare provider will fill out most of the enrollment form for you and will send the form to *Actelion Pathways*®. *Actelion Pathways* runs the Opsumit REMS Program

What are the Opsumit® REMS Program requirements for me?

- Females who can get pregnant must have a negative pregnancy test before starting Opsumit, each month for as long as they are being treated with Opsumit, and for one month after they stop taking Opsumit. Your healthcare provider will order the pregnancy tests for you
 - 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)
- You must use reliable birth control at all times when taking Opsumit and for one month after stopping Opsumit. Your birth control options are listed on page 5
- 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 (eg, 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
- Opsumit is not available at your local pharmacy. You must receive Opsumit through a certified pharmacy (sometimes called a specialty pharmacy)
 - Your pharmacy will call you every month to ask if you have completed a pregnancy test before shipping your Opsumit to your home or another shipping address you choose
- You may not receive your Opsumit refill on time if you do not confirm with the pharmacy that you have had your monthly pregnancy test

What are my birth control options?

Your healthcare provider will talk with you about your birth control options before starting Opsumit. 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.

Acceptable birth control options

Option 1	OR	Option 2	OR	Option 3	OR	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

How will I receive Opsumit®?

Opsumit is available only through a certified pharmacy (sometimes called a specialty pharmacy).

- *Actelion Pathways*® provides support and services that help patients with their PAH medicines. Once you are enrolled, a Patient Case Manager will work with you to get your Opsumit prescription filled by a pharmacy
- Before your first prescription is filled, the pharmacy will call you to schedule a shipment of Opsumit that will come right to your home
- The *Opsumit Medication Guide* will be included in the package
- Read the *Opsumit Medication Guide* each time you receive it. Important information may have been added or changed

For a list of certified pharmacies, please call *Actelion Pathways* at **1-866-ACTELION (1-866-228-3546)**.

Your steps to treatment with Opsumit

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

FIRST:

- Review the *Opsumit REMS Guide for Females Who Can Get Pregnant* and the *Opsumit Medication Guide* with your healthcare provider
- Make sure you understand the risks and benefits of taking Opsumit
- Go for your pregnancy test
- Enroll in the Opsumit REMS Program

NEXT:

- Expect a call from your Patient Case Manager. He or she will help you get your Opsumit prescription filled by one of the certified pharmacies
- Expect a call from the pharmacy to schedule your first shipment

EVERY MONTH:

- Read the *Opsumit Medication Guide* that comes with every shipment
- Use reliable birth control method(s) agreed upon with your healthcare provider—during treatment and for one month after you stop taking Opsumit
- 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 Opsumit. 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



The Opsumit® REMS Program is administered by *Actelion Pathways*®.

You can reach *Actelion Pathways* by calling toll free at
1-866-ACTELION (1-866-228-3546).

For more information about the Opsumit REMS Program,
please visit www.OpsumitREMS.com.

*Please see accompanying full Prescribing Information, including
BOXED WARNING for birth defects, and Medication Guide.*

The logo for Opsumit macitentan tablets 10 mg. It features a stylized graphic of a red and blue arrow pointing right, above the word "Opsumit" in a large, blue, sans-serif font. Below "Opsumit" is the text "macitentan tablets 10 mg" in a smaller, blue, sans-serif font.

Opsumit.
macitentan tablets 10 mg

Prescriber and Pharmacy Guide for the Opsumit[®] REMS Program

(Risk Evaluation and Mitigation Strategy)

Changes to the Opsumit Risk Evaluation and Mitigation Strategy (REMS) Program November 2015

- New definition of Female of Non-Reproductive Potential (page 4)
- Revised Form: *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*
- Audits will be performed for a select number of inpatient pharmacies



Please see accompanying full Prescribing Information,
including **BOXED WARNING** for teratogenicity.

ACTELION
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Introduction to Opsumit® (macitentan)

Indication

Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression. Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). Opsumit also reduced hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients were treated with Opsumit monotherapy or in combination with phosphodiesterase-5 inhibitors or inhaled prostanoids. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

Risk of teratogenicity

Opsumit is contraindicated in females who are pregnant. Opsumit may cause fetal harm when administered to a pregnant woman. Opsumit was consistently shown to have teratogenic effects when administered to animals. If Opsumit is used during pregnancy, apprise the patient of the potential hazard to a fetus. To prevent pregnancy, females of reproductive potential must use reliable contraception during treatment and for one month after stopping Opsumit. Patients must not become pregnant while taking Opsumit.

Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program

Due to the risk of teratogenicity, Opsumit is only available to females through a restricted distribution program required by the FDA called the Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program.

