

Initial REMS Approved: 02/2010  
Most Recent Modification: 10/2014

**BLA 125338**  
**XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum)**  
**Drug Class: Bacterial collagenase enzyme**

Auxilium Pharmaceuticals, Inc.  
640 Lee Road  
Chesterbrook, PA 19087  
1-877-663-0412

**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](http://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](http://www.XIAFLEXREMS.com).
- XIAFLEX REMS Program website ([www.XIAFLEXREMS.com](http://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 prescribe<sup>1</sup> 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.

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<sup>1</sup> 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](http://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](http://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](http://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](http://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 dispense<sup>2</sup> 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.

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<sup>2</sup> 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](http://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.



## IMPORTANT DRUG WARNING

Dear Healthcare Provider,

The purpose of this letter is to inform you of updated important safety information about XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum), a biologic medication indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. XIAFLEX is administered by intra-lesional injection into a palpable Dupuytren's cord by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for XIAFLEX to ensure that the benefits of XIAFLEX outweigh its risks of tendon rupture and other serious adverse reactions of the injected extremity, and its potential risk of serious hypersensitivity reactions (including the potential for anaphylaxis).

### **New Important Safety Information**

The Prescribing Information for XIAFLEX was recently revised to incorporate new information regarding

- The safety of administering two concurrent injections into the same hand
- Extending the timing of the finger extension procedure to approximately 24 to 72 hours.
- Risk of skin lacerations



## **Contraindication**

- XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

## **Tendon Rupture or Other Serious Injury to the Injected Extremity**

- Injection of XIAFLEX into collagen-containing structures, such as tendons or ligaments of the hand, may result in damage to those structures and possible permanent injury, such as tendon rupture, ligament damage, or skin laceration.
- Out of 1,082 XIAFLEX-treated patients in the XIAFLEX clinical studies, serious adverse events of the injected extremity occurred in 11 (1%) patients, including 3 (0.3%) patients who had flexor tendon ruptures and other events of the injected extremity (pulley rupture, ligament injury, recurrence of complex regional pain syndrome, tendonitis, sensory abnormality of the hand). The incidence of XIAFLEX-associated serious adverse events of the injected extremity, including tendon ruptures, in clinical practice may be different than the incidence seen in the clinical studies.
- To reduce the risk of serious injury to the injected extremity, XIAFLEX should be injected only into a palpable Dupuytren's cord with a metacarpophalangeal (MP) or proximal interphalangeal (PIP) joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting XIAFLEX into a Dupuytren's cord affecting a PIP joint of the fifth finger, special precautions should be taken.
- In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared with subjects treated with up to three single injections in the placebo-controlled studies (9%). Cases of skin laceration



requiring skin graft after finger extension procedures have been reported post-marketing.

### **Hypersensitivity Reactions, Including Anaphylaxis**

- Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture.
- Healthcare providers should be prepared to address severe hypersensitivity reactions (including anaphylaxis) following XIAFLEX injections.
- In the controlled portions of the XIAFLEX clinical trials, a greater proportion of XIAFLEX-treated patients (15%) compared with placebo-treated patients (1%) had mild allergic reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections.

### **Healthcare Provider Action**

- Review training materials (procedure training video, training guide) on the proper preparation and injection of XIAFLEX, and on the finger extension procedures to facilitate cord disruption as described in the FDA-approved Prescribing Information, and the special precautions and potential risk with injection of a cord affecting the PIP joint of the fifth finger.

### **Patient Counseling**

- Counsel and communicate with patients about the potential risks associated with XIAFLEX before treatment.

### **Medication Guide**

- The Medication Guide contains information that can be used to facilitate discussions about the potential risks of XIAFLEX. Provide a copy to each patient before each injection.



**Reporting Adverse Events**

To report any adverse events with the use of XIAFLEX contact:

- Auxilium Drug Information Center at 1-877-663-0412; or
- FDA MedWatch program by phone at 1-800-FDA-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

Training materials are available at [www.XIAFLEXREMS.com](http://www.XIAFLEXREMS.com) or by calling 1-877-XIAFLEX (1-877-942-3539).

Read the accompanying FDA-approved Prescribing Information for XIAFLEX for a complete understanding of the benefits and risks of XIAFLEX in the treatment of adult patients with Dupuytren's contracture with a palpable cord.

Sincerely,

Auxilium Pharmaceuticals, Inc.  
640 Lee Road  
Chesterbrook, PA 19087

# XIAFLEX®

collagenase clostridium histolyticum



## TRAINING GUIDE FOR THE ADMINISTRATION OF XIAFLEX® FOR DUPUYTREN'S CONTRACTURE

This Training Guide for the use of XIAFLEX for the treatment of adult patients with Dupuytren's contracture with a palpable cord is required and approved by the Food and Drug Administration (FDA) as part of the XIAFLEX Risk Evaluation and Mitigation Strategy (REMS). A REMS is a strategy to manage known or potential serious risks associated with a drug and is required by the FDA to ensure that the benefits of the drug outweigh its risks.

Auxilium has worked with the FDA to develop this Training Guide to inform healthcare providers about the risks of XIAFLEX, including tendon rupture and other serious adverse events of the injected extremity, and the potential risk of severe hypersensitivity events. This Training Guide also provides instructions on the proper preparation and administration of XIAFLEX for the treatment of Dupuytren's contracture to reduce the risks of serious adverse events of the injected extremity.

**Please see Prescribing Information and Medication Guide.**

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**Please see Prescribing Information and Medication Guide.**

## Dupuytren's Contracture Overview

Dupuytren's contracture, a slowly progressive fibroproliferative disease of the palmar fascia in the hand, is characterized by increased collagen production and deposition that commonly results in cord formation. The Dupuytren's cord(s) may cause the affected fingers to bend or contract toward the palm of the hand, resulting in the inability to fully extend the affected fingers and a reduced range of motion.

XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. XIAFLEX consists of 2 microbial collagenases that are isolated and purified from the fermentation of *Clostridium histolyticum*. The collagenases work in a synergistic fashion to provide hydrolyzing activity to collagen in the Dupuytren's cords. This guide demonstrates the steps necessary to prepare and administer XIAFLEX. It also outlines the finger extension procedure(s) that may be required approximately 24 to 72 hours after injection to help disrupt the cord. The guide also includes special precautions for injection of a cord affecting the PIP joint of the fifth finger.

XIAFLEX should be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of Dupuytren's contracture.

## XIAFLEX® Dosing for Dupuytren's Contracture

- XIAFLEX® (collagenase clostridium histolyticum), supplied as a lyophilized powder, **must be reconstituted with the supplied sterile diluent in the appropriate volume prior to use**
- The dose for XIAFLEX is 0.58 mg per injection into a palpable cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint, according to the injection procedure
- Up to two concurrent injections may be administered in the same hand at one treatment visit to treat two joints affected by one or two cords
- XIAFLEX treatment of cords associated with contractures of distal interphalangeal (DIP) joints or the joints of the thumb has not been evaluated in clinical trials
- Finger extension procedure(s) may be performed approximately 24 to 72 hours after injection in the event the cord has not spontaneously ruptured
- Four weeks after the XIAFLEX injection and finger extension procedure(s), if an MP or PIP contracture remains, the cord may be re-injected with a single dose of 0.58 mg of XIAFLEX and the finger extension procedure(s) may be repeated (approximately 24 to 72 hours after re-injection)

**Please see Prescribing Information and Medication Guide.**

- Injection and finger extension procedure(s) may be administered up to **3 times per cord at approximately 4-week intervals**
- Perform up to two injections in the same hand according to the injection procedure appropriate for each joint type during a treatment visit for a total dose of up to 1.16 mg per visit. Two palpable cords affecting two joints may be injected or one palpable cord affecting two joints in the same finger may be injected at two locations during a treatment visit. When injecting a cord affecting the PIP joint of the fifth finger, special precautions should be taken (see WARNINGS AND PRECAUTIONS in the FDA-approved Prescribing Information)

## XIAFLEX® Preparation for Administration for Dupuytren's Contracture

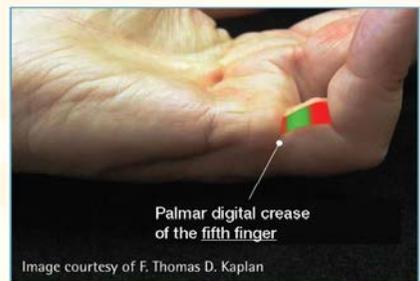
This section summarizes the procedure for reconstitution of the lyophilized XIAFLEX® (collagenase clostridium histolyticum) powder.

### Important Considerations

- XIAFLEX should be injected into the cord at the point of maximal separation between the cord and the underlying tendon to prevent accidental injection into the tendon or surrounding tissue
- Care must be taken to place the needle in the cord and not through the cord
- Special care also should be taken when treating the PIP joint of the fifth finger (see below)

If injecting into a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in

depth and care should be taken to inject as close to the palmar digital crease as possible (as far proximal to the digital PIP joint crease). Tendon ruptures have occurred after XIAFLEX injections near the digital fifth finger PIP joint crease.



**Please see Prescribing Information and Medication Guide.**

### Additional Important Considerations

- Prior to reconstitution, the vials of lyophilized XIAFLEX powder and sterile diluent should be stored in a refrigerator at 2° to 8°C (36° to 46°F)
- If the vials have been at room temperature for more than 60 minutes, they should not be used
- The preparation procedure varies slightly depending on whether the palpable cord is associated with an MP or PIP joint contracture and is described in detail below
- Visually inspect the vial containing XIAFLEX. The cake of lyophilized powder should be intact and white in color.

If the cake has been eroded, it should not be used and should be reported to Auxilium by calling 1-877-663-0412



## XIAFLEX® Preparation for Administration for Dupuytren's Contracture (continued)

XIAFLEX is supplied in a single-use glass vial containing 0.9 mg of a sterile, lyophilized powder for reconstitution. The vial of lyophilized XIAFLEX powder should be reconstituted with the



sterile diluent (0.3 mg/mL calcium chloride dihydrate in 0.9% sodium chloride) provided in a single-use vial in the package. Syringes are not included in the package. Each vial of XIAFLEX and sterile diluent should only be used for a single injection. If a second joint requires treatment, separate vials and syringes should be used for the second injection.

### Before Use

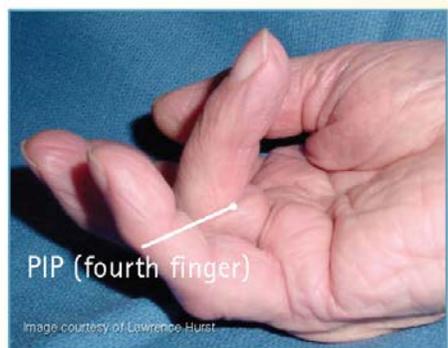
Before removing the vials from the refrigerator, confirm that the joint to be treated has a palpable cord. This is important particularly when performing a second or third XIAFLEX injection.

The vial containing the lyophilized XIAFLEX powder and the vial containing the sterile diluent for reconstitution should be removed from the refrigerator and allowed to stand at room temperature for at least 15 minutes, but no longer than 60 minutes prior to reconstitution.

**Please see Prescribing Information and Medication Guide.**

Using an aseptic technique, the following procedure for reconstitution should be followed:

1. Identify the joint contracture that is associated with the palpable cord (ie, MP or PIP) — the volume of sterile diluent required for reconstitution is determined by the type of joint contracture. When injecting XIAFLEX into a Dupuytren's cord affecting the PIP joint of the fifth finger, special precautions should be taken (see WARNINGS AND PRECAUTIONS in the FDA-approved Prescribing Information)



2. Remove the protective covering from both vials
3. Using sterile alcohol, swab the rubber stoppers and surrounding surface of the vial containing lyophilized XIAFLEX powder and the vial containing the sterile diluent for reconstitution

## XIAFLEX® Preparation for Administration for Dupuytren's Contracture (continued)



4. Using a syringe that contains 0.01 mL graduations with a 27-gauge  $\frac{1}{2}$ -inch needle (not supplied), withdraw the appropriate amount of **sterile diluent required for reconstitution** as follows:
  - **0.39 mL for a cord affecting an MP joint or**
  - **0.31 mL for a cord affecting a PIP joint**
5. When reconstituting XIAFLEX powder, inject the sterile diluent slowly into the sides of the vial containing the lyophilized XIAFLEX powder



**Please see Prescribing Information and Medication Guide.**

6. Slowly swirl the solution to ensure that all of the lyophilized powder has gone into the solution. Do not shake the solution because it can denature the proteins



7. The reconstituted XIAFLEX solution is now ready for injection (see “XIAFLEX Injection Procedure” for the appropriate injection volumes)

8. Discard the sterile diluent vial and the syringe and needle used for reconstitution

# XIAFLEX<sup>®</sup> Preparation for Administration for Dupuytren's Contracture (continued)

## Important Considerations

- The reconstituted XIAFLEX solution should be clear. Inspect the solution for particulate matter and discoloration prior to administration. If the solution contains particulates, is cloudy, or is discolored, do not inject it
- Reconstituted XIAFLEX solution can be kept at room temperature (20° to 25°C / 68° to 77°F) for up to 1 hour or refrigerated (2° to 8°C / 36° to 46°F) for up to 4 hours prior to administration. If refrigerated, the reconstituted XIAFLEX solution should be allowed to return to room temperature for approximately 15 minutes before use



**Please see Prescribing Information and Medication Guide.**

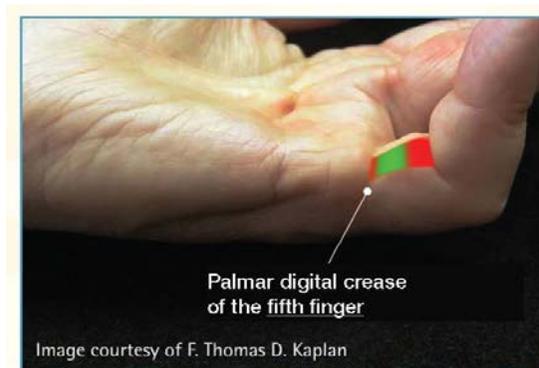
## XIAFLEX® Injection Procedure for Dupuytren's Contracture

This section outlines the procedure for injecting the reconstituted XIAFLEX® (collagenase clostridium histolyticum) solution into the Dupuytren's cord.

