Bosentan REMS Program

Fact Sheet

Phone: 1-866-359-2612
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BACKGROUND

The single shared Bosentan REMS Program was approved by the Food and Drug Administration (FDA) for all bosentan products. In the Bosentan REMS Program:

Patients must be enrolled in the Bosentan REMS Program. Prescribers must complete the ***Bosentan REMS Program Patient Enrollment Form*** for each patient.

Prescribers must be certified in the Bosentan REMS Program.

Pharmacies must be certified in the Bosentan REMS Program.

Prescriptions require a Pre-dispense Authorization (PDA) from the Bosentan REMS Program before a certified outpatient pharmacy can dispense bosentan. A PDA is verification sent to outpatient and chain pharmacies by the Bosentan REMS Program, authorizing the pharmacy to dispense bosentan to an eligible patient.

STAKEHOLDER	BOSENTAN REMS PROGRAM REQUIREMENTS
OUTPATIENT PHARMACIES[i]	• **Designate an authorized representative to oversee the implementation of and compliance with the Bosentan REMS Program** • **To become certified, the authorized representative must:** 1. Complete and sign the ***Bosentan REMS Program Outpatient Pharmacy Enrollment Form*** on behalf of the pharmacy, and submit the form to the Bosentan REMS Program 2. Review the ***Bosentan REMS Program Pharmacy Guide*** 3. Ensure all relevant staff involved in the dispensing of bosentan are trained on the Bosentan REMS Program requirements as described in the ***Bosentan REMS Program Pharmacy Guide*** and maintain a record of the training 4. Recertify in the Bosentan REMS Program if the pharmacy designates a new authorized representative 5. Report all adverse events including those suggestive of hepatotoxicity to the Bosentan REMS Program 6. Report any pregnancy and all available information during treatment with bosentan to the Bosentan REMS Program 7. Maintain documentation that all processes and procedures are in place and are being followed for the Bosentan REMS Program and provide upon request to the Bosentan Sponsors or a third party acting on behalf of the Bosentan Sponsors 8. Comply with audits by the Bosentan Sponsors or a third party acting on behalf of the Bosentan Sponsors to ensure that all processes and procedures are in place and are being followed for the Bosentan REMS Program 9. Put processes and procedures in place to ensure the following requirements are completed prior to dispensing bosentan: o Obtain a pre-dispense authorization 10. Outpatient pharmacies that support electronic telecommunication verification with the Bosentan REMS Program system must: o Ensure the pharmacy enables its pharmacy management system to support communication with the Bosentan REMS Program system, using established telecommunication standards, and runs the standardized validation test transactions to validate the system enhancements o Dispense bosentan to patients only after obtaining a pre-dispense authorization by processing the prescription, including cash claims, through their pharmacy management system to electronically: ▪ Verify the prescriber is certified and the patient is enrolled ▪ Verify the patient has completed the liver function tests and each female of reproductive potential has completed the pregnancy test or the prescriber has authorized a refill for patients if testing could not be confirmed ▪ Verify if patient has been counseled on the risk of hepatotoxicity and each female of reproductive potential has been counseled on the risk of embryo-fetal toxicity and the need to use reliable contraception o If counseling was not completed, call the Bosentan REMS Program Contact Center to complete the counseling requirement before dispensing bosentan o Dispense up to a 30-day supply of bosentan o Provide the Medication Guide to the patient every time bosentan is dispensed o Not transfer bosentan to any pharmacy, practitioner, or any healthcare setting not certified in the Bosentan REMS Program 11. Outpatient pharmacies that do NOT support electronic telecommunication verification with the Bosentan REMS Program system must: o Dispense bosentan to patients only after obtaining a pre-dispense authorization by calling the Bosentan REMS Program Contact Center or accessing the ***Bosentan REMS Program Website***