The purpose of the Opsumit REMS Program is to:

1. Inform prescribers, patients, and pharmacists about the serious risk of teratogenicity and safe-use conditions for Opsumit
2. Minimize the risk of fetal exposure and adverse fetal outcomes in females of reproductive potential who are prescribed Opsumit
 - a. Females who are pregnant must not be prescribed Opsumit
 - b. Females taking Opsumit must not become pregnant

Opsumit REMS Program overview

- All healthcare providers must enroll in the Opsumit REMS Program and comply with the requirements to prescribe Opsumit
- All female patients must enroll in the Opsumit REMS Program to receive Opsumit
- Prescribers must counsel Females of Reproductive Potential and Pre-pubertal Females of Non-Reproductive Potential about the risks of Opsumit, including the risk of serious birth defects
- Prescribers must order and review pregnancy testing for Females of Reproductive Potential prior to initiation of treatment, monthly during treatment, and one month after stopping treatment
- Prescribers must report any change or misclassification in a female's reproductive potential status to the Opsumit REMS Program

- Definitions of Reproductive Potential Status

- Females of Reproductive Potential

- Females of reproductive potential include girls who have entered puberty and all females who have a uterus and have not passed through menopause (as defined below)

- For the purposes of this REMS, puberty includes those girls who are at least Tanner Stage 3 and have not yet had a menses (premenarchal)

- Females of Non-Reproductive Potential

- Pre-pubertal Females: Females who are at Tanner Stages 1 and 2 are not considered to be of reproductive potential

- Post-menopausal Females: Females who have passed through menopause. Menopause is defined as 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy) or post-surgical form bilateral oophorectomy

- Females with other medical reasons for permanent, irreversible infertility

- For Females of Reproductive Potential:

- Pregnancy must be ruled out prior to drug initiation, monthly during treatment, and one month after stopping treatment

- She must agree to be contacted by *Actelion Pathways*® if she becomes pregnant either while on Opsumit® or within one month of treatment discontinuation

- Only pharmacies certified in the Opsumit REMS Program can dispense Opsumit to outpatients

- Only inpatient pharmacies that are certified in the Opsumit REMS Program may stock Opsumit for inpatient use

Summary of Opsumit REMS Program requirements for female patients

All prescribers must be enrolled in the Opsumit REMS Program. To become enrolled, a healthcare provider must complete an *Opsumit REMS Prescriber Enrollment and Agreement Form* agreeing to follow the Opsumit REMS Program requirements. This form must be submitted to the Opsumit REMS Program.

All females must be enrolled in the Opsumit REMS Program in order to receive Opsumit. To become enrolled a patient must complete an *Opsumit Patient Enrollment and Consent Form* with her prescriber. This form must be submitted to the Opsumit REMS Program.

Prescribers must determine whether the patient is a Female of Reproductive Potential or a Female of Non-Reproductive Potential (Pre-pubertal Female, Post-menopausal Female, or a female with other medical reasons for permanent, irreversible infertility). **This category must be documented on the *Opsumit Patient Enrollment and Consent Form*.** (See definitions of Reproductive Potential Status.)

Based on whether the patient is a Female of Reproductive Potential or a Female of Non-Reproductive Potential (Pre-pubertal Female, Post-menopausal Female, or a female with other medical reasons for permanent, irreversible infertility), the prescriber must perform certain actions before initiating treatment, during treatment, and after the patient stops taking Opsumit.

Summary of Opsumit® REMS Program requirements for female patients (continued)

Requirement	Females of Reproductive Potential	Females of Non-Reproductive Potential	
		Pre-pubertal	Post-menopausal or other medical reasons for permanent, irreversible infertility
Prescriber enrolls female patients into Opsumit REMS Program	●	●	●
Prescriber counsels with <i>Opsumit REMS Guide for Females Who Can Get Pregnant</i>	●		
Prescriber counsels with <i>Opsumit Medication Guide</i> , including the risk of teratogenicity	●	●*	
Prescriber must order and review pregnancy tests prior to initiation of treatment, monthly during treatment, and for 1 month after stopping treatment	●		
Prescriber must verify reproductive status annually in Pre-pubertal patients 8 years of age or older by completing the <i>Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form</i>		●	
Prescriber must complete the <i>Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form</i> upon becoming aware of any change or misclassification in reproductive potential status within 10 business days of awareness	●	●	●

*Counsel Pre-pubertal Female patient and/or parent/guardian.

Prescriber's role in the Opsumit REMS Program

Healthcare providers must complete the following steps in the Opsumit REMS Program:

1. **Read** the Opsumit Prescribing Information and this guide to understand the risks of Opsumit and to learn about the Opsumit REMS Program
2. **Complete** an *Opsumit REMS Prescriber Enrollment and Agreement Form*
3. **Determine** the reproductive potential of female patients
4. **Educate and counsel** female patients about the risks of Opsumit
5. **Enroll** female patients into the Opsumit REMS Program by completing an *Opsumit Patient Enrollment and Consent Form*
6. **Check** patient's pregnancy status (if patient is a Female of Reproductive Potential)
7. **Monitor** pregnancy and reproductive potential status for female patients throughout treatment

The next section provides specific information on each step:

1. **Read** the Opsumit Prescribing Information and this guide to understand the risks of Opsumit and to learn about the Opsumit REMS Program
 - Prescribers must understand the risks of Opsumit and become familiar with the Opsumit REMS Program
2. **Complete** an *Opsumit REMS Prescriber Enrollment and Agreement Form*
 - By signing the form, you attest to understanding the risks of Opsumit and agree to comply with the Opsumit REMS Program
3. **Determine** the reproductive potential for female patients
 - Prescribers should identify female patients (captured on the *Opsumit Patient Enrollment and Consent Form*) as belonging to one of the following categories:
 - Female of Reproductive Potential (FRP)
 - or**
 - Female of Non-Reproductive Potential (FNRP) (choose one of the options below)
 - Pre-pubertal Female of Non-Reproductive Potential
 - Post-menopausal Female of Non-Reproductive Potential
 - Female with other medical reasons for permanent, irreversible infertility

Definitions are provided in the section "Opsumit REMS Program overview."