### Important Considerations

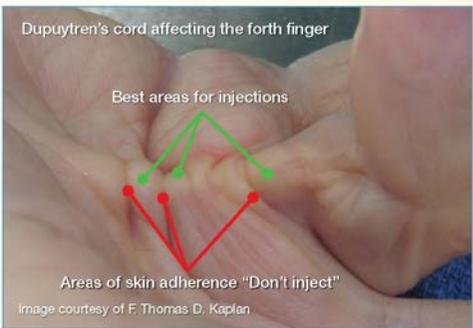
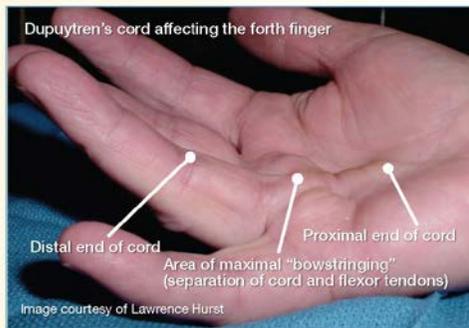
- XIAFLEX should be injected into the cord at the point of maximal separation between the cord and the underlying tendon to prevent accidental injection into the tendon or surrounding tissue
- Care must be taken to place the needle in the cord and not through the cord
- Special care also should be taken when treating the PIP of the fifth finger (see below)

If injecting into a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and care should be taken to inject as close to the palmar digital crease as possible (as far proximal to the digital PIP joint crease). Tendon ruptures have occurred after XIAFLEX injections near the digital fifth finger PIP joint crease.



## XIAFLEX® Injection Procedure for Dupuytren's Contracture (continued)

Administration of a local anesthetic agent prior to injection of XIAFLEX is not recommended because it may interfere with proper injection placement.



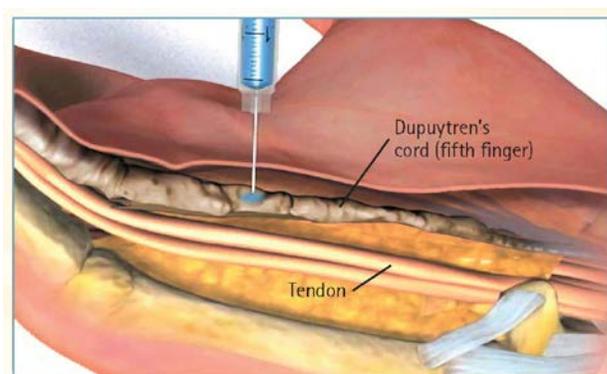
1. Reconfirm the cord and site chosen for injection. It should be the area where the contracting cord is separated maximally from the underlying flexor tendons and where the skin is not adhered intimately to the cord
2. Instruct patient to remove any jewelry from the hand to be treated
3. Prepare the skin with an antiseptic and allow it to dry

**Please see Prescribing Information and Medication Guide.**

4. Withdraw the volume of **reconstituted XIAFLEX solution\*** required for injection using a hubless syringe with 0.01-mL graduations and a permanently fixed, 27-gauge ½-inch needle

- **Cord affecting an MP joint: Withdraw 0.25 mL of the reconstituted solution**
- **Cord affecting a PIP joint: Withdraw 0.20 mL of the reconstituted solution**

5. Secure the patient's hand to be treated while simultaneously applying tension to the cord. Place the needle into the cord, using caution to keep the needle within the cord, which has a gritty and gristly consistency. Avoid passing the needle tip completely through the cord to minimize the potential for injection of XIAFLEX into other tissues



\* Each reconstituted volume withdrawn will contain the required dose of 0.58 mg of XIAFLEX. The entire reconstituted XIAFLEX solution contains 0.9 mg of XIAFLEX. Reconstituted XIAFLEX solution remaining in the vial after the injection should be discarded.

## XIAFLEX<sup>®</sup> Injection Procedure for Dupuytren's Contracture (continued)

6. After needle placement, if there is any concern that the needle is in the flexor tendon, apply a small amount of passive motion at the distal interphalangeal (DIP) joint to ascertain that the needle does not move with fingertip motion. If insertion of the needle into a tendon is suspected or paresthesia is noted by the patient, withdraw the needle and reposition it into the Dupuytren's cord
7. After confirming that the needle is placed correctly in the cord, inject approximately one-third of the dose. It is important to stabilize the needle while pushing the plunger to prevent accidental injection through the cord
8. Withdraw the needle tip from the cord and reposition it in a slightly more distal location to the initial injection in the cord (approximately 2 to 3 mm) and inject another one-third of the dose

**Please see Prescribing Information and Medication Guide.**

9. Again, withdraw the needle tip from the cord and reposition it proximal to the initial injection (approximately 2 to 3 mm) and inject the final portion of the dose into the cord



An alternate method of injection may be used, in which the needle is completely withdrawn from the skin when being repositioned in the cord (approximately 2 to 3 mm to each side of the initial injection).

10. When injecting a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and avoid injecting more than 4 mm distal to the palmar digital crease

## XIAFLEX® Injection Procedure for Dupuytren's Contracture (continued)

11. Administer up to two injections in the same hand according to the injection procedure during a treatment visit.

When injecting two cords in the same hand concurrently, begin with the affected finger in the most lateral aspect of the hand and continue toward the medial aspect (eg, fifth finger to index finger).

Within each finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (eg, MP to PIP).

Where a single cord affects both the MP and PIP joint in the same finger, administer one injection into the cord at the MP level and administer a second injection into the cord at the PIP level during the treatment visit. Each injection contains a 0.58 mg dose.

When administering two injections in the same hand during a treatment visit, use a new syringe and needle and separate vial of reconstituted solution for the second injection.

**Please see Prescribing Information and Medication Guide.**

12. After the injections are completed, wrap the patient's treated hand with a soft, bulky gauze dressing. Instruct the patient to return the next day and keep the treated hand elevated until bedtime



13. Patients should be informed that the injection may result in swelling, bruising, bleeding and/or pain at the injection site and surrounding tissue. Patients should be instructed to limit motion of the injected finger and promptly contact their physician if there is evidence of infection, sensory changes, or trouble bending the finger after swelling has gone down

#### Important Considerations

- Discard the unused portion of the reconstituted solution after injection
- Do not store, pool, or use any vials with unused, reconstituted solution

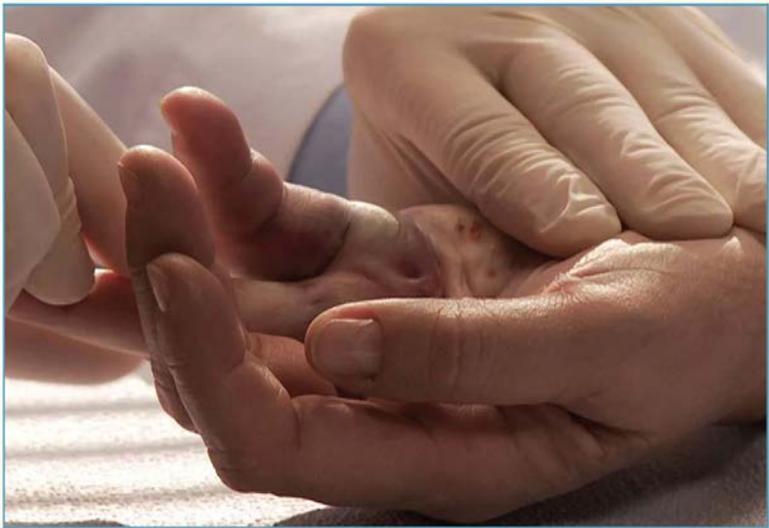
## Finger Extension Procedure(s)

This section describes the finger extension procedure(s) that are usually performed approximately 24 to 72 hours after the XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) injection to rupture the Dupuytren's cord.

1. Determine if the contracture has resolved at the follow-up visit approximately 24 to 72 hours after XIAFLEX injection
2. If a contracture remains, a passive finger extension procedure should be undertaken in an attempt to disrupt the cord
3. Local anesthesia may be used during the finger extension procedure since the procedure can be painful for the patient

**Please see Prescribing Information and Medication Guide**

4. With the patient's wrist in a flexed position, apply moderate stretching pressure to the injected cord by extending the finger for approximately 10 to 20 seconds. For cords affecting the PIP joint, perform the finger extension procedure when the MP joint is in the flexed position. Do not jerk the finger to attempt to disrupt the cord, as this may contribute to tendon rupture. If two joints in one finger were treated, perform the finger extension procedure on the affected MP joint before performing the finger extension procedure on the affected PIP joint.

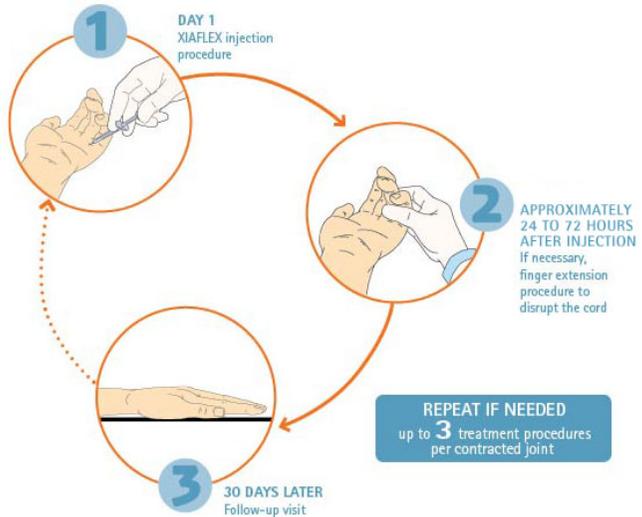


## Finger Extension Procedure(s) (continued)

5. During this visit (approximately 24 to 72 hours after the XIAFLEX injection), if the first finger extension procedure does not result in rupture of the cord, a second and third attempt can be performed in 5- and 10-minute intervals. However, no more than 3 attempts to rupture a cord are recommended during this visit.

**Please see Prescribing Information and Medication Guide**

6. If the cord has not ruptured after 3 attempts of extension per joint, a follow-up visit should be scheduled in approximately 4 weeks. If the contracted cord persists at that subsequent visit, an additional XIAFLEX<sup>®</sup> injection and subsequent finger extension procedure may be repeated



In 2 XIAFLEX clinical trials, 64% and 44% of the XIAFLEX-treated patients, compared to 7% and 5% of the placebo-treated patients, achieved reduction in contracture of the primary joint (MP or PIP) to 0° to 5° after up to 3 injections.

## Finger Extension Procedure(s) (continued)

7. Care should be taken during release of contracture, as some patients may experience skin splitting. If this occurs, cover the area with gauze and apply gentle pressure until bleeding stops. Standard wound care with regular dressings should be applied



8. Following the finger extension procedure(s), patients should be fitted with a splint and provided instructions for use at bedtime for up to 4 months to maintain finger extension. Instruct the patient to perform finger extension and flexion exercises several times a day for several months. Patients can be instructed to resume normal activities, but should not perform strenuous activity with the injected hand until instructed to do so

**Please see Prescribing Information and Medication Guide**

## XIAFLEX<sup>®</sup> Indication and Important Safety Information for the treatment of Dupuytren's contracture

### INDICATION

XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.

### IMPORTANT SAFETY INFORMATION

XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

In the controlled and uncontrolled portions of clinical trials, flexor tendon ruptures occurred after XIAFLEX injection. Injection of XIAFLEX into collagen-containing structures such as tendons or ligaments of the hand may result in damage to those structures and possible permanent injury such as tendon rupture, ligament damage, or skin laceration. Therefore, XIAFLEX<sup>®</sup> should be injected only into the collagen cord with a MP or PIP joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting a cord affecting a PIP joint of the fifth finger, insert the needle no more than 2 to 3 mm in depth, and avoid injecting more than 4 mm distal to the palmar digital crease.