	to: • Verify the prescriber is certified and the patient is enrolled • Verify the patient has completed the liver function tests and each female of reproductive potential has completed the pregnancy test or the prescriber has authorized a refill for patients if testing could not be confirmed • Verify if patient has been counseled on the risk of hepatotoxicity and each female of reproductive potential has been counseled on the risk of embryo-fetal toxicity and the need to use reliable contraception o If counseling was not completed, call the Bosentan REMS Program Contact Center to complete the counseling requirement before dispensing bosentan o Dispense up to a 30-day supply of bosentan o Provide the patient the Medication Guide every time bosentan is dispensed o Not transfer bosentan to any pharmacy, practitioner, or any healthcare setting not certified in the Bosentan REMS Program
CHAIN PHARMACIES[ii]	• **Designate an authorized representative to oversee the implementation of and compliance with the Bosentan REMS Program** • **To become certified the authorized representative must:** 1. Complete and sign the ***Bosentan REMS Program Chain Pharmacy Headquarters Enrollment Form*** on behalf of the pharmacy, and submit the form to the Bosentan REMS Program 2. Comply with requirements #2 through #10 in the Outpatient Pharmacies section above 3. Once the ***Bosentan REMS Program Chain Pharmacy Headquarters Enrollment Form*** has been processed, the authorized representative will receive instructions on submitting test transactions to the Bosentan REMS Program to ensure that the pharmacy management system has been successfully configured/updated to communicate with the Bosentan REMS Program 4. After successful completion of the test transactions, the authorized representative will receive a pharmacy certification confirmation. Upon receipt, the chain pharmacy headquarters is certified and dispensing locations are now eligible to complete their training 5. Once each dispensing location is trained, the authorized representative must report confirmation of training to the Bosentan REMS Program online through **www.BosentanREMSProgram.com**, or by calling the Bosentan REMS Program Contact Center at 1-866-359-2612 to obtain instructions on providing a list of trained pharmacy locations. Once the Bosentan REMS Program confirms the required dispensing information, the dispensing location will be authorized to purchase, receive, and dispense bosentan
INPATIENT PHARMACIES[iii]	• **Designate an authorized representative to oversee the implementation of and compliance with the Bosentan REMS Program** • **To become certified the authorized representative must:** 1. Complete and sign the ***Bosentan REMS Program Inpatient Pharmacy Enrollment Form*** on behalf of the pharmacy, and submit the form to the Bosentan REMS Program 2. Review the ***Bosentan REMS Program Pharmacy Guide*** 3. Ensure that all pharmacy staff involved in the dispensing of bosentan are trained on the Bosentan REMS Program requirements as described in the ***Bosentan REMS Program Pharmacy Guide*** and maintain a record of the training 4. Recertify in the Bosentan REMS Program if the pharmacy designates a new authorized representative 5. Report all adverse events including those suggestive of hepatotoxicity to the Bosentan REMS Program 6. Report any pregnancy and all available information during treatment with bosentan to the Bosentan REMS Program 7. Maintain documentation that all processes and procedures are in place and are being followed for the Bosentan REMS Program and provide upon request to the Bosentan Sponsors or a third party acting on behalf of the Bosentan Sponsors 8. Comply with audits by the Bosentan Sponsors or a third party acting on behalf of the Bosentan Sponsors to ensure that all processes and procedures are in place and are being followed for the Bosentan REMS Program 9. Put processes and procedures in place to ensure the following requirements are completed prior to dispensing bosentan: o Verify the patient is under the supervision and care of a prescriber who is certified o Verify the patient is enrolled or will be enrolled prior to discharge o Dispense no more than a 15-day supply of bosentan upon discharge 10. Verify the requirements by the following mechanisms, including but not limited to calling the Bosentan REMS Program Contact Center, accessing the ***Bosentan REMS Program Website***, or by accessing the patient's medical records 11. Not transfer bosentan to any pharmacy, practitioner, or any healthcare setting not certified in the