4. **Educate and counsel** female patients about the risks of Opsumit®

- For all females, prescribers must:
 - Advise the patient that Opsumit is only available through a restricted distribution program called the Opsumit REMS Program
 - Educate and counsel patients about the risks of Opsumit
- For Females of Reproductive Potential (FRP), prescribers must:
 - Review with her the *Opsumit Medication Guide* and the *Opsumit REMS Guide for Females Who Can Get Pregnant*
 - Educate her about the risk of teratogenicity; the need to use reliable contraception during Opsumit treatment and for one month following treatment discontinuation; and her need to consider medical options in the event of unprotected sexual intercourse or known or suspected contraception failure
 - Advise the patient of the requirement for initial and monthly pregnancy tests to confirm they are not pregnant, so they can begin and continue to receive Opsumit
 - Counsel her to immediately contact her healthcare provider if she misses a menstrual period or suspects she is pregnant
 - Counsel her that she must agree to be contacted prior to each shipment to confirm that a pregnancy test has been completed
- For Females of Non-Reproductive Potential (FNRP)
 - For a Post-menopausal Female or a female with other medical reasons for permanent, irreversible infertility, prescribers must provide the *Opsumit Medication Guide*—and instruct her to read it
 - For Pre-pubertal Females, prescribers must:
 - Review with her and her parent/guardian the *Opsumit Medication Guide*
 - Educate her and her parent/guardian about the risk of serious birth defects
 - Counsel her and her parent/guardian to immediately contact her healthcare provider if she gets her menstrual period
- Prescribers must counsel any patient who fails to comply with the program requirements

5. **Enroll** female patients into the Opsumit REMS Program by completing the *Opsumit Patient Enrollment and Consent Form*

- Confirm patient has agreed to comply with program requirements and has signed the form where indicated

- Fax the completed form, along with all patient insurance information, including prescription drug benefits and medical benefits, to *Actelion Pathways*® at 1-866-279-0669. *Actelion Pathways* administers the Opsumit REMS Program

- Keep the original form with patient's records

6. **Check** patients' pregnancy status (for Females of Reproductive Potential)

- Order and review pregnancy tests for the patient:
 1. Prior to initiating treatment
 2. Monthly during treatment
 3. One month after stopping treatment

7. **Monitor** patients throughout treatment

- For FRPs, prescribers must:
 - Order and review pregnancy tests monthly during treatment with Opsumit and for one month after stopping treatment
 - Notify the patient and Actelion if a patient's pregnancy test is positive
 - Monitor patients' reproductive status during treatment with Opsumit and report any changes or misclassifications to the Opsumit REMS Program by completing and submitting the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change
- For FNRPs, prescribers must:
 - Monitor patients' reproductive status during treatment with Opsumit and report any changes or misclassifications to the Opsumit REMS Program by completing and submitting the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change
 - For each Pre-pubertal Female who is at least 8 years of age and older, annually verify and report the reproductive status by completing and submitting the *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*

Contraception options for FRPs

All FRPs must use reliable contraception during Opsumit® treatment and for one month after stopping treatment. They should also have contraceptive counseling with either the prescriber or another designated healthcare provider trained in contraceptive counseling. Please refer to the table below for a complete list of acceptable contraceptive methods. A similar table can be found in the *Opsumit REMS Guide for Females Who Can Get Pregnant* and should be used to discuss acceptable birth control options with patients. The patient should be instructed to select one of the options listed below.

- Educate and counsel females of reproductive potential about medical options in the event of unprotected sex or known or suspected contraceptive failure
- Remind patients to report any delay in getting a period or any other reason of suspected pregnancy during treatment to you immediately
- If pregnancy is suspected for any reason, a pregnancy test must be performed
- The prescriber must notify Actelion at 1-866-228-3546 of any pregnancies that occur during treatment or within 1 month of discontinuation

Contraceptive options for Females of Reproductive Potential

Acceptable birth control options

Option 1	OR	Option 2	OR	Option 3	OR	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

Please see accompanying full Prescribing Information, including **BOXED WARNING** for teratogenicity.

Certified pharmacies

Due to the risk of serious birth defects, Opsumit® is only available via a network of certified pharmacies. For a list of certified pharmacies please call *Actelion Pathways*® at 1-866-228-3546.

Actelion Pathways is Actelion's services and support program that administers the Opsumit REMS Program.