Other serious local adverse reactions in clinical trials include: pulley rupture, ligament injury, complex regional pain syndrome (CRPS), and sensory abnormality of the hand.

## XIAFLEX<sup>®</sup> Indication and Important Safety Information for the treatment of Dupuytren's contracture (continued)

In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared with subjects treated with up to three single injections in the placebo-controlled studies (9%). Cases of skin laceration requiring skin graft after finger extension procedures have been reported post-marketing.

In the controlled portions of the clinical trials (Studies 1 and 2), a greater proportion of XIAFLEX-treated patients (15%) compared to placebo-treated patients (1%) had mild allergic reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections.

Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial (Study 3) in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture. Healthcare providers should be prepared to address severe allergic reactions following XIAFLEX injections.

**Please see Prescribing Information and Medication Guide**

In the XIAFLEX trials (Studies 1 and 2), 70% and 38% of XIAFLEX-treated patients developed an ecchymosis/contusion or an injection site hemorrhage, respectively. The efficacy and safety of XIAFLEX in patients receiving anticoagulant medications (other than low-dose aspirin) within 7 days prior to XIAFLEX administration is not known. Therefore, use with caution in patients with coagulation disorders including patients receiving concomitant anticoagulants (except for low-dose aspirin).

The most frequently reported adverse drug reactions ( $\geq 5\%$ ) in the XIAFLEX clinical trials and at an incidence greater than placebo included: edema peripheral, contusion, injection site hemorrhage, injection site reaction, pain in extremity, tenderness, injection site swelling, pruritus, lymphadenopathy, skin laceration, lymph node pain, erythema, and axillary pain.

## XIAFLEX<sup>®</sup> Indication and Important Safety Information for the treatment of Dupuytren's contracture (continued)

Read the FDA-approved Prescribing Information for XIAFLEX for an understanding of the benefits and risks of XIAFLEX in the treatment of adult patients with Dupuytren's contracture with a palpable cord.

Distribute the XIAFLEX Medication Guide to your patients and counsel each on the associated risks of treatment.

If you have product-related questions, please contact the Auxilium Drug Information Center at 1-877-663-0412.

**To report adverse events, please contact either of the following:**

- Auxilium Drug Information Center at 1-877-663-0412
- FDA MedWatch reporting system by telephone (1-800-FDA-1088), fax (1-800-FDA-0178), online (<https://www.accessdata.fda.gov/scripts/medwatch/>), or by mail using the postage-paid MedWatch Voluntary Reporting Form 3500.

Please mail to:

FDA Safety Information and Adverse Event  
Reporting Program  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD, 20852-9787

**Please see Prescribing Information and Medication Guide.**

## Frequently Asked Questions

### **1. What are the risks of XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) use in the treatment of Dupuytren's contracture?**

In the XIAFLEX clinical studies, serious injury of the injected extremity including flexor tendon ruptures occurred after XIAFLEX injection.

Injection of XIAFLEX into collagen-containing structures, such as tendons or ligaments of the hand, may result in damage to those structures and possible permanent injury, such as tendon rupture or ligament damage.

Therefore, XIAFLEX should be injected only into the collagen cord causing an MP or PIP joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. Other events of the injected extremity included pulley rupture, ligament injury, recurrence of complex regional pain syndrome, tendonitis, and sensory abnormality of the hand.

Because XIAFLEX contains foreign proteins, severe allergic reactions, including anaphylaxis, can occur following XIAFLEX injections.

Healthcare providers should be prepared to address severe allergic reactions following XIAFLEX injections. Please see the Prescribing Information for additional information concerning XIAFLEX use.

## Frequently Asked Questions (continued)

### **2. Why is a Risk Evaluation and Mitigation Strategy (REMS) program required for XIAFLEX for the treatment of Dupuytren's contracture?**

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. The FDA has determined that a REMS is necessary to help mitigate the risks associated with XIAFLEX.

Auxilium has worked with the FDA to develop the XIAFLEX REMS program to inform healthcare providers and patients about the potential risks with XIAFLEX. The XIAFLEX REMS materials for healthcare providers, including this Training Guide and the Training Video, were designed to reduce the risk of tendon rupture and other serious adverse events.

### **3. What is the likelihood of tendon rupture?**

Of the 1,082 patients who received 0.58 mg of XIAFLEX in the controlled and uncontrolled portions of the XIAFLEX studies (2,630 XIAFLEX injections), 3 (0.3%) patients had a flexor tendon rupture of the injected finger. The incidence of XIAFLEX-associated tendon ruptures in clinical practice may be different than the incidence seen in the XIAFLEX clinical studies.

**Please see Prescribing Information and Medication Guide**

#### **4. Were there any allergic reactions to XIAFLEX®?**

Anaphylaxis was reported in a post-marketing clinical trial in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture. Healthcare providers should be prepared to address severe hypersensitivity reactions (including anaphylaxis) following XIAFLEX injections.

In the controlled portions of the clinical trials (Studies 1 and 2), a greater proportion of XIAFLEX-treated patients (15%) compared with placebo-treated patients (1%) had mild hypersensitivity reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections.

#### **5. What is my responsibility when I prescribe/administer XIAFLEX for the treatment of Dupuytren's contracture?**

You should read the Prescribing Information. The Prescribing Information and training materials include important information regarding the proper injection of XIAFLEX and the finger extension procedure(s) designed to mitigate the risks of tendon rupture, special precautions for injection of a cord

## Frequently Asked Questions (continued)

affecting the PIP joint of the fifth finger, and other serious adverse events of the injected extremity. Secondly, a Medication Guide should be dispensed to each patient receiving XIAFLEX. This Medication Guide contains information that can be used to facilitate discussions about the potential risks of XIAFLEX. It is important to counsel patients about the risks associated with XIAFLEX including tendon rupture, other serious adverse events of the injected extremity, and the potential risk of serious hypersensitivity reactions (including the potential for anaphylaxis).

The Prescribing Information and the Medication Guide will be included in the product packaging and also can be found at [www.XIAFLEX.com](http://www.XIAFLEX.com). For additional information, visit [www.XIAFLEX.com](http://www.XIAFLEX.com) or contact the toll-free medical information line (1-877-XIAFLEX; 1-877-942-3539).

To report adverse events, please contact either of the following: Auxilium Drug Information Center at 1-877-663-0412 or the FDA MedWatch reporting system by telephone (1-800-FDA-1088), fax (1-800-FDA-0178), or online (<https://www.accessdata.fda.gov/scripts/medwatch/>).

**Please see Prescribing Information and Medication Guide.**

## Access to XIAFLEX<sup>®</sup> for the treatment of Dupuytren's contracture

XIAFLEX<sup>®</sup> is only available through a managed distribution program for the treatment of Dupuytren's contracture.

The enrollment process consists of 3 steps:

1. Review the training materials
2. Complete, sign, and fax or mail the healthcare provider enrollment form to be able to order XIAFLEX
3. Complete, sign, and fax or mail the site enrollment form to register site(s) for shipping

More details can be found at [www.XIAFLEXREMS.com](http://www.XIAFLEXREMS.com).

**Please see Prescribing Information and Medication Guide**



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RMX-00068

# XIAFLEX Training Video for Treatment of Dupuytren's Contracture

NARRATIVE	VISUAL
<b>OPENING</b>	
<p><i>Narrator:</i> Welcome to the XIAFLEX training video. XIAFLEX, or collagenase clostridium histolyticum is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.</p> <p><b>PI/p2/Indications and Usage</b></p> <p>XIAFLEX should be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of Dupuytren's contracture.</p> <p><b>PI/p1/c1/Dosage and Administration/bullet 1</b></p> <p>This video demonstrates the steps necessary to prepare and administer XIAFLEX. It also outlines the finger extension procedures that may be required approximately 24 to 72 hours after injection to help disrupt the cord. This video also includes special precautions for injection of a cord affecting the proximal interphalangeal, or PIP, joint of the fifth finger.</p>	 <p><small>This Training Video is prepared and approved by the Food and Drug Administration (FDA) as part of the XIAFLEX® (collagenase clostridium histolyticum) (CCH) Kit. XIAFLEX is a sterile, lyophilized, injectable enzyme in a sterile, single-use vial. XIAFLEX is indicated for the treatment of Dupuytren's contracture with a palpable cord in the hand and is approved by the FDA to ensure that the benefits of the drug outweigh its risks.</small></p> <p><small>Accutane has worked with the FDA to develop this Training Video to inform healthcare providers about the risks of XIAFLEX including tendon rupture and other serious adverse events of the ligament complex and the possible risk of severe hypotension events. This Training Video also provides instructions on the proper preparation and administration of XIAFLEX to reduce the risk of serious adverse events of the ligament complex.</small></p>

**NARRATIVE**

**VISUAL**

**INTRODUCTION**

[TRANSITION SLIDE]



*KOL:* Hello, I'm Dr. Lawrence Hurst, Professor and Chair of the Department of Orthopedic Surgery at the State University of New York at Stony Brook.



*KOL:* In the early 1980s, researchers established the central role of collagen in the pathogenesis of Dupuytren's disease.

Dr Marie Badalamente and I felt that collagen would be a serious therapeutic target and began investigating the role of a clostridial collagenase that could be injected into the cords that cause Dupuytren's disease.

XIAFLEX contains 2 different classes of clostridial collagenase, which break down collagen at different locations along the collagen fiber. [panel #1]

**PI/p10/"Description" and "Clinical Pharmacology"**

Once the collagen is broken into these smaller, disorganized units, endogenous enzymes are able to assist in further breaking down the fibrous material. [panel #2]

Panel #1



Panel #2



**INTRODUCTION**

*KOL:* Since collagen also exists in tissues other than the cords that cause Dupuytren’s disease, it is vitally important that XIAFLEX be injected properly. This video will demonstrate the proper injection technique, preparation and follow-up finger-extension procedure used to disrupt the Dupuytren’s cord after the administration of XIAFLEX.

Also, there is important safety information at the end of the video that should be reviewed carefully.



*Narrator:* XIAFLEX should be injected into the cord at the point of maximal separation between the cord and the underlying flexor tendon in order to prevent accidental injection into the flexor tendon sheath.

Care must be taken to place the needle in the cord, and not through the cord.

Special care should also be taken when injecting the PIP joint of the fifth finger.



*Narrator:* If injecting into a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and care should be taken to avoid injecting more than 4 mm distal to the palmar digital crease. Tendon ruptures have occurred after XIAFLEX injections near the fifth finger digital PIP joint crease.

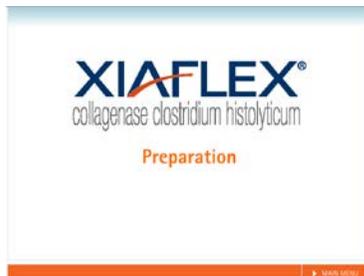


**NARRATIVE**

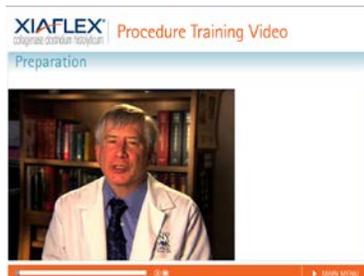
**VISUAL**

**PREPARATION**

[TRANSITION SLIDE]



*KOL:* In the next section, we will discuss how to properly prepare XIAFLEX for injection. It is important to note that preparation will be slightly different depending on whether you are treating an MP or PIP joint.



*Narrator:* XIAFLEX is supplied in a single-use glass vial containing 0.9 mg of a sterile, lyophilized powder for reconstitution. The vial of lyophilized XIAFLEX powder should be reconstituted only with the sterile diluent provided in a single-use glass vial in the package. **PI/p5”Dosage Forms and Strengths”;** **PI/p3”Reconstitution of the Lyophilized Powder”/c**

Each vial of XIAFLEX and sterile diluent should only be used for a single injection. If two concurrent injections in the same hand are planned, separate vials should be reconstituted using separate syringes for each injection. Different preparation is required if you are concurrently treating both an MP joint and a PIP joint.



## NARRATIVE

## VISUAL

### PREPARATION

Preparation of each vial of XIAFLEX will require a syringe with 0.01 mL graduations with a 27 gauge, ½-inch needle.

**PI/p3/”Reconstitution of the Lyophilized Powder”/d; p4/”Injection Procedure”/a**  
Syringes are not included in the package. Prior to reconstitution, the vials of lyophilized XIAFLEX powder and sterile diluent should be stored in the upright position in a refrigerator [**panel #1**].

Before removing the vials from the refrigerator, confirm that each joint to be treated has a palpable cord. This is particularly important when performing a 2<sup>nd</sup> or 3<sup>rd</sup> XIAFLEX injection for an affected joint.

Once a palpable cord has been identified, the XIAFLEX and sterile diluent vials should be removed from the refrigerator and allowed to stand at room temperature for at least 15 minutes and no longer than 60 minutes [**panel #2**]. **PI/p3/”Reconstitution of the Lyophilized Powder”/a**

If the vials have accidentally been allowed to stand at room temperature for over 60 minutes, they should not be used.

