

Initial REMS Approved: 02/2010
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BLA 125338
XIAFLEX[®] (collagenase clostridium histolyticum)
Drug Class: Bacterial collagenase enzyme

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. TREATMENT OF DUPUYTREN'S CONTRACTURE

A. GOALS

The goals of the XIAFLEX REMS for the treatment of Dupuytren's contracture are:

- To mitigate the risks of tendon rupture and serious adverse reactions affecting the injected extremity associated with the use of XIAFLEX by informing healthcare providers about how to properly inject XIAFLEX and perform finger extension procedures.
- To inform healthcare providers about the potential risk of serious hypersensitivity reactions (including the potential for anaphylaxis) associated with XIAFLEX treatment.

B. COMMUNICATION PLAN FOR THE TREATMENT OF DUPUYTREN'S CONTRACTURE

Auxilium will implement a communication plan targeted to healthcare providers who are likely to prescribe XIAFLEX for the treatment of Dupuytren's contracture (for example: hand surgeons, orthopedic surgeons, plastic surgeons, general surgeons, and rheumatologists) to convey important information about the serious risks associated with XIAFLEX and to disseminate educational materials about how to properly inject XIAFLEX and perform finger extension procedures.

The communication plan will include the following:

1. A Dear Healthcare Provider Letter will be distributed via hardcopy mailings within 60 days of the most recent REMS modification approval. The Prescribing Information will also be distributed in this communication. This letter will also include information about how to obtain the Training Guide and Training Video educational materials (see below). Auxilium will send the Dear Healthcare Provider Letter to MedWatch at the same time it is disseminated to the target audience. In addition, any new healthcare providers inquiring about the use of XIAFLEX will receive the Dear Healthcare Provider Letter, Prescribing Information, and information about how to obtain the Training Guide or how to access the Training Video.

The Training Guide or the Training Video may be used as an educational tool by a healthcare provider, since each provides complete training instructions and information regarding the risks addressed in the REMS. These materials are available through the following distribution methods:

- Accessed through the www.XIAFLEXREMS.com website
- Hard copy available upon request, from the XIAFLEX REMS Program call center (1-877-313-1235).

The following materials are part of the REMS, and are appended:

- Dear Healthcare Provider Letter
- Training Guide for the Administration of XIAFLEX for Dupuytren's contracture is appended.
- XIAFLEX Procedure Training Video for Dupuytren's Contracture can be accessed at www.XIAFLEXREMS.com.
- XIAFLEX REMS Program website (www.XIAFLEXREMS.com), main landing page of the REMS website and landing pages for Dupuytren's contracture and Peyronie's disease.

II. TREATMENT OF PEYRONIE'S DISEASE

A. GOALS

The goals of the XIAFLEX REMS for Peyronie's disease are:

- To mitigate the risks of corporal rupture (penile fracture) and other serious penile injuries associated with the use of XIAFLEX by:
 - Training healthcare providers in how to properly administer XIAFLEX.
 - Informing healthcare providers about the risks of corporal rupture (penile fracture) and other serious injuries to the penis.
 - Informing healthcare providers about the need to counsel patients to communicate that risks of corporal rupture and other serious penile injuries are associated with the use of XIAFLEX in treating Peyronie's disease and that patient adherence to post-injection instructions is important for the drug's safety and effectiveness.
 - Ensuring that XIAFLEX is dispensed only in certified pharmacies or healthcare settings.
 - Informing patients about the risks of corporal rupture and other serious penile injuries associated with the use of XIAFLEX in treating Peyronie's disease and that adherence to post-injection instructions is important for the drug's safety and effectiveness.

B. ELEMENTS TO ASSURE SAFE USE FOR THE TREATMENT OF PEYRONIE’S DISEASE

1. Healthcare providers who prescribe XIAFLEX for Peyronie’s disease are specially certified.

- a. Auxilium will ensure that healthcare providers who prescribe¹ XIAFLEX for the treatment of Peyronie’s disease are specially certified.
- b. To become specially certified to prescribe XIAFLEX for the treatment of Peyronie’s disease, healthcare providers must:
 - i. Read the Prescribing Information for XIAFLEX.
 - ii. Complete the XIAFLEX REMS Healthcare Provider Training Program for Peyronie’s disease by:
 - a. viewing the entire REMS Training Video for Administering XIAFLEX for Peyronie’s disease **or**
 - b. reading the entire REMS Training Guide for Administering XIAFLEX for Peyronie’s disease
 - iii. Agree to review with and provide a copy of the Patient Counseling Tool, “*What You Need to Know About XIAFLEX Treatment for Peyronie’s Disease: A Patient Guide*”, to each patient to inform patients about the risks associated with the use of XIAFLEX and the need to follow important post-injection instructions.
 - iv. Acknowledge that my practice setting must be a certified healthcare setting, or that I will use a certified pharmacy, enrolled in the XIAFLEX REMS Program.
 - v. Complete and sign the Healthcare Provider Enrollment Form for Peyronie’s disease and submit it to the XIAFLEX REMS Program.
- c. Auxilium will:
 - i. Ensure that healthcare providers complete the *Healthcare Provider Training Program for Peyronie’s Disease* and *Healthcare Provider Enrollment Form for Peyronie’s Disease* before activating healthcare providers’ certification in the XIAFLEX REMS Program.
 - ii. Ensure that healthcare providers are notified when they have been successfully certified by the XIAFLEX REMS Program for Peyronie’s disease.
 - iii. Maintain a validated secure database of healthcare providers who prescribe XIAFLEX and their specialties in the XIAFLEX REMS Program. Auxilium will ensure that the prescribers’ certification requirements are met and may de-certify non-compliant prescribers until the requirements are met.