OUTPATIENT PHARMACY CERTIFICATION:

Only a limited number of certified pharmacies will dispense Opsumit for outpatients. Prior to dispensing Opsumit to any female, the pharmacy will confirm that the female and the prescriber who wrote the prescription are enrolled in the Opsumit REMS Program. If either the female or prescriber is not enrolled, Opsumit will not be dispensed.

Females of Reproductive Potential and Pre-pubertal Females will only be able to get a 30-day supply of Opsumit at one time. The *Opsumit Medication Guide* will be provided to all patients each time Opsumit is dispensed.

Females of Reproductive Potential will be contacted each month by the pharmacy to arrange dispensing of Opsumit. The pharmacy will:

- Ask if she has had a pregnancy test within the last month
- Counsel her on the need to use reliable contraception during Opsumit treatment and for one month after stopping treatment
- Counsel her to inform her prescriber immediately if she misses a menstrual period or suspects that she may be pregnant, or if her reproductive status changes

For Pre-pubertal Females, pharmacies will:

- Counsel her to inform her prescriber immediately if her reproductive status changes

INPATIENT PHARMACY CERTIFICATION:

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

- Dispense only to those patients under the supervision and care of a healthcare provider who is enrolled in the Opsumit REMS Program
- Dispense to a female patient only after she has been enrolled in the Opsumit REMS Program or if she will be enrolled prior to discharge from this healthcare facility. A female who has not been enrolled by the certified prescriber will not have access to Opsumit in the outpatient setting until such time that registration has been completed
- Dispense no more than a fifteen- (15-) day temporary supply of Opsumit upon discharge of any patient
- Not transfer Opsumit to any pharmacy, practitioner, or healthcare setting not certified by *Actelion Pathways*

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

- Read the Opsumit Prescribing Information, *Opsumit Medication Guide*, and *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
- Put processes and procedures in place to ensure the Opsumit REMS Program requirements are met
- Ensure training of dispensing staff on the Opsumit REMS Program procedures and materials, including the *Prescriber and Pharmacy Guide for the Opsumit REMS Program* prior to dispensing Opsumit
- Notify Actelion Pharmaceuticals US, Inc. ("Actelion") or FDA if any patient becomes pregnant during Opsumit treatment
- Develop a process to track compliance with the conditions above and provide information about its compliance to Actelion
- Agree that this pharmacy may be audited by the FDA, Actelion, or a designated third-party
- Agree to follow the REMS requirements by completing and submitting an *Opsumit REMS Inpatient Pharmacy Enrollment Form* to the Opsumit REMS Program
 - Authorized representatives can complete the *Opsumit REMS Inpatient Pharmacy Enrollment Form*:
 - By fax at 1-866-279-0669
 - By calling the Opsumit REMS Program at 1-866-228-3546

If an inpatient pharmacy needs Opsumit and is not enrolled in the Opsumit REMS Program, the inpatient pharmacy can contact *Actelion Pathways* at 1-866-228-3546 for assistance in obtaining a 15-day supply of Opsumit for a specific inpatient while initiating enrollment.

To learn more about the serious risks associated with Opsumit, please refer to the full Prescribing Information including BOXED WARNING, *Opsumit Medication Guide*, and the *Prescriber and Pharmacy Guide for the Opsumit REMS Program* and the *Opsumit REMS Guide for Females Who Can Get Pregnant*. These materials are available at www.OpsumitREMS.com.

If you have questions about Opsumit REMS Program enrollment, or if you would like more information about Opsumit, you can reach *Actelion Pathways* by calling toll-free at 1-866-ACTELION (1-866-228-3546).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.



The Opsumit® REMS Program is administered by *Actelion Pathways*®.

You can reach *Actelion Pathways* by calling toll free
1-866-ACTELION (1-866-228-3546).

For more information about the Opsumit REMS Program,
please visit www.OpsumitREMS.com.

*Please see accompanying full Prescribing Information,
including **BOXED WARNING** for teratogenicity.*



Opsumit® REMS Prescriber Enrollment and Agreement Form

Complete and fax this form to *Actelion Pathways*® at 1-866-279-0669.

You can also reach *Actelion Pathways* via phone at 1-866-ACTELION (1-866-228-3546)



PO2201512

Prescriber Information (please print)

First name _____ MI _____ Last name _____
Email address _____ NPI # _____ Professional designation _____
 MD DO PA NP

In the event you are unavailable, is there another person we can contact on your behalf? Yes No
If yes, please indicate.

Name _____ Phone _____

Office Practice/Clinic Information (please print)

Primary

Office practice/Clinic name _____ Affiliated hospital _____
Specialty _____ Office contact name _____ Office contact phone _____
Office email address _____ Phone _____ Fax _____
Address _____ City _____
State _____ ZIP _____ Preferred method of contact _____
 Phone Fax Email

Secondary

Office practice/Clinic name _____ Affiliated hospital _____
Specialty _____ Office contact name _____ Office contact phone _____
Office email address _____ Phone _____ Fax _____
Address _____ City _____
State _____ ZIP _____ Preferred method of contact _____
 Phone Fax Email

Opsumit REMS Prescriber Agreement

By signing below, you signify your understanding of the risks of Opsumit treatment and your obligation as an Opsumit prescriber to educate your female patients about the Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program, monitor them appropriately, and report any pregnancies to the Opsumit REMS Program.