Visually inspect the vial containing XIAFLEX. The cake of lyophilized powder should be intact and white in color. If the cake has been eroded, it should not be used, and should be reported to Auxilium by calling 1-877-663-0412. [**panel #3**]

### Panel #1



### Panel #2



### Panel #3



**PREPARATION**

*Narrator:* To begin preparing the solution, first identify the joint contracture that is associated with the palpable cord as the volume of sterile diluent required for reconstitution is determined by the type of joint contracture. When injecting XIAFLEX into a Dupuytren’s cord affecting the PIP joint of the fifth finger, special precautions should be taken. Please see the “Warnings and Precautions” section in the FDA-approved Prescribing Information. For a cord affecting an MP joint use 0.39 mL of diluent for reconstitution [**panel #1**] and for a cord affecting a PIP joint use 0.31 mL [**panel #2**]. **PI/p2/Table 1**

When injecting two cords in the same hand concurrently, begin with the affected finger in the most lateral aspect of the hand and continue toward the medial aspect (eg, fifth finger to index finger). Within each finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (eg, MP to PIP).

*Narrator:* Next, remove the protective covering from both vials...  
**PI/p3/”Reconstitution of the Lyophilized Powder”/b**

**Panel #1**



**Panel #2**



**NARRATIVE****VISUAL****PREPARATION**

*Narrator:* ... and, using aseptic technique, swab the rubber stoppers and surrounding surface of both vials with sterile alcohol. No other antiseptics should be used.

**PI/p3”Reconstitution of the Lyophilized Powder”/b**



*Narrator:* Using a syringe that contains 0.01 mL graduations, with a 27 gauge ½ inch needle, withdraw the appropriate amount of sterile diluent required for reconstitution. Again, for a cord affecting an MP joint use 0.39 mL of diluent [panel #1] and for a cord affecting a PIP joint use 0.31 mL [panel #2]. **PI/p3”Reconstitution of the Lyophilized Powder”/d**

**Panel #1****Panel #2**

*Narrator:* Then, inject the diluent slowly into the sides of the vial containing the lyophilized powder of XIAFLEX.

**PI/p3”Reconstitution of the Lyophilized Powder”/e**



**PREPARATION**

*Narrator:* Slowly swirl the solution to ensure that all of the lyophilized powder has gone into solution [**panel #1**].

**PI/p3/”Reconstitution of the Lyophilized Powder”/e** Do not shake the solution because it can denature the proteins.

The reconstituted XIAFLEX solution should be clear. Inspect the solution visually for particulate matter and discoloration prior to administration. If the solution contains particulates, is cloudy, or is discolored, do not inject it [**panel #2**].

**PI/p3/”Reconstitution of the Lyophilized Powder”/e** If particulate matter is detected report it to Auxilium by calling 1-877-663-0412.

**Panel #1**



**Panel #2**



*Narrator:* As a final step, discard the sterile diluent vial and the syringe and needle used for reconstitution. **PI/p3/”Reconstitution of the Lyophilized Powder”/g**

If a second concurrent injection is planned, prepare a second vial of reconstituted XIAFLEX using new needles according to the instructions, keeping in mind that the second joint could require a different reconstitution volume based on the joint type.



**PREPARATION**

*Narrator:* The solution is now ready for injection. [panel #1]

Reconstituted XIAFLEX solution can be kept at room temperature for up to one hour or refrigerated for up to 4 hours prior to administration [panel #2]. If refrigerated, the reconstituted XIAFLEX solution should be allowed to return to room temperature for approximately 15 minutes before use.

**PI/p3”Reconstitution of the Lyophilized Powder”/f**

Panel #1



Panel #2



**PREPARATION***[Self-Learning Versions]*

*Narrator:* This completes the section on Preparation of the XIAFLEX injection. To confirm understanding of the key points in this section, please answer the following self-test questions.

After answering these questions you may continue to the next section.

**XIAFLEX** Procedure Training Video

## Preparation Questions

- 1) Before use, for how long should the vial containing XIAFLEX and the diluent be left to stand at room temperature?
- a. 0-10 minutes
  - b. 10-20 minutes
  - c. 30-60 minutes
  - d. At least 2 hours

[Next slide](#)**XIAFLEX** Procedure Training Video

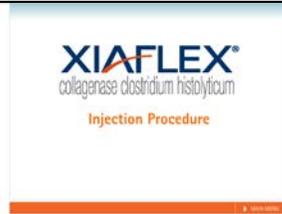
## Preparation Questions

- 2) The amount of diluent that should be used for reconstitution when treating a PJP joint is:
- a. 0.10 mL
  - b. 0.20 mL
  - c. 0.21 mL
  - d. 0.30 mL

[Next slide](#)

**NARRATIVE****VISUAL****INJECTION PROCEDURE**

[TRANSITION SLIDE]



*KOL:* In the next section, we will discuss how to properly inject XIAFLEX into the cord.

There are three very important points that I wanted to stress here:

First, XIAFLEX should be injected into the cord at the point of maximal separation between the cord and the underlying flexor tendon in order to prevent accidental injection into the flexor tendon sheath.

Second, care must be taken to place the needle in the cord, and not through the cord.

And third, special care should also be taken when injecting the PIP joint of the fifth finger.

Let's now look at the procedure in more detail.



**INJECTION PROCEDURE**

*Narrator:* As you prepare for injection, first reconfirm the cord to be injected [**panel #1**]. The site chosen for injection should be the area where the contracting cord is maximally separated from the underlying flexor tendons [**panel #2**] and where the skin is not intimately adhered to the cord [**panel #3**]. **PI/p3/”Preparation Prior to Injection”/d**

**Panel #1**



**Panel #2**



**Panel #3**



*Narrator:* If injecting into a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and care should be taken to avoid injecting more than 4 mm distal to the palmar digital crease. Tendon ruptures have occurred after XIAFLEX injections near the fifth finger digital PIP joint crease. **PI/p3/”Preparation Prior to Injection”/c**



**NARRATIVE****VISUAL****INJECTION PROCEDURE**

*Narrator:* Begin by preparing the skin with an antiseptic and allowing it to dry.

**PI/p3/Preparation Prior to Injection/e**  
Make sure that any jewelry on the affected hand has been removed.

Administration of a local anesthetic agent prior to injection of XIAFLEX is not recommended, as it may interfere with proper placement of the injection.

**PI/p3/Preparation Prior to Injection/b**  
It is also not recommended because it may be just as painful as the injection of XIAFLEX.



*Narrator:* Next, using a new 1 mL hubless syringe with 0.01 mL graduations and a permanently fixed, 27 gauge, ½-inch needle, withdraw the volume of reconstituted XIAFLEX solution required for injection. For a cord affecting an MP joint, withdraw 0.25 mL [**panel #1**] and for a cord affecting a PIP joint withdraw 0.20 mL [**panel #2**]. **PI/p4/Injection Procedure/a**

**Panel #1****Panel #2**

If two affected joints are treated concurrently, be sure to use the reconstituted solution prepared for each specific joint since the preparation for MP and PIP joints is different.



**INJECTION PROCEDURE**

*Narrator:* When injecting two cords in the same hand concurrently, begin with the affected finger in the most lateral aspect of the hand and continue toward the medial aspect (eg, fifth finger to index finger). Within each finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (eg, MP to PIP).

Where a single cord affects both the MP and PIP joint in the same finger, administer one injection into the cord at the MP level and administer a second injection into the cord at the PIP level during the treatment visit. Each injection contains a 0.58 mg dose.

When administering two injections in the same hand during a treatment visit, use a new syringe and needle and separate vial of reconstituted solution for the second injection.



**INJECTION PROCEDURE**

*Narrator:* After withdrawing the correct volume of reconstituted XIAFLEX, carefully place the needle into the cord [panel #1]. The cord has a gritty, gristly consistency [panel #2]. It is important to keep the needle within the cord and not allow the needle tip to pass completely through the cord [panel #3]. This will help minimize the potential for injection of XIAFLEX into tissues other than the cord. After needle placement, if there is any concern that the needle is in the flexor tendon, apply a small amount of passive motion at the distal interphalangeal joint to ascertain that the needle does not move with finger tip motion. If insertion of the needle into a tendon is suspected or paresthesia is noted by the patient, withdraw the needle and reposition it into the Dupuytren's cord. **PI/p4"Injection Procedure"/b**

**Panel #1****Panel #2****Panel #3**

*Narrator:* After confirming that the needle is correctly placed in the cord, inject approximately one-third of the dose. **PI/p4"Injection Procedure"/c** When injecting, it is important to stabilize the needle while pushing the plunger to prevent accidental injection through the cord.



## NARRATIVE

## VISUAL

### INJECTION PROCEDURE

*Narrator:* Next, withdraw the needle tip from the cord, reposition it in the cord approximately 2-3 mm distal to the initial injection and inject another one-third of the dose [panel #1]. **PI/p4/Injection Procedure"/d**

For ease of repositioning, it may be helpful to not completely withdraw the needle tip from the skin.

*Narrator:* Withdraw the needle tip from the cord again and reposition it in the cord, this time approximately 2-3 mm proximal to the initial injection and inject the final portion of the dose. **PI/p4/Injection Procedure"/e**

*Narrator:* An alternate method of injection may be used in which the needle is completely withdrawn from the skin when being repositioned in the cord.

Again, when injecting a cord affecting the PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and avoid injecting more than 4 mm distal to the palmar digital crease.

### Panel #1



**NARRATIVE****VISUAL****INJECTION PROCEDURE**

*Narrator:*

After the injections are completed, wrap the patient's treated hand with a soft, bulky, gauze dressing **PI/p4/"Injection Procedure"/f**

Instruct the patient to return the next day and to keep the hand elevated until bedtime. Patients should be instructed not to attempt to disrupt the injected cord by self manipulation. **PI/p14/"Patient Counseling Information"**



**INJECTION PROCEDURE**

*Narrator:* Patients should be informed that the injection may result in swelling, bruising, bleeding, and/or pain at the injection site and surrounding tissue. **[panel #1]** They should be instructed to limit motion of the injected finger until the return visit, usually the following day. **[panel #2]** Patients should also be instructed to promptly contact their physician if there is evidence of infection, sensory changes, or trouble bending the finger after the swelling goes down.

**PI/p14/“Patient Counseling Information”**

Panel #1



Panel#2



## INJECTION PROCEDURE

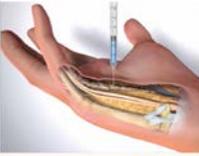
[Self-Learning Versions]

*Narrator:* This completes the section on the proper injection procedure for the XIAFLEX injection. To confirm understanding of the key points in this section, please answer the following self-test questions.

After answering these questions you may continue to the next section.

**XIAFLEX**  
Chondroitin Sulfate Sodium Procedure Training Video

Injection Procedure



**BEFORE INJECTION**

**INJECTION**

**AFTER INJECTION**

- Instruct patient to limit motion of the injected finger
- Instruct patient to contact physician if there is evidence of:
  - Infection
  - Sensory changes
  - Trouble holding the finger after the swelling goes down

▶ [VIEW TESTS](#)

**XIAFLEX**  
Chondroitin Sulfate Sodium Procedure Training Video

Injection Procedure Questions

3) The proper site of injection for XIAFLEX is:

- the proximal end of the cord
- the point of maximal separation of the cord from the underlying tendons
- the distal end of the cord
- the tissue surrounding the cord

▶ [VIEW TESTS](#)

**XIAFLEX**  
Chondroitin Sulfate Sodium Procedure Training Video

Injection Procedure Questions

4) The amount of reconstituted XIAFLEX that should be injected when treating an MP joint is:

- 0.20 mL
- 0.25 mL
- 0.31 mL
- 0.39 mL

▶ [VIEW TESTS](#)

**XIAFLEX**  
Chondroitin Sulfate Sodium Procedure Training Video

Injection Procedure Questions

5) When injecting XIAFLEX, it is important to:

- Use an anesthetic before injection
- Inject the entire dose all at once without repositioning the needle
- Ensure that the tip of the needle is in the cord and has not gone through the cord
- Place a tight dressing over the hand to allow patients to move their fingers as soon as the procedure is completed

▶ [VIEW TESTS](#)

**NARRATIVE****VISUAL****FINGER EXTENSION PROCEDURE**

[TRANSITION SLIDE]



*KOL:* This final section will briefly describe the finger extension procedure that should be used to disrupt the Dupuytren's cord. It should be performed on the follow-up visit approximately 24 to 72 hours after the injection.

In some patients, the cord may rupture on its own.

If this is not the case, the following procedure should be followed.



## NARRATIVE

## VISUAL

### FINGER EXTENSION PROCEDURE

*Narrator:* Determine if the contracture has resolved at the follow-up visit the day after XIAFLEX injection. [panel #1]

If a contracture remains on the follow-up visit, a passive finger extension procedure should be undertaken in an attempt to disrupt the cord. **PI/p4''Finger Extension Procedure''/a** Local anesthesia may be used during the finger extension procedure since the procedure can be painful for the patient. **PI/p4''Finger Extension Procedure''/b**

If two joints in one finger were treated, perform the finger extension procedure on the affected MP joint before performing the finger extension procedure on the affected PIP joint.