	Bosentan REMS Program
PRESCRIBERS	• **To become certified to prescribe bosentan, each prescriber must:** 1. Review the Prescribing Information for bosentan 2. Review the ***Bosentan REMS Program Prescriber Guide*** 3. Enroll in the Bosentan REMS Program by completing the ***Bosentan REMS Program Prescriber Enrollment Form*** and submitting it to the Bosentan REMS Program 4. Enroll each patient in the Bosentan REMS Program by performing the following: o Counsel the patient about the risk of hepatotoxicity associated with bosentan, the signs and symptoms of hepatotoxicity, and program requirements including the need to complete liver function testing and, as appropriate, pregnancy testing by reviewing and providing the ***Bosentan REMS Program Guide for Patients*** o Determine the reproductive potential status of each female patient as defined in the ***Bosentan REMS Program Prescriber Guide*** o For pre-pubertal females, counsel the patient and/or parent/legal guardian about (i) the risk of embryo-fetal toxicity, (ii) the need to immediately contact the prescriber if the patient begins to menstruate o For females of reproductive potential, counsel the patient about (i) the risk of embryo-fetal toxicity, (ii) the need to use reliable contraception as defined in the ***Bosentan REMS Program Prescriber Guide*** during treatment and for one month following treatment discontinuation, (iii) the need to immediately contact her prescriber if she misses a menstrual period or suspects she is pregnant, and (iv) her medical options in the event of unprotected sexual intercourse or known or suspected contraception failure o Complete the ***Bosentan REMS Program Patient Enrollment Form*** for each patient and provide a completed copy to the patient. Submit the completed form to the Bosentan REMS Program 5. Report all adverse events including those suggestive of hepatotoxicity to the Bosentan REMS Program 6. Report any pregnancy and all available information during treatment with bosentan to the Bosentan REMS Program 7. Perform the following on an ongoing basis for each female patient: Report a change or misclassification in the reproductive status of any female patient by completing the ***Bosentan REMS Program Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*** within 10 business days of becoming aware of the change 8. Perform the following requirements on an ongoing basis for each patient: o Order and review liver function test results before bosentan treatment initiation and monthly during treatment o Counsel patients who fail to comply with program requirements 9. Perform the following monitoring on an ongoing basis for each pre-pubertal female: Evaluate patients age 8 years and older at least annually for any change in reproductive status and complete the ***Bosentan REMS Program Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form*** verifying their reproductive potential status 10. Perform the following monitoring on an ongoing basis for each female patient of reproductive potential: Order and review pregnancy test results before bosentan treatment initiation, monthly during treatment, and for one month following treatment discontinuation
PATIENTS/PARENTS/LEGAL GUARDIANS	• **Each patient and/or parent/legal guardian must complete and sign the *Bosentan REMS Program Patient Enrollment Form* with the prescriber to indicate that he/she has:** 1. Received and has read the ***Bosentan REMS Program Guide for Patients*** 2. Received counseling from the prescriber regarding: o the risk of liver damage, the signs and symptoms of liver damage and, as appropriate, the risk of serious birth defects, and the need to use reliable contraception o the need to complete liver function testing and, as appropriate, pregnancy testing, as outlined in the ***Bosentan REMS Program Guide for Patients*** o contact by the Bosentan REMS Program prior to each dispense of bosentan to obtain confirmation that liver function tests and, as appropriate, pregnancy test were completed and provide counseling

BOSENTAN REMS PROGRAM PDA SCENARIOS FOR PHARMACIES	PDA ISSUED*
Pharmacy is certified, prescriber is certified, patient is enrolled, patient has completed the required test(s), and current appropriate counseling is confirmed	✓
Patient liver function test is not on file, but later confirmed to have taken place If patient does not have a current completed liver function test confirmed with the Bosentan REMS Program, a PDA will not be issued. The pharmacy can contact the Bosentan REMS Program to notify the patient or patient's prescriber that a liver function test is required. The Bosentan REMS Program Contact Center will update completion of testing for the patient.	✓
Pregnancy test for a female of reproductive potential is not on file, but later confirmed to have taken place If patient does not have a current completed pregnancy test confirmed with the Bosentan REMS Program, a PDA will not be issued. The pharmacy can contact the Bosentan REMS Program to notify the patient or patient's prescriber that a pregnancy test is required. The Bosentan REMS Program Contact Center will update completion of testing for the patient.	✓
Confirmation of counseling is not on file If all safe use conditions are met but the patient does not have current appropriate counseling confirmed with the Bosentan REMS Program, a PDA will be issued by the Bosentan REMS Program, with a message instructing the pharmacist or patient to call the Bosentan REMS Program Contact Center to complete the counseling requirement.	✓
Pharmacy is not certified If a pharmacy is not certified in the Bosentan REMS Program, a PDA will not be issued.	✗
Prescriber is not certified If a prescriber is not certified in the Bosentan REMS Program, a PDA will not be issued.	✗
Patient is not enrolled If a patient is not enrolled in the Bosentan REMS Program, a PDA will not be issued.	✗
Patient liver function test is not confirmed If a patient does not have a current completed liver function test confirmed with the Bosentan REMS Program, a PDA will not be issued.	✗
Pregnancy test for females of reproductive potential is not confirmed If a female of reproductive potential does not have a current pregnancy test confirmed with the Bosentan REMS Program, a PDA will not be issued.	✗

*A green checkmark indicates approval to dispense bosentan to the patient. A red 'X" indicates safe use conditions have not been met and bosentan should not be dispensed to the patient.

[i] For the purposes of this REMS, outpatient pharmacies include but are not limited to retail, specialty, mail order, and closed system pharmacies.

[ii] For the purposes of this REMS, chain pharmacies are retail pharmacies with multiple locations that dispense bosentan for outpatient use and have a pharmacy headquarters that coordinates pharmacy enrollment in the Bosentan REMS Program.

[iii] For the purposes of this REMS, inpatient pharmacies include but are not limited to pharmacies in hospitals, hospices, long-term care facilities, and prisons.