Specifically, you attest to the following:

- I have read the Opsumit Prescribing Information, the *Opsumit Medication Guide*, and the *Prescriber and Pharmacy Guide for the Opsumit REMS Program* and agree to comply with the Opsumit REMS Program requirements
- I agree to enroll all female patients into the Opsumit REMS Program
- I will:
 - Determine the reproductive potential status of all female patients using the definitions provided in the *Prescriber and Pharmacy Guide for the Opsumit REMS Program*
 - Advise all females that Opsumit is only available through a restricted distribution program called the Opsumit REMS Program
 - Counsel Females of Reproductive Potential (FRP) on the risks of Opsumit, including the risk of serious birth defects, and review the *Opsumit Medication Guide* and the *Opsumit REMS Program Guide for Females Who Can Get Pregnant* with the patient
 - Counsel the Pre-pubertal Female patients and parent/guardian on the risks of Opsumit, including the risk of serious birth defects, and review the *Opsumit Medication Guide* with the patient and parent/guardian
 - Counsel FRPs to immediately contact their healthcare provider if they miss a menstrual period or suspect pregnancy
 - Counsel Pre-pubertal Female patients and parent/guardian to immediately contact her healthcare provider if the patient begins to menstruate
 - Verify the reproductive potential status annually for Pre-pubertal Females who are at least 8 years of age and older by submitting an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*
 - Order and review pregnancy tests for Females of Reproductive Potential prior to initiating treatment with Opsumit, monthly during treatment, and for one month after stopping treatment
 - Counsel FRPs to use reliable contraception during Opsumit treatment, and for one month after stopping treatment; and discuss their medical options in the event of unprotected sexual intercourse or known or suspected contraceptive failure
 - Report any change or misclassification in reproductive potential status by submitting an *Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* within 10 business days of becoming aware of the change
 - Counsel female patients who fail to comply with the Opsumit REMS Program requirements
 - Notify Actelion of any pregnancies at 1-866-ACTELION (1-866-228-3546)

Signature _____ Date _____

Please visit www.OpsumitREMS.com or call 1-866-ACTELION (1-866-228-3546) for more information about the Opsumit REMS Program.

Opsumit® REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form

**NOTE: THIS FORM SHOULD NOT BE USED TOGETHER WITH THE ENROLLMENT FORM.
USE IT ONLY TO REPORT A CHANGE IN REPRODUCTIVE STATUS OR FOR PRE-PUBERTAL ANNUAL VERIFICATION.**

Complete this form to:

- 1) Change the reproductive status of any female patient within 10 business days of awareness of the change in reproductive status
- 2) Complete the annual verification of the reproductive potential status for Pre-pubertal Females 8 years of age or older

Fax this form to *Actelion Pathways®* at 1-866-279-0669.

Prescriber must complete this form within 10 business days of awareness of the change in reproductive status.

Patient Information (please print)

Patient Opsumit ID _____

First name _____ MI _____ Last name _____

Address _____

City _____ State _____ ZIP _____

Birth date _____ Phone _____

Prescriber Information (please print)

First name _____ MI _____ Last name _____

NPI # _____

Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

Opsumit Prescriber ID (if available) _____

Office contact and email address (optional) _____

Definitions of Reproductive Potential Status

Females of Reproductive Potential

- Females of reproductive potential include girls who have entered puberty and all females who have a uterus and have not passed through menopause (as defined below)
- For the purposes of this REMS, puberty includes those girls who are at least Tanner Stage 3 and have not yet had a menses (premenarchal)

Females of Non-Reproductive Potential

- Pre-pubertal females: Females who are at Tanner Stages 1 and 2 are not considered to be of reproductive potential
- Post-menopausal females: Females who have passed through menopause. Menopause is defined as 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy) or post-surgical form bilateral oophorectomy
- Females with other medical reasons for permanent, irreversible infertility

Select the most appropriate reason for submitting this form. (For reference, please see the Definitions of Reproductive Potential Status)

Change in Status

- Based on definitions of reproductive potential status, patient is (please check one):

- Female of Reproductive Potential
- Female of Non-Reproductive Potential – Patient is pre-pubertal
- Female of Non-Reproductive Potential – Patient is post-menopausal
- Female of Non-Reproductive Potential – Other medical reasons for permanent, irreversible infertility

- Reason for change in classification (please check one):

- Physiological transition
- Medical/surgical (please specify): _____
- Other (please specify): _____

- Annual Verification

- Patient remains a Pre-pubertal Female (8 years of age or older)

Prescriber acknowledgement (REQUIRED)

By signing, I certify that the patient's reproductive status as noted above is accurate, and that I will comply with the REMS requirements for my patient's reproductive potential status.