With the patient's wrist in a flexed position, apply moderate stretching pressure to the injected cord by extending the finger for approximately 10 to 20 seconds. For cords affecting the PIP joint, perform the finger extension procedure when the MP joint is in the flexed position. **PI/p4''Finger Extension Procedure''/c** Do not jerk the finger to attempt to disrupt the cord as this may contribute to tendon rupture. Sometimes, disruption of the cord might not occur. In other instances, the cord will be disrupted without a sound. Additionally, there may be cases in which there will be an audible "pop" when the cord is disrupted [panel #2].

During this visit, approximately 24 to 72 hours after the XIAFLEX injection, if the first finger extension procedure does not result in rupture of the cord, a second and third attempt can be performed in 5- and 10-minute intervals. However, no more than 3 attempts to rupture a cord are recommended during this visit. [panel #3] **PI/p5''Finger Extension Procedure''/d**

#### Panel #1



#### Panel #2



#### Panel #3



## NARRATIVE

## VISUAL

### FINGER EXTENSION PROCEDURE

If the cord has not disrupted after 3 attempts of extension per joint, a follow-up visit should be scheduled in approximately 4 weeks [panel #4]. If, at that subsequent visit the contracted cord persists, an additional XIAFLEX injection and subsequent finger extension procedure, or procedures, may be repeated [panel #5]. **PI/p5”Finger Extension Procedure”/e**

It is not unusual for patients to require more than one injection, and in fact, they can receive up to 3 injections per cord at 4 week intervals [panel #6]. **PI/p2”Dosing Overview”/paragraph 3**

### Panel #4

**XIAFLEX**  
Ceftriaxone sodium 1000mg

### Procedure Training Video

#### Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection

30 Days Later  
Follow-up visit

In the XIAFLEX clinical trials, 84% and 84% of the XIAFLEX treated patients, compared to 7% and 23% of the placebo-treated patients, achieved reduction in length of the primary cord. 50% of patients up to 2” after up to 3 injections.

MAIN MENU

### Panel #5

**XIAFLEX**  
Ceftriaxone sodium 1000mg

### Procedure Training Video

#### Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection

Injection procedure

MAIN MENU

### Panel #6

**XIAFLEX**  
Ceftriaxone sodium 1000mg

### Procedure Training Video

#### Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection
- Up to 3 injections can be administered per cord

Up to 3 injections can be administered per cord

MAIN MENU

## NARRATIVE

## VISUAL

### FINGER EXTENSION PROCEDURE

During release of contracture, some patients may experience skin splitting. If this occurs, standard wound care with regular dressings should be applied [panel #7].

Following the finger extension procedure, or procedures, patients should be fitted with a splint and provided instructions for use at bedtime for up to 4 months to maintain finger extension [panel #8]. **PI/p5”Finger Extension Procedure”f** Instruct the patient to perform finger extension and flexion exercises several times a day for several months. Patients can be instructed to resume normal activities, but should not perform strenuous activity with the injected hand until told to do so. **PI/p14”Patient Counseling Information”**

### Panel #7

**XIAFLEX**  
Cialis (tadalafil) injection

#### Procedure Training Video

Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection
- Up to 3 injections can be administered per cord



▶ LEARN MORE

### Panel #8

**XIAFLEX**  
Cialis (tadalafil) injection

#### Procedure Training Video

Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection
- Up to 3 injections can be administered per cord
- Fit patient with a splint



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**XIAFLEX**  
Cialis (tadalafil) injection

#### Procedure Training Video

Finger Extension Procedure(s)

**FOLLOW-UP**

- Apply moderate stretching pressure for 10-20 seconds
- Second and third attempts can be made at 5-10 minute intervals
- No more than 3 attempts
- Follow up in 4 weeks if cord is not disrupted; consider additional injection
- Up to 3 injections can be administered per cord
- Fit patient with a splint



▶ LEARN MORE

**FINGER EXTENSION PROCEDURE**

*[Self-learning Versions]*

*Narrator: This concludes the section on finger extension. To confirm understanding of the key points in this section, please answer the following self-test questions.*

*After answering these questions you may continue to the next section.*



**XIAFLEX** Procedure Training Video

Finger Extension Procedure(s) Questions

- 6) How long should moderate stretching pressure be applied during passive extension?
- 5-10 seconds
  - 10-20 seconds
  - 30-60 seconds
  - 1-2 minutes

▶ NEXT VIDEO



**XIAFLEX** Procedure Training Video

Finger Extension Procedure(s) Questions

- 7) What is the maximum number of attempts that should be made to disrupt the cord during the follow up visit?
- 3
  - 4
  - 5
  - 6

▶ NEXT VIDEO



**XIAFLEX** Procedure Training Video

Finger Extension Procedure(s) Questions

- 8) Injections and finger extension procedures may be administered up to \_\_\_ times per cord at approximately 4-week intervals.
- 1
  - 2
  - 3
  - 4

▶ NEXT VIDEO

**NARRATIVE****VISUAL****SUMMARY**

[TRANSITION SLIDE]



*KOL:* Thank you for taking time out to learn about the preparation and injection of XIAFLEX. Here's a recap of some key points.



SUMMARY

Narrator:

**Preparation stage**

- Before preparing XIAFLEX, allow vials to stand at room temperature for at least 15 minutes and no longer than 60 minutes [**panel #1**]
- **PI/p3/”Reconstitution of the Lyophilized Powder”/a**
- Identify the joint contracture that is associated with the palpable cord as the volume of sterile diluent required for reconstitution is determined by the type of joint contracture. For a cord affecting an MP joint use 0.39 mL of diluent for reconstitution [**panel #2**] and for a cord affecting a PIP joint use 0.31 mL. [**panel #3**] **PI/p2/****Table 1**
- If two concurrent injections in the same hand are planned, use a new syringe and needle to prepare a second injection of XIAFLEX for the second injection according to the instructions for the specific joint type.

Panel #1



Panel #2



Panel #3



**SUMMARY**

**Injection procedure**

- Using a new needle, withdraw and inject the volume of reconstituted XIAFLEX solution required for injection. For a cord affecting an MP joint, withdraw 0.25 mL [panel #4] and for a cord affecting a PIP joint withdraw 0.20 mL [panel #5] **PI/p2/Table 1**
- Inject XIAFLEX at the site of maximal separation of the cord from underlying tendons [panel #6] **PI/p3/“Preparation Prior to Injection”/d**
- When injecting a cord affecting a PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and avoid injecting more than 4 mm distal to the palmar digital crease. [panel #7] **PI/p3/“Preparation Prior to Injection”/c**

**Panel #4**

Joint to be Treated	Volume to be Withdrawn from Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

**Panel #5**

Joint to be Treated	Volume to be Withdrawn from Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

**Panel #6**

Joint to be Treated	Volume to be Withdrawn from Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

**Panel #7**

Joint to be Treated	Volume to be Withdrawn from Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

SUMMARY

- Confirm that the needle tip is placed in the cord [panel #8] **PI/p4/”Injection Procedure”/b**
- To maximize contact with the cord, XIAFLEX should be injected into the cord at 3 adjacent locations with one-third of the total dose being injected at each location [panels #9, 10] **PI/p4/”Injection Procedure”/c,d,e**
- When administering two injections in the same hand during a treatment visit, use a new syringe and needle and separate vial of reconstituted solution for the second injection.
- When injecting two cords in the same hand concurrently, begin with the affected finger in the most lateral aspect of the hand and continue toward the medial aspect (eg, fifth finger to index finger). Within each finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (eg, MP to PIP).

Panel #8



Panel #9



Panel #10



## SUMMARY

**Finger extension procedure**

- A passive finger extension procedure can be performed approximately 24 to 72 hours after injection if a contracture persists. Local anesthesia may be used during the finger extension procedure since the procedure can be painful for the patient.
- If two joints in one finger were treated, perform the finger extension procedure on the affected MP joint before performing the finger extension procedure on the affected PIP joint.
- For finger extension, apply moderate stretching pressure for 10-20 seconds, waiting 5-10 minutes between attempts **[panel #11]**  
**PI/p4''Finger Extension Procedure''/c; p5''Finger Extension Procedure''/d**
- No more than 3 attempts per joint should be made in a single visit  
**PI/p5''Finger Extension Procedure''/d**
- Following the finger extension procedure, patients should be fitted with a splint **[panel #12]**  
**PI/p5''Finger Extension Procedure''/f**

**Panel #11****Panel #12**

## NARRATIVE

## VISUAL

### IMPORTANT SAFETY INFORMATION

*Narrator:* In this section, we will review the indication and important safety information for XIAFLEX, collagenase clostridium histolyticum.

XIAFLEX is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. **PI/p2/Indications and Usage**

### IMPORTANT SAFETY INFORMATION

XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

In the controlled and uncontrolled portions of clinical trials, flexor tendon ruptures occurred after XIAFLEX injection. Injection of XIAFLEX into collagen-containing structures such as tendons or ligaments of the hand may result in damage to those structures and possible permanent injury such as tendon rupture, ligament damage, or skin laceration. Therefore, XIAFLEX should be injected only into the collagen cord with an MP or PIP joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting a cord affecting a PIP joint of the fifth finger, insert the needle no more than 2 to 3 mm in depth, and avoid injecting more than 4 mm distal to the palmar digital crease.

Other serious local adverse reactions in clinical trials include: pulley rupture, ligament injury, complex regional pain syndrome (CRPS), and sensory abnormality of the hand.

In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared

**XIAFLEX**<sup>®</sup>  
collagenase clostridium histolyticum

Indication and  
Important Safety Information

▶ NEXT MENU

**XIAFLEX**<sup>®</sup>  
collagenase clostridium histolyticum

Procedure Training Video

Indication

XIAFLEX is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.

▶ NEXT MENU

**XIAFLEX**<sup>®</sup>  
collagenase clostridium histolyticum

Procedure Training Video

Important Safety Information

XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

In the controlled and uncontrolled portions of clinical trials, flexor tendon ruptures occurred after XIAFLEX injection. Injection of XIAFLEX into collagen-containing structures such as tendons or ligaments of the hand may result in damage to those structures and possible permanent injury such as tendon rupture, ligament damage, or skin laceration. Therefore, XIAFLEX should be injected only into the collagen cord with an MP or PIP joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting a cord affecting a PIP joint of the fifth finger, insert the needle no more than 2 to 3 mm in depth, and avoid injecting more than 4 mm distal to the palmar digital crease.

Other serious local adverse reactions in clinical trials include: pulley rupture, ligament injury, complex regional pain syndrome (CRPS), and sensory abnormality of the hand.

In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared with subjects treated with up to three single injections in the placebo-controlled studies (21%). Cases of skin laceration requiring skin graft after finger contracture procedures have been reported post-marketing.

In the controlled portions of the clinical trials (Studies 1 and 2), a greater proportion of XIAFLEX-treated patients (17%) compared to placebo-treated patients (1%) had one or more adverse events reported after up to 3 injections. The incidence of XIAFLEX-reported events increased after more XIAFLEX injections. Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial (Study 3) in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture. Healthcare providers should be prepared to address serious allergic reactions (including anaphylaxis) following XIAFLEX injections.

In the XIAFLEX Study 3 (Study 3) and 2), only one year of post-treatment follow-up was available for patients who were injected with XIAFLEX. Regardless of the efficacy and safety of XIAFLEX in patients receiving anti-infective medications (other than those listed against which it is given) or XIAFLEX administration to local tissues. Therefore, use with caution in patients with immunosuppressive diseases including patients receiving immunosuppressive therapy for the same condition.

The most frequently reported adverse drug reactions (≥ 5%) in the XIAFLEX clinical trials and at an incidence greater than placebo included: edema proximal to the injection site, hematoma, discoloration, skin reaction, pain in softening conditions, injection site swelling, pruritus, lymphadenopathy, skin laceration, lymph node pain, tendinitis, and dactylitis pain.

Please see the Prescribing Information and Medication Guide.

▶ NEXT MENU

**NARRATIVE****VISUAL**

with subjects treated with up to three single injections in the placebo-controlled studies (9%). Cases of skin laceration requiring skin graft after finger extension procedures have been reported post-marketing.

In the controlled portions of the clinical trials (Studies 1 and 2), a greater proportion of XIAFLEX-treated patients (15%) compared to placebo-treated patients (1%) had mild allergic reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections.

Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial (Study 3) in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture. Healthcare providers should be prepared to address severe allergic reactions (including anaphylaxis) following XIAFLEX injections.

In the XIAFLEX trials (Studies 1 and 2), 70% and 38% of XIAFLEX-treated patients developed an ecchymosis/contusion or an injection site hemorrhage, respectively. The efficacy and safety of XIAFLEX in patients receiving anticoagulant medications (other than low-dose aspirin) within 7 days prior to XIAFLEX administration is not known. Therefore, use with caution in patients with coagulation disorders including patients receiving concomitant anticoagulants (except for low-dose aspirin).