¹ For the purposes of this REMS, the terms “prescribe” and “prescription” include medication orders in outpatient settings or hospital settings.

- iv. Ensure that the XIAFLEX REMS Healthcare Provider Training Program for Peyronie's disease, Healthcare Provider Enrollment Form for Peyronie's disease, and Patient Counseling Tool for Peyronie's disease are available on the XIAFLEX REMS program website at www.XIAFLEXREMS.com or from the XIAFLEX REMS Program call center (1-877-313-1235).

These materials will be available within 60 days of the most recent REMS modification approval (12/6/2013) through the following distribution methods:

- Accessed through the www.XIAFLEXREMS.com website
- Hard copy is available, upon request, through the XIAFLEX REMS Program call center (1-877-313-1235).

The following materials are part of the REMS and are appended:

- REMS Training Guide for Administering XIAFLEX for Peyronie's disease
- REMS Training Video for Administering XIAFLEX for Peyronie's disease (accessed at www.XIAFLEXREMS.com)
- Healthcare Provider Enrollment Form for Peyronie's disease
- Patient Counseling Tool, *What You Need to Know About XIAFLEX Treatment for Peyronie's disease: A Patient Guide*
- XIAFLEX REMS Program website (www.XIAFLEXREMS.com), main landing page of the REMS website and landing pages for Dupuytren's contracture and Peyronie's disease

2. Pharmacies and healthcare settings that dispense² XIAFLEX for Peyronie's disease are specially certified.

a. Auxilium will:

- i. Ensure that XIAFLEX is only distributed to and dispensed for the treatment of Peyronie's disease from pharmacies or healthcare settings (e.g., hospitals, and outpatient clinics, and healthcare providers' offices) that are specially certified.
 - ii. Ensure that pharmacies or healthcare settings are recertified in the XIAFLEX REMS Program every two years.
- b. To become certified to dispense XIAFLEX for the treatment of Peyronie's disease, the pharmacy or healthcare setting must designate an Authorized Representative to coordinate the pharmacy or healthcare setting's activities and assure compliance with the XIAFLEX REMS Program. The Authorized Representative must agree to the following:
- i. Complete and sign the *Pharmacy/Healthcare Setting Enrollment Form for Peyronie's Disease* and submit it to the XIAFLEX REMS Program.

² For the purposes of this REMS, "dispense" in an outpatient setting includes dispensing for administration in a provider's office.

- ii. Put processes and procedures in place to verify, prior to dispensing XIAFLEX, that the healthcare provider prescribing XIAFLEX for Peyronie's disease is certified in the XIAFLEX REMS Program
- iii. Maintain a record of current certified prescribers.
- iv. Agree not to loan, sell or transfer XIAFLEX to another pharmacy, healthcare setting, prescriber, institution or distributor.
- v. To be audited to ensure compliance with the XIAFLEX REMS Program for Peyronie's disease.

The following materials are part of the REMS and are appended:

- *XIAFLEX REMS Pharmacy/Healthcare Setting Enrollment Form for Peyronie's disease*

C. IMPLEMENTATION SYSTEM

An implementation system will be established for the XIAFLEX REMS for the treatment of Peyronie's disease to monitor and evaluate whether the elements to assure safe use are meeting the program's goals.

1. Auxilium will ensure that pharmacies or healthcare settings that dispense XIAFLEX for Peyronie's disease are specially certified.
2. Auxilium will maintain, monitor, and evaluate the implementation of the XIAFLEX REMS Program for Peyronie's disease.
 - a. Auxilium will maintain a validated secure database of all certified pharmacies or healthcare settings.
 - b. Auxilium will send confirmation of certification to each certified pharmacy or healthcare setting.
 - c. The database of certified healthcare providers will be accessible by the Authorized Representative at a pharmacy or certified healthcare setting and by contract distributors.
 - d. Contract distributors will verify pharmacy or healthcare setting certification prior to distributing XIAFLEX.
 - e. Auxilium will maintain a XIAFLEX REMS Program call center (1-877-313-1235) to respond to questions from healthcare providers, pharmacies, and healthcare settings.
 - f. Auxilium will ensure that all materials listed in or appended to the XIAFLEX REMS Program will be available through the XIAFLEX REMS Program website at www.XIAFLEXREMS.com or through the XIAFLEX REMS Program call center (1-877-313-1235).
 - g. Auxilium will audit the certified pharmacies or healthcare settings to ensure that all processes and procedures are in place and functioning to support the requirements of the XIAFLEX REMS Program. Auxilium will correct noncompliance with XIAFLEX REMS Program requirements.

- h. Auxilium will take reasonable steps to improve implementation of these elements and to maintain compliance with the XIAFLEX REMS Program requirements, as applicable.
3. Auxilium will ensure that contract distributors maintain distribution records of all shipments of XIAFLEX.
4. Auxilium will take reasonable steps to improve implementation of these elements and to maintain compliance with the XIAFLEX REMS Program requirements, as applicable.

III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS FOR THE TREATMENT OF DUPUYTREN'S CONTRACTURE AND FOR THE TREATMENT OF PEYRONIE'S DISEASE

Auxilium will submit REMS Assessments for Peyronie's disease to FDA at 6 months and 12 months from the date of the approval of the modified REMS (12/2013) and annually thereafter. The REMS Assessment for Dupuytren's contracture should be submitted at 6 months and then 2 years and 4 years from the date of the approval of the modified REMS (12/2013). 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. Auxilium will submit each assessment so that it will be received by the FDA on or before the due date.