Prescriber signature _____

Title (MD/PA/NP, etc) _____

Date _____

Please visit www.OpsumitREMS.com or call 1-866-ACTELION (1-866-228-3546) for more information about the Opsumit REMS Program.



Opsumit® REMS Inpatient Pharmacy Enrollment Form

Complete and fax this form to **Actelion Pathways®** at 1-866-279-0669.

You can also reach **Actelion Pathways** via phone at 1-866-ACTELION (1-866-228-3546)



H02201512

Due to the risk of teratogenicity for female patients, Opsumit is available only through a restricted program called the Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program. In order for inpatients to receive Opsumit, females, as well as inpatient pharmacies that wish to stock this product, must enroll in the Opsumit REMS Program 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.

Inpatient pharmacy information (please print)

Name

- Hospital Nursing home Hospice Asylum/Mental facility Assisted Living Prison Rehabilitation
 Other (please specify): _____

Identification (please complete one of the following):

- Health Industry Number (HIN #) _____ National Provider Identifier (NPI #) _____
 Other identifier: _____

Address

City _____ State _____ ZIP _____

Phone # _____ Fax # _____

Ship to address (if different from above)

Address

City _____ State _____ ZIP _____

Phone # _____ Fax # _____

Authorized Representative information (please print)

Title:

- Hospital pharmacist Head of Pharmacy and Therapeutics (P&T) committee
 Other title: _____

Name

Authorized Representative phone # _____ Fax # _____

Authorized Representative email _____

Authorized Representative consent

This inpatient pharmacy will:

- Put processes and procedures in place to ensure the Opsumit REMS Program requirements are met
- Dispense only to those patients under the supervision and care of a healthcare provider who is enrolled in the Opsumit REMS Program
- Dispense to a female patient only after she has been enrolled in the Opsumit REMS Program or if she will be enrolled prior to discharge from this healthcare facility. A female who has not been enrolled by the certified prescriber will not have access to Opsumit in the outpatient setting until such time that registration has been completed
- Dispense no more than a fifteen- (15-) day temporary supply of Opsumit upon discharge of any patient
- Notify Actelion Pharmaceuticals US, Inc. ("Actelion") or FDA if any patient becomes pregnant during Opsumit treatment
- Not transfer Opsumit to any pharmacy, practitioner, or any healthcare setting not certified by *Actelion Pathways*
- Develop a process to track compliance with the conditions above and provide information about its compliance to Actelion

I attest that I have read the Opsumit Prescribing Information, *Medication Guide*, and *Prescriber and Pharmacy Guide for the Opsumit REMS Program* available at www.OpsumitREMS.com.

I will ensure training of dispensing staff on the Opsumit REMS Program procedures and materials, including the *Prescriber and Pharmacy Guide for the Opsumit REMS Program* prior to dispensing Opsumit.

I agree that this pharmacy may be audited by the FDA, Actelion, or a designated third-party.

Note: If your inpatient pharmacy needs Opsumit and is not enrolled in the Opsumit REMS Program, contact *Actelion Pathways* at 1-866-228-3546 for assistance in obtaining a 15-day supply of Opsumit for a specific inpatient while initiating enrollment.

Signature _____

Date _____

Please visit www.OpsumitREMS.com or call 1-866-ACTELION (1-866-228-3546) for more information about the Opsumit REMS Program.

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Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program

A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to manage serious risks associated with a drug product.

The Opsumit REMS Program is for females only. Male patients are not required to enroll in the Opsumit REMS Program.

The goals of the Opsumit REMS are:

- To inform prescribers, patients, and pharmacists about the risk of serious birth defects and safe-use conditions for Opsumit
- To minimize the risk of fetal exposure and adverse fetal outcomes in females of reproductive potential prescribed Opsumit:
 - a. Females who are pregnant must not be prescribed Opsumit
 - b. Females taking Opsumit must not become pregnant

Prescribers

For Prescriber Information

[Click Here](#)

Female Patients

For Patient Information

[Click Here](#)

Opsumit REMS Program Overview:

- All healthcare providers must enroll in the Opsumit REMS Program and comply with requirements to prescribe Opsumit
- All female patients must be enrolled in the Opsumit REMS Program to receive Opsumit
- Females of Reproductive Potential and Pre-pubertal Females of Non-Reproductive Potential are required to be counseled on the risks of Opsumit
- Females of Reproductive Potential are required to get monthly pregnancy testing
- A limited number of certified pharmacies will dispense Opsumit for outpatients. They must enroll in the Opsumit REMS Program and agree to the REMS requirements
- Pharmacies that supply inpatient use of Opsumit must also be certified by enrolling in the Opsumit REMS Program and agreeing to the REMS requirements

Changes to the Opsumit Risk Evaluation and Mitigation Strategy (REMS) Program November 2015

- New definition of Female of Non-Reproductive Potential
- Revised Form: [Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form](#)
- Audits will be performed for a select number of inpatient pharmacies