The most frequently reported adverse drug reactions ( $\geq 5\%$ ) in the XIAFLEX clinical trials and at an incidence greater than placebo included: edema peripheral, contusion, injection site hemorrhage, injection site reaction, pain in extremity, tenderness, injection site swelling, pruritus, lymphadenopathy, skin laceration, lymph

<b>NARRATIVE</b>	<b>VISUAL</b>
<p>node pain, erythema, and axillary pain.</p> <p>Please see the Prescribing Information and Medication Guide.</p>	

FREQUENTLY ASKED QUESTIONS



XIAFLEX<sup>®</sup> collagenase clostridium histolyticum Procedure Training Video

**FAQ**

1. What are the risks of XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) use?
2. Why is a Risk Evaluation and Mitigation Strategy (REMS) program required for XIAFLEX?
3. What is the likelihood of tendon rupture?
4. Have there any allergic reactions to XIAFLEX?
5. What is my responsibility when I prescribe/administer XIAFLEX?

In the XIAFLEX clinical studies, serious injury of ligament (including those ligament systems associated with XIAFLEX use), fracture of distal radius, wrist, or carpometacarpal joint, or fracture of distal radius, wrist, or carpometacarpal joint, or fracture of distal radius, wrist, or carpometacarpal joint may result in damage to these structures and possible permanent injury to the ligament system. Systemic toxicity, or even toxicity, fracture, XIAFLEX should be injected only into the collagen used with an MP or RP joint conditions, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. Other risks of the injected enzyme include pain, redness, swelling, bruising, redness, redness of complex regional pain syndrome, tendonitis, and unclear etiology of the hand.

Because XIAFLEX contains foreign proteins, some hypersensitivity reactions, including anaphylaxis, could occur following XIAFLEX injection. Healthcare providers should be prepared to address serious allergic reactions following XIAFLEX injection. Please see Full Prescribing Information for additional information concerning XIAFLEX use.

▶ MAIN MENU

XIAFLEX<sup>®</sup> collagenase clostridium histolyticum Procedure Training Video

**FAQ**

1. What are the risks of XIAFLEX<sup>®</sup> (collagenase clostridium histolyticum) use?
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4. Have there any allergic reactions to XIAFLEX?
5. What is my responsibility when I prescribe/administer XIAFLEX?

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to control known or potential serious risks associated with a drug that is essential for the health and drug administration (FDA) to ensure that the benefits of the drug outweigh the risks. The FDA has determined that a REMS is necessary to help mitigate the risks associated with XIAFLEX.

Anatomical factors, such as the size of the hand, may increase the risk of tendon rupture. XIAFLEX should be injected only into the collagen used with an MP or RP joint conditions, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. Other risks of the injected enzyme include pain, redness, swelling, bruising, redness, redness of complex regional pain syndrome, tendonitis, and unclear etiology of the hand.

▶ MAIN MENU

XIAFLEX<sup>®</sup> collagenase clostridium histolyticum Procedure Training Video

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3. What is the likelihood of tendon rupture?
4. Have there any allergic reactions to XIAFLEX?
5. What is my responsibility when I prescribe/administer XIAFLEX?

Of the 1,000 patients who received 100 mg of XIAFLEX in the controlled and uncontrolled portions of the XIAFLEX studies (L100, XIAFLEX, and XIAFLEX-2), 3 (0.3%) patients had a severe tendon rupture of the injected finger. The incidence of XIAFLEX-associated tendon rupture in clinical practice may be different than the incidence seen in the XIAFLEX clinical studies.

▶ MAIN MENU

**XIAFLEX**  
gabapentin extended-release tablets Procedure Training Video

FAQ

1. What are the risks of XIAFLEX (gabapentin extended-release tablets) use?
2. Why is a Risk Evaluation and Mitigation Strategy (REMS) program required for XIAFLEX?
3. What is the likelihood of misuse/abuse?
4. What does any change mean to XIAFLEX?
5. What is my responsibility when I prescribe XIAFLEX?

In the attached portion of the clinical trials (Studies 1 and 2), a greater proportion of XIAFLEX-treated patients (21%) compared with placebo-treated patients (17%) had mild to moderate adverse reactions (reported) after up to 12 weeks. The incidence of XIAFLEX-associated adverse reactions after more XIAFLEX treatment.

Because XIAFLEX contains benzoyl peroxide, more adverse reactions to XIAFLEX use occur. An algorithm was required in a post-marketing clinical trial to use patients who had previous exposure to XIAFLEX for the treatment of Rheumatoid Arthritis. Healthcare providers should be alerted to adverse events associated with XIAFLEX use (including emergency) following XIAFLEX treatment.

▶ MORE INFO

**XIAFLEX**  
gabapentin extended-release tablets Procedure Training Video

FAQ

1. What are the risks of XIAFLEX (gabapentin extended-release tablets) use?
2. Why is a Risk Evaluation and Mitigation Strategy (REMS) program required for XIAFLEX?
3. What is the likelihood of misuse/abuse?
4. What does any change mean to XIAFLEX?
5. What is my responsibility when I prescribe XIAFLEX?

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Because XIAFLEX contains benzoyl peroxide, more adverse reactions to XIAFLEX use occur. An algorithm was required in a post-marketing clinical trial to use patients who had previous exposure to XIAFLEX for the treatment of Rheumatoid Arthritis. Healthcare providers should be alerted to adverse events associated with XIAFLEX use (including emergency) following XIAFLEX treatment.

The prescribing information and the Mitigation Plan will be included in the product packaging and also can be found at [www.xiaflex.com](http://www.xiaflex.com). For additional information, visit [www.xiaflex.com](http://www.xiaflex.com) or contact the toll-free medical information line (1-877-XIAFLEX), 9 AM-5 PM (EST).

To report adverse events, please contact either of the following: American Drug Information Center at (800)833-6343 or the FDA MedWatch reporting system by telephone (1-800-FDA-1088), Fax (1-800-833-6343).

▶ MORE INFO

**XIAFLEX**  
gabapentin extended-release tablets Procedure Training Video

FAQ

1. What are the risks of XIAFLEX (gabapentin extended-release tablets) use?
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▶ MORE INFO

CONTACT US



XIAFLEX<sup>®</sup> Procedure Training Video

Contact Us

Read the Risk-Adjusted Prescribing Information for XIAFLEX for an understanding of the benefits and risks of XIAFLEX in the treatment of adult patients with Dupuytren's contracture with a possible link.

Obtain the XIAFLEX MEDICATION GUIDE to your patients and insert each on the associated risks of treatment.

• You have product-related questions, please contact the  
Auxilium Drug Information Center at 1-877-852-2413.

• Report adverse events, please contact one of the following:  
• National Drug Information Center at 1-877-852-2413  
• FDA MedWatch reporting system by telephone 1-800-FDA-1088, fax 1-800-FDA-0178,  
online 1789a/online.fda.gov/cpr/cdr/cdr.html, or by mail using the average postcard MedWatch Voluntary Reporting Form 2006.

Place and in:  
FDA Safety Information and Adverse Event Reporting Program  
Head of Drug Administration  
1085 Willow Road  
Baltimore, MD 21204-6369

Web center

▶ Slide Show



# **REMS Training Guide** **for Administering** **Xiaflex for** **Peyronie's Disease**

This guide discusses:

- the Xiaflex REMS and the risks of penile fracture or other serious injury to the penis
- the steps necessary to prepare and administer Xiaflex
- the in-office penile modeling procedure that is part of each Xiaflex treatment cycle
- the daily, at-home penile modeling activities that are performed by the patient for approximately 6 weeks after each treatment cycle
- counseling your patient with the Xiaflex Patient Counseling Tool

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## Background

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

A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Xiaflex is only available under a restricted distribution program called the Xiaflex REMS because of the risks of penile fracture and other serious penile injury associated with using Xiaflex in treating Peyronie's Disease.

This training guide is part of the Xiaflex REMS program. This guide discusses:

- the steps necessary to prepare and administer Xiaflex
- the in-office penile modeling procedure that is part of each Xiaflex treatment cycle
- the daily, at-home penile modeling activities that are performed for 5 to 6 weeks after each treatment cycle
- counseling your patient with the Xiaflex Patient Counseling Tool

### Peyronie's Disease

Peyronie's disease is a localized connective tissue disorder characterized by changes in collagen composition in the tunica albuginea.<sup>1</sup> These changes cause an abnormal scar formation known as Peyronie's plaque, which is typically a palpable bump under the skin.<sup>2-4</sup> The Peyronie's plaque is composed predominantly of collagen, and replaces the normally elastic fibers of the tunica albuginea. Microvascular trauma resulting from excessive bending or injury to the penis (possibly during sexual activity) is thought to be an important trigger for the inflammatory response and plaque development characteristic of Peyronie's disease. Genetic predisposition and autoimmunity may also play a role in its development.

One of the hallmarks of Peyronie's disease is penile curvature deformity. Peyronie's disease may also cause other types of deformities, including narrowing, indentation, and shortening of the penis.

### Indication

Xiaflex is indicated for the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy. Xiaflex is also indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. Use of Xiaflex for Dupuytren's contracture is covered under the REMS, but with separate requirements. (A separate letter to healthcare providers describing Important Drug Warnings for use in Dupuytren's contracture is available at [www.XIAFLEXREMS.com](http://www.XIAFLEXREMS.com) or by calling 1-877-313-1235.)

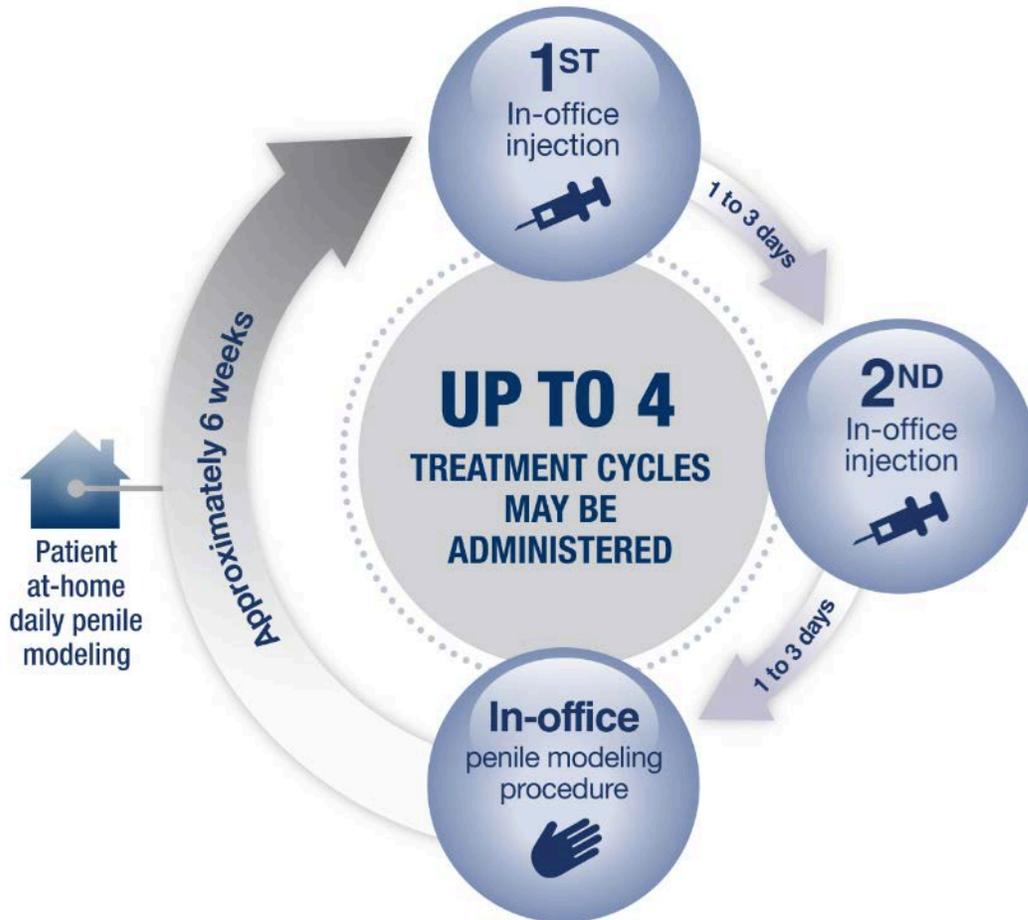
Xiaflex contains 2 different types of purified collagenase clostridium histolyticum (AUX-I and AUX-II), in a defined mass ratio. Injection of Xiaflex into a Peyronie's plaque, which is composed mostly of collagen, may result in enzymatic disruption of the collagen found in Peyronie's plaque. Following this disruption of the collagen-containing plaque, penile curvature deformity may improve while Patient-Reported Bother may be reduced.

Xiaflex should be administered by a healthcare provider experienced in the treatment of male urological diseases, **who has completed required training for use of Xiaflex in the treatment of Peyronie's disease.**

## Xiaflex Treatment Overview

- Xiaflex, supplied as a lyophilized powder, **must be reconstituted with the provided diluent prior to use**
- The dose of Xiaflex is 0.58 mg per injection administered into a Peyronie's plaque. If more than one plaque is present, inject into the plaque causing the curvature deformity
- A treatment course consists of a maximum of 4 treatment cycles. Each treatment cycle consists of 2 Xiaflex injection procedures and one in-office penile modeling procedure. The second Xiaflex injection procedure occurs 1 to 3 days after the first. The in-office penile modeling procedure is performed 1 to 3 days after the second injection of the treatment cycle. (See diagram on next page.) It is necessary to identify the treatment area prior to each treatment cycle
- Healthcare providers must counsel patients on:
  - the risks of penile fractures or other serious injuries of the penis
  - how to perform the at-home penile modeling activities as appropriate
- After the third office visit of each treatment cycle, the patient performs approximately 6 weeks of daily, at-home penile modeling activities

- Up to 4 treatment cycles (for a total of 8 injection procedures and 4 modeling procedures) may be administered per plaque causing the curvature deformity. If the curvature deformity is less than 15 degrees after the first, second or third treatment cycle, or if the healthcare provider determines that further treatment is not clinically indicated, then the subsequent treatment cycles should not be administered
- The safety of more than one treatment course of Xiaflex (comprising 4 treatment cycles) is not known



## Preparing for Administration

This section summarizes the procedure for reconstituting the lyophilized powder of Xiaflex.

Xiaflex is supplied in single-use glass vials containing 0.9 mg of collagenase clostridium histolyticum as a sterile, lyophilized powder for reconstitution. Sterile diluent for reconstitution is supplied in the package in a single-use glass vial containing 3 mL of 0.3 mg/mL calcium chloride dihydrate in 0.9% sodium chloride. **Xiaflex must be reconstituted with the provided diluent prior to use.**



Prior to reconstitution, the vials of lyophilized powder of Xiaflex and sterile diluent should be stored in a refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze.

### Before Use

1. Remove the vial containing the lyophilized powder of Xiaflex and the vial containing the diluent for reconstitution from the refrigerator and check the labels on both the diluent vial and the lyophilized powder vial to make sure they have not expired. Allow the 2 vials to stand at room temperature for at least 15 minutes but no longer than 60 minutes.



2. Visually inspect the vial containing Xiaflex. The cake of lyophilized powder should be intact and white in color. If the cake has been eroded, it should not be used and should be reported to Auxilium by calling 1-877-663-0412.



3. After removing the flip-off cap from each vial, using aseptic technique swab the rubber stopper and surrounding surface of the vial containing Xiaflex and the vial containing the diluent for reconstitution with sterile alcohol (no other antiseptics should be used). Use only the supplied diluent for reconstitution. The diluent contains calcium, which is required for the activity of Xiaflex.
4. Using a 1-mL syringe with 0.01-mL graduations with a 27-gauge ½-inch needle (not supplied), withdraw a volume of 0.39 mL of the **diluent supplied**.



5. Inject the diluent slowly into the sides of the vial containing the lyophilized powder of Xiaflex.



6. Do not invert the vial or shake the solution. Slowly swirl the solution to ensure that all of the lyophilized powder has gone into the solution. Do not use if opaque particles, discoloration, or other foreign particles are present.



7. The reconstituted Xiaflex solution is now ready for injection.

8. The reconstituted Xiaflex solution can be kept at room temperature (20°C to 25°C [68°F to 77°F]) for up to 1 hour or refrigerated at 2°C to 8°C (36°F to 46°F) for up to 4 hours prior to administration. If the reconstituted Xiaflex solution is refrigerated, allow the solution to return to room temperature for approximately 15 minutes before use and no longer than 60 minutes.



9. Do not recap the needle. Discard the syringe, needle, and diluent used for reconstitution using medical waste disposal procedures.

## Self-Test Questions

1. Before use, for how long should the vials containing Xiaflex and the diluent be left to stand at room temperature?
  - a) Five to ten minutes
  - b) At least fifteen but no more than sixty minutes
  - c) Sixty to ninety minutes
  - d) At least two hours
  
2. The amount of diluent that should be used for reconstituting the lyophilized powder of Xiaflex is:
  - a) 0.15 mL
  - b) 0.25 mL
  - c) 0.31 mL
  - d) 0.39 mL
  
3. The reconstituted Xiaflex solution can be kept at room temperature for up to 1 hour or refrigerated for up to:
  - a) Two hours
  - b) Three hours
  - c) Four hours
  - d) Five hours

## Answers to Self-Test Questions

1. Before use, for how long should the vials containing Xiaflex and the diluent be left to stand at room temperature?
  - a) Five to ten minutes
  - b) At least fifteen but no more than sixty minutes**
  - c) Sixty to ninety minutes
  - d) At least two hours
  
2. The amount of diluent that should be used for reconstituting the lyophilized powder of Xiaflex is:
  - a) 0.15 mL
  - b) 0.25 mL
  - c) 0.31 mL
  - d) 0.39 mL**
  
3. The reconstituted Xiaflex solution can be kept at room temperature for up to 1 hour or refrigerated for up to:
  - a) Two hours
  - b) Three hours
  - c) Four hours**
  - d) Five hours

## Identifying the Treatment Area and Injecting Xiaflex

This section outlines the procedures for identifying the treatment area and injecting the reconstituted Xiaflex solution into the Peyronie's plaque.

NOTE: Prior to administering Xiaflex and as part of every treatment-related visit, use the Patient Counseling Tool, *What You Need to Know About Xiaflex Treatment for Peyronie's Disease* to discuss important information with each patient. Patients should be given this counseling tool to take home for reference along with a Medication Guide. See page 25 for details.

### *Identifying the Treatment Area*

Prior to each treatment cycle, identify the treatment area as follows:

1. Induce a penile erection. A single intracavernosal injection of 10 mcg or 20 mcg of alprostadil may be used for this purpose. Apply antiseptic at the site of injection and allow the skin to dry prior to the intracavernosal injection.
2. Locate the plaque at the point of maximum concavity (or focal point) in the bend of the penis.



3. Mark the point with a surgical marker. This indicates the target area in the plaque for Xiaflex deposition.



4. The penis should be in a flaccid state before Xiaflex is injected.

### ***Injection Procedure***

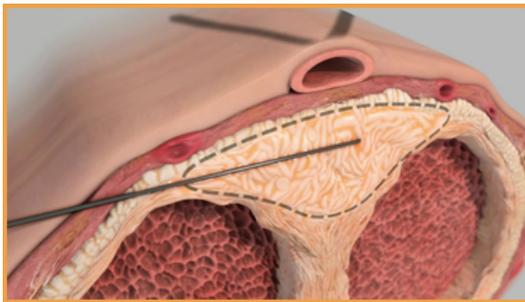
The reconstituted Xiaflex solution should be clear. Inspect the solution visually for particulate matter and discoloration prior to administration. If the solution contains particulates, is cloudy, or is discolored, do not inject the reconstituted solution.

1. Apply antiseptic at the site of the injection and allow the skin to dry. Administer suitable local anesthetic, if desired.
2. Using a new hubless syringe containing 0.01-mL graduations with a permanently fixed 27-gauge ½-inch needle (not supplied), withdraw a volume of 0.25 mL of **reconstituted solution (containing 0.58 mg of Xiaflex)**. There will be reconstituted solution left in the vial.

3. The penis should be in a flaccid state before Xiaflex is injected. Place the needle tip on the side of the target plaque in alignment with the point of maximal concavity. Orient the needle so that it enters the plaque from the side, NOT downwards or perpendicularly towards the corpora cavernosum.



4. Insert and advance the needle transversely through the width of the plaque, towards the opposite side of the plaque without passing completely through it. Proper needle position is confirmed by carefully noting resistance to minimal depression of the syringe plunger.



5. With the tip of the needle placed within the plaque, initiate the injection, maintaining steady pressure to slowly inject the drug into the plaque. Withdraw the needle slowly, so as to deposit the full dose along the needle track within the plaque. For plaques that are only a few millimeters in width, the distance of withdrawal of the syringe may be very minimal. The goal is always to deposit the full dose entirely within the plaque.

6. Upon complete withdrawal of the needle, apply gentle pressure at the injection site. Apply a dressing as necessary.



7. Discard the unused portion of the reconstituted solution and diluent after each injection. Do not store, pool, or use any vials containing unused reconstituted solution or diluent.
8. The second injection of each treatment cycle should be made approximately 2 mm to 3 mm apart from the first injection and within the plaque.

At each patient visit, counsel the patient as appropriate on the following:

- The risks of penile fracture and other serious injury to the penis
- That their penis may appear bruised and/or swollen
- That they may have mild-to-moderate penile pain that can be relieved by taking over-the-counter pain medications
- To promptly contact their physician if, at any time, they have any of these symptoms:
  - a popping sound or sensation in an erect penis
  - sudden loss of the ability to maintain an erection
  - severe purple bruising and swelling of the penis
  - difficulty urinating or blood in the urine
  - severe pain in the penis

These symptoms may indicate penile fracture, and may require surgery.

- To return to their healthcare provider's office when directed for further injection(s) and/or penile modeling procedure(s)
- **To wait 2 weeks after the second injection of each treatment cycle before resuming sexual activity, provided pain and swelling have subsided**

## Self-Test Questions

1. The proper site of injection for Xiaflex is:
  - a) Laterally into the distal two-thirds of the penis
  - b) At the point of minimal concavity in the bend of the penis
  - c) At the point of maximal concavity in the bend of the penis
  - d) Two millimeters from the base of the erect penis
2. The amount of reconstituted Xiaflex that should be injected into the Peyronie's plaque is:
  - a) 0.20 mL
  - b) 0.25 mL
  - c) 0.31 mL
  - d) 0.39 mL
3. When marking the treatment area the penis should be:
  - a) flaccid or
  - b) erect
4. When injecting Xiaflex the penis should be:
  - a) flaccid or
  - b) erect
5. The needle needs to be inserted in which direction into the plaque?
  - a) Perpendicular to
  - b) Transversely through the width of
  - c) Parallel to
  - d) Adjacent to, but not within
6. The goal of injection is always to deposit the full dose of drug:
  - a) Entirely within the plaque
  - b) Mostly within the plaque
  - c) Entirely outside of the plaque
  - d) Both inside and outside of the plaque

## Answers to Self-Test Questions

1. The proper site of injection for Xiaflex is:
  - a) Laterally into the distal two-thirds of the penis
  - b) At the point of minimal concavity in the bend of the penis
  - c) At the point of maximal concavity in the bend of the penis**
  - d) Two millimeters from the base of the erect penis
  
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  - a) 0.20 mL
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  - b) Mostly within the plaque
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  - d) Both inside and outside of the plaque

## Penile Modeling (In-Office and At-Home)

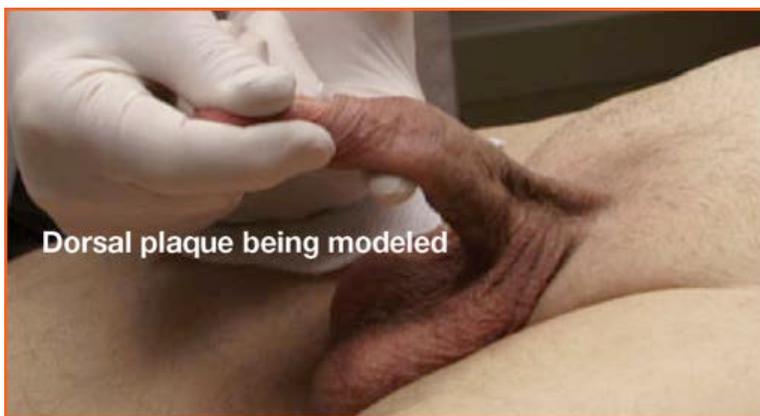
This section outlines the in-office penile modeling procedure, which, in conjunction with Xiaflex, helps relieve curvature deformity and straighten the penile shaft. At a follow-up visit 1 to 3 days after the second injection of each treatment cycle, perform a penile modeling procedure (as described below) on the flaccid penis to stretch and elongate the treated plaque.

This section also outlines instructions to give to patients on how to perform daily, at-home penile modeling activities for 5 to 6 weeks following each treatment cycle.

NOTE: Prior to administering Xiaflex and as part of every treatment-related visit, use the Patient Counseling Tool, *What You Need to Know About Xiaflex Treatment for Peyronie's Disease* to discuss important information with each patient. See page 21 for details.

### *In-Office Penile Modeling Procedure*

1. Administer suitable local anesthetic, if desired.
2. Wearing gloves, grasp the plaque or indurated portion of the flaccid penis about 1 cm proximal and distal to the injection site. Avoid direct pressure on the injection site.
3. Using the target plaque as a fulcrum point, use both hands to apply firm, steady pressure to elongate and stretch the plaque. The goal is to gradually create bending opposite to the patient's penile curvature, with stretching to the point of moderate resistance.



4. Hold pressure for 30 seconds, then release.
5. After a 30-second rest period, repeat the penile modeling technique for a total of 3 modeling attempts at 30 seconds for each attempt.

## *At-Home Penile Modeling Activities*

There are 2 types of at-home penile modeling activities. One is a gentle stretching activity; the other is a gentle straightening activity. Discuss with patients the best time to perform these activities. Patients will do these for approximately 6 weeks after each treatment cycle.