Opsumit® is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression. Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). Opsumit also reduced hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients were treated with Opsumit monotherapy or in combination with phosphodiesterase-5 inhibitors or inhaled prostanoids. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

Materials for Healthcare Providers

- ↓ [Prescriber and Pharmacy Guide for the Opsumit REMS Program](#)
- ↓ [Opsumit REMS Prescriber Enrollment and Agreement Form](#)
- ↓ [Opsumit Patient Enrollment and Consent Form](#)
- ↓ [Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form](#)

Materials for Female Patients

- ↓ [Opsumit REMS Guide for Females Who Can Get Pregnant](#)
- ↓ [Opsumit Medication Guide](#)

Prescriber Roles & Responsibilities

Healthcare providers must complete the following steps in the Opsumit REMS Program:

1. Read the [Opsumit Prescribing Information](#) and the [Prescriber and Pharmacy Guide for the Opsumit REMS Program](#) to understand the risks of Opsumit, and to learn about the Opsumit REMS Program

- Prescribers must understand the risks of Opsumit, and become familiar with the Opsumit REMS Program

2. Complete an [Opsumit REMS Prescriber Enrollment and Agreement Form](#)

- By signing the form, you will attest to understanding the risks of Opsumit and agree to comply with the Opsumit REMS Program. You can download the [Opsumit REMS Prescriber Enrollment and Agreement Form](#) here and fax it to [Actelion Pathways](#)* at 1-866-279-0669. [Actelion Pathways](#) administers the Opsumit REMS Program

3. Determine the reproductive potential for female patients

- Prescribers should identify female patients (captured on the [Opsumit Patient Enrollment and Consent Form](#)) as one of the following categories:
 - Female of Reproductive Potential
 - Or
 - Female of Non-Reproductive Potential (choose one of the options below)
 - Pre-pubertal Female of Non-Reproductive Potential
 - Post-menopausal Female of Non-Reproductive Potential
 - Female with other medical reasons for permanent, irreversible infertility

Definitions are provided in the "Opsumit REMS Program Overview" section of the [Prescriber and Pharmacy Guide for the Opsumit REMS Program](#).

4. Educate and counsel female patients about the risks of Opsumit

- For all females, prescribers must:
 - Advise the patient that Opsumit is only available through a restricted distribution program called the Opsumit REMS Program
 - Educate and counsel patients about the risks of Opsumit
- For Females of Reproductive Potential, prescribers must:
 - Review with her the [Opsumit Medication Guide](#) and the [Opsumit REMS Guide for Females Who Can Get Pregnant](#)
 - Educate her about
 - the risk of teratogenicity;
 - the need to use reliable contraception during Opsumit treatment and for one month following treatment discontinuation; and
 - her need to consider medical options in the event of unprotected sexual intercourse or known or suspected contraception failure.
 - Advise the patient of the requirement for initial and monthly pregnancy tests to confirm they are not pregnant, so they can begin and continue to receive Opsumit
 - Counsel her to immediately contact her healthcare provider if she misses a menstrual period or suspects she is pregnant
 - Counsel her that she must agree to be contacted prior to each shipment to confirm that the pregnancy tests have been completed
- For Females of Non-Reproductive Potential
 - For a Post-menopausal Female or a female with other medical reasons for permanent, irreversible infertility, prescribers must:
 - Provide the [Opsumit Medication Guide](#) and instruct her to read it
 - For Pre-pubertal Females, prescribers must:
 - Review with her and her parent/guardian the [Opsumit Medication Guide](#)
 - Educate her and her parent/guardian about the risk of serious birth defects
 - Counsel her and her parent/guardian to immediately contact her healthcare provider if she gets her menstrual period
- Prescribers must counsel any patient who fails to comply with the program requirements.

5. Enroll female patients into the Opsumit REMS Program by completing the [Opsumit Patient Enrollment and Consent Form](#)

- Confirm patient has agreed to comply with program requirements and has signed the form where indicated
- Fax the completed form to [Actelion Pathways](#) at 1-866-279-0669. [Actelion Pathways](#) administers the Opsumit REMS Program
- Keep the original form with patient's records

6. Check patients' pregnancy status (for Females of Reproductive Potential)

- Order and review pregnancy tests for the patient:
 1. prior to initiating treatment
 2. monthly during treatment
 3. one (1) month after stopping treatment

7. Monitor patients throughout treatment

- For Females of Reproductive Potential, prescribers must:
 - Order and review pregnancy tests monthly during treatment with Opsumit and for one month after stopping treatment
 - Notify the patient and Actelion if a patient's pregnancy test is positive
 - Monitor patients' reproductive status during treatment with Opsumit and report any changes or misclassifications to the Opsumit REMS Program by completing and submitting an [Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form](#) within 10 business days of becoming aware of the change.
- For Females of Non-Reproductive Potential, prescribers must:
 - Monitor patients' reproductive status during treatment with Opsumit and report any changes or misclassifications to the Opsumit REMS Program by completing and submitting the [Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form](#) within 10 business days of becoming aware of the change
 - For each Pre-pubertal Female who is at least 8 years of age and older, annually verify and report the reproductive status by completing and submitting the [Opsumit REMS Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form](#)



Reporting to Actelion
To report any pregnancies and suspected adverse reactions, contact Actelion at 1-866-228-3546.

Reporting to FDA MedWatch
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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Information for Female Patients

What is Opsumit (macitentan)?

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

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

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

What are the serious risks of Opsumit?

Opsumit can cause **serious birth defects** if taken during pregnancy. Women must not be pregnant when they start taking Opsumit or become pregnant while taking Opsumit.

What is the Opsumit REMS (Risk Evaluation and Mitigation Strategy) Program?

The Opsumit REMS Program is a program to tell patients and healthcare providers about the risk of serious birth defects when taking Opsumit. This program is required by the Food and Drug Administration (FDA). All females must enroll in the Opsumit REMS Program to receive Opsumit. REMS stands for **R**isk **E**valuation and **M**itigation **S**trategy.

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

- Talk to your healthcare provider about the risks and benefits of Opsumit
- Read:
 - a. The [Opsumit Medication Guide](#) and
 - b. The [Opsumit REMS Guide for Females Who Can Get Pregnant](#)
- Have a pregnancy test before you start taking Opsumit
- Have a pregnancy test before you receive your refill each month
- Use reliable forms of birth control during Opsumit treatment and for one month after stopping treatment with Opsumit
- Immediately notify your healthcare provider if you miss a menstrual period or suspect you are pregnant

Please see the resources below to learn more about taking Opsumit and the Opsumit REMS Program.



- Home
- Prescriber Roles & Responsibilities
- Information for Female Patients
- Pharmacy Certification
- Enrollment Forms & Other Resources
- Changes to the Opsumit REMS Program

Pharmacy Certification

Due to the risk of serious birth defects, Opsumit is only available through a network of certified pharmacies. For information on Opsumit certified pharmacies or wholesale distributors, please call *Actelion Pathways*® at 1-866-228-3546.

Outpatient Pharmacy Certification

Opsumit will be dispensed to outpatients by a limited number of certified pharmacies. Prior to dispensing Opsumit 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 Opsumit REMS Program. If either the female or prescriber is not enrolled, Opsumit will not be dispensed.

For Females of Reproductive Potential, pharmacies will:

- Ask the patient if she has had a pregnancy test within the last month
- Counsel her on the need to use reliable contraception during Opsumit treatment and for one month after stopping treatment
- Counsel her to inform her prescriber immediately if she misses a menstrual period or suspects that she may be pregnant or if her reproductive status changes

For Pre-pubertal Females, pharmacies will:

- Counsel her to inform her healthcare provider immediately if her reproductive status changes

Females of Reproductive Potential and Pre-pubertal Females will only be able to get a 30 day supply of Opsumit at one time. The [Opsumit Medication Guide](#) will be provided to all patients each time Opsumit is dispensed.

Inpatient Pharmacy Certification

This inpatient pharmacy will:

- Dispense only to those patients under the supervision and care of a healthcare provider who is enrolled in the Opsumit REMS Program
- Dispense to a female patient only after she has been enrolled in the Opsumit REMS Program or if she will be enrolled prior to discharge from this healthcare facility. A female who has not been enrolled by the certified prescriber will not have access to Opsumit in the outpatient setting until such time that registration has been completed
- Dispense no more than a fifteen (15) day temporary supply of Opsumit upon discharge of any patient
- Not transfer Opsumit to any pharmacy, practitioner, or healthcare setting not certified by *Actelion Pathways*

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

- Read the Opsumit Prescribing Information, [Opsumit Medication Guide](#) and [Prescriber and Pharmacy Guide for the Opsumit REMS Program](#)
- Put processes and procedures in place to ensure the Opsumit REMS Program requirements are met
- Ensure training of dispensing staff on the Opsumit REMS program procedures and materials, including the [Prescriber and Pharmacy Guide for the Opsumit REMS Program](#) prior to dispensing Opsumit
- Notify Actelion Pharmaceuticals US, Inc. ("Actelion") or FDA if any patient becomes pregnant during Opsumit treatment
- Develop a process to track compliance with the conditions above and provide information about its compliance to Actelion
- Agree that this pharmacy may be subject to an audit by the FDA, Actelion, or a designated third party
- Agree to follow the REMS requirements by completing and submitting an [Opsumit REMS Inpatient Pharmacy Enrollment Form](#) to the Opsumit REMS Program
 - Authorized representatives can complete the [Opsumit REMS Inpatient Pharmacy Enrollment Form](#):
 - By fax at 1-866-279-0669
 - By calling the Opsumit REMS Program at 1-866-228-3546

If an inpatient pharmacy needs Opsumit and is not enrolled in the Opsumit REMS Program, the inpatient pharmacy can contact *Actelion Pathways* at 1-866-228-3546 for assistance in obtaining a 15 day supply of Opsumit for a specific inpatient while initiating enrollment.



You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

To learn more about the serious risks associated with Opsumit, please refer to the resources below.



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