Patients should perform the penis-stretching activity daily, three times per day, with a nonerect penis.

For the **stretching activity**, instruct the patient to:

1. Grasp the tip of the penis with the fingers of one hand and hold the base of the penis with the fingers of the other.
2. **Gently** pull the penis away from the body to its full length.
3. Hold the stretch for 30 seconds.
4. Let go and allow the penis to return to its normal, unstretched length.



Side view of penis stretching activity

Patients should perform the penis-straightening activity no more than once per day only if a spontaneous erection occurs. If the patient does not have a spontaneous erection, he should not attempt the penis straightening.

For the **straightening activity**, instruct the patient to:

1. **Gently** attempt to bend the shaft of the erect penis in the opposite direction of the curve, but not so forcefully as to produce significant pain or discomfort.
2. Hold the penis in this more straightened position for 30 seconds, then let go.
3. Perform this no more than once per day, if a spontaneous erection unrelated to sexual activity occurs.



Top view of penis straightening activity

## Self-Test Questions

1. How soon should the in-office penile modeling procedure be performed after the second injection of each treatment cycle?
  - a) Immediately
  - b) Fifteen to sixty minutes
  - c) One to three days
  - d) Five to seven days
  
2. When performing in-office penile modeling procedure, hold the pressure for thirty seconds and rest for thirty seconds for a total of:
  - a) Two times
  - b) Three times
  - c) Five times
  - d) Ten times
  
3. The patient should be instructed to perform at-home penile straightening activity on a spontaneous erection unrelated to sexual activity no more than once daily for thirty seconds. How often should the patient perform the stretching activity on the flaccid penis?
  - a) At no time
  - b) Once daily for a total of one minute
  - c) Five times daily for thirty seconds at a time
  - d) Three times daily for thirty seconds at a time

## Answers to Self-Test Questions

1. How soon should the in-office penile modeling procedure be performed after the second injection of each treatment cycle?
  - a) Immediately
  - b) Fifteen to sixty minutes
  - c) One to three days**
  - d) Five to seven days
  
2. When performing in-office penile modeling procedure, hold the pressure for thirty seconds and rest for thirty seconds for a total of:
  - a) Two times
  - b) Three times**
  - c) Five times
  - d) Ten times
  
3. The patient should be instructed to perform at-home penile straightening activity on a spontaneous erection unrelated to sexual activity no more than once daily for thirty seconds. How often should the patient perform the stretching activity on the flaccid penis?
  - a) At no time
  - b) Once daily for a total of one minute
  - c) Five times daily for thirty seconds at a time
  - d) Three times daily for thirty seconds at a time**

## Patient Counseling

A Patient Counseling Tool is a part of the Xiaflex REMS Program. This Tool called *What You Need to Know About Xiaflex Treatment for Peyronie's Disease: A Patient Guide* must be given to the patient at each visit. The Tool contains the following information that you should discuss with each patient:

- The risks of corporal rupture (penile fracture) and other serious penile injury
- Precautions related to the patient's actions to reduce these adverse outcomes (eg, advising patients to wait two weeks until after the second injection of each treatment cycle before resuming sexual activity)
- Symptoms to look for and conditions under which patients should promptly contact their healthcare provider
- Clear instructions on at-home penile modeling activities

The patient must be given a copy of the Patient Counseling Tool to take home.

In addition, provide a Medication Guide to each patient prior to each injection of Xiaflex.

To obtain copies of the Patient Counseling Tool,

- Visit [www.XIAFLEXREMS.com](http://www.XIAFLEXREMS.com)
- Call 1-877-XIAFLEX (1-877-942-3539)
- Or contact your Xiaflex sales representative

Convenient tear pads are also available for your office.

## Self-Test Questions

1. A Peyronie's patient receiving Xiaflex should be advised to wait how long following the second injection of each treatment cycle before resuming sexual activity?
  - a. 1-2 days
  - b. 2 weeks
  - c. 3 weeks
  - d. 2 months
  
2. True or False. The Patient Counseling Tool, "*What You Need to Know About Xiaflex Treatment for Peyronie's Disease: A Patient Guide*," must be given to the patient at EACH visit.
  - a. True
  - b. False
  
3. True or False. The Medication Guide should be provided to each patient PRIOR to EACH injection of Xiaflex.
  - a. True
  - b. False

## Answers to Self-Test Questions

1. A Peyronie's patient receiving Xiaflex should be advised to wait how long following the second injection of each treatment cycle before resuming sexual activity?
  - a. 1-2 days
  - b. 2 weeks**
  - c. 3 weeks
  - d. 2 months
  
2. True or False. The Patient Counseling Tool, "*What You Need to Know About Xiaflex Treatment for Peyronie's Disease: A Patient Guide*," must be given to the patient at EACH treatment visit.
  - a. True**
  - b. False
  
3. True or False. The Medication Guide should be provided to each patient PRIOR to EACH injection of Xiaflex.
  - a. True**
  - b. False

**References:** 1. Hellstrom WJ. Medical management of Peyronie's disease. *J Androl.* 2009;30(4):397-405. 2. Ralph D, Gonzalez-Cadavid N, Mirone V, et al. The management of Peyronie's disease: evidence-based 2010 guidelines. *J Sex Med.* 2010;7(7):2359-2374. 3. Moreland RB, Nehra A. Pathophysiology of Peyronie's disease. *Int J Impot Res.* 2002;14(5):406-410. 4. Bella AJ, Perelman MA, Brant WO, Lue TF. Peyronie's disease (CME). *J Sex Med.* 2007;4(6):1527-1538.



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## XIAFLEX REMS Video (Peyronie’s Disease)

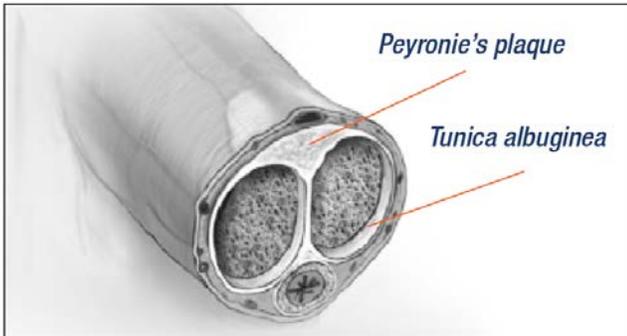
VISUAL	AUDIO
<p><b>TITLE FRAME</b></p>  <p><b>ON-SCREEN COPY:</b> REMS training video for administering Xiaflex for Peyronie’s disease.</p> <p><b>VISUAL:</b> REMS description scrolls</p> <p>A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks.</p> <p>Xiaflex, or collagenase clostridium histolyticum, is indicated for the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least thirty degrees at the start of therapy</p> <p>Xiaflex is only available under a restricted distribution program called the Xiaflex REMS because of the risks of penile fracture and other serious penile injury associated with using Xiaflex in treating Peyronie’s disease.</p> <p>This training video is part of the Xiaflex REMS program. This video discusses:</p> <ul style="list-style-type: none"><li>• the steps necessary to prepare and administer Xiaflex</li><li>• the in-office penile modeling procedure that is part of each Xiaflex treatment cycle</li><li>• the daily, at-home penile modeling activities</li></ul>	<p><b>VO:</b></p> <p>Welcome to the REMS training video for administering Xiaflex for Peyronie’s disease. A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Xiaflex, or collagenase clostridium histolyticum, is indicated for the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least thirty degrees at the start of therapy [Ref: <a href="#">PI/p.3/§1/¶ 2</a>].</p> <p>Xiaflex is only available under a restricted distribution program called the Xiaflex REMS because of the risks of penile fracture and other serious penile injury associated with using Xiaflex in treating Peyronie’s disease.</p> <p>This training video is part of the Xiaflex REMS program. This video discusses:</p> <ul style="list-style-type: none"><li>• the steps necessary to prepare and administer Xiaflex</li><li>• the in-office penile modeling procedure that is part of each Xiaflex treatment cycle</li><li>• the daily, at-home penile modeling activities that are performed for approximately 6 weeks after each treatment cycle</li><li>• counseling your patient with the Xiaflex Patient Counseling Tool</li></ul> <p>Xiaflex is also indicated for the treatment of adult patients with Dupuytren’s contracture with a palpable cord. [Ref: <a href="#">PI/p.3/§1/¶ 1</a>] Use of Xiaflex for Dupuytren’s contracture is covered under separate REMS requirements. Information on Dupuytren’s contracture is available by visiting <a href="http://www.XIAFLEX.com">www.XIAFLEX.com</a> or by calling 1-877-313-1235.</p>

## Introduction—Mechanism of Action

<p>that are performed for approximately 6 weeks after each treatment cycle</p> <ul style="list-style-type: none"><li>• counseling your patient with the Xiaflex Patient Counseling Tool</li></ul> <p>Xiaflex is also indicated for the treatment of adult patients with Dupuytren’s contracture with a palpable cord. <a href="#">[Ref: PI/p.3/§1/¶ 1]</a> Use of Xiaflex for Dupuytren’s contracture is covered under separate REMS requirements. Information on Dupuytren’s contracture is available by visiting <a href="http://www.Xiaflex.com">www.Xiaflex.com</a> or by calling 1-877-313-1235.</p> <p>Xiaflex® (collagenase clostridium histolyticum)</p> <p>© 2013 Auxilium Pharmaceuticals, Inc. All rights reserved RMX-00008</p>	
<p><b>Frame 1</b></p> <div data-bbox="131 1010 761 1346"><hr data-bbox="170 1220 729 1226"/></div> <p><b>VISUAL:</b> REMS headline fades away and Xiaflex logo moves to center of screen.</p> <p><b>ON-SCREEN COPY:</b> Xiaflex® collagenase clostridium histolyticum</p> <p><a href="http://www.XiaflexREMS.com">www.XiaflexREMS.com</a>.</p>	<p><b>VO:</b></p> <p>For the treatment of Peyronie’s disease, Xiaflex should be administered by a healthcare provider experienced in the treatment of male urological diseases who has completed the required training. <a href="#">[Ref: PI/p.6/§2.2/¶ 1]</a></p> <p>This video demonstrates the steps necessary to prepare and administer Xiaflex. It also describes the in-office penile modeling procedure that is part of each Xiaflex treatment cycle, as well as the daily, at-home penile modeling activities that are performed for approximately six weeks after each cycle. <a href="#">[Ref: PI/p.9/§2.2/Penile Modeling for PD/¶1; PI/p.9/§2.2/Penile Modeling for PD/¶2]</a> It also includes directions for utilizing the Xiaflex Patient Counseling Tool. The full Prescribing Information and Medication Guide are available at <a href="http://www.XiaflexREMS.com">www.XiaflexREMS.com</a>.</p>

## Introduction—Mechanism of Action

### Frame 2



**VISUAL:** Cut to cross-section illustration of penis with callouts for Peyronie's plaque and tunica albuginea

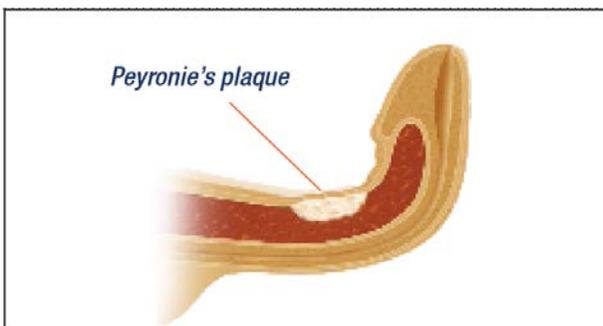
**ON-SCREEN COPY:** Peyronie's plaque; Tunica albuginea

### VO:

Peyronie's disease is a localized connective tissue disorder characterized by changes in collagen composition in the tunica albuginea. [Ref: Hellstrom, p. 397/col 1/¶2/lines 1-4] These changes cause an abnormal scar formation known as Peyronie's plaque, which is typically a palpable bump under the skin. [Ref: Ralph, p 1, col 1, ¶1, lines 6-7; Ref: Moreland, p.408/col 2/¶1; Ref: Bella/p. 1529/col 1/¶ 2/lines 10-11] The Peyronie's plaque is composed predominantly of collagen, and replaces the normally elastic fibers of the tunica albuginea. [Ref: CSR/p.14/¶1/lines 2-3]

Microvascular trauma resulting from excessive bending or injury to the erect penis (possibly during sexual activity) is thought to be an important trigger for the inflammatory response and plaque development characteristic of Peyronie's disease. [Ref 3:Moreland, p.407/col 2/¶2; p.408/col.1/¶1] Genetic predisposition and autoimmunity may also play a role in its development. [Moreland, p.406/col 2/¶2/lines 3-8; lines 21-31]

### Frame 3



**VISUAL:** Animation changes perspective to illustrate penis profile with Peyronie's plaque causing curvature

**ON-SCREEN COPY:** Peyronie's plaque

### VO:

One of the hallmarks of Peyronie's disease is curvature deformity. Peyronie's disease may also cause other types of deformities, including narrowing, indentation, and shortening of the penis. [Ref 4: Bella/p. 1527/col 1/¶1/lines 4-8]

## Mechanism of Action

### Frame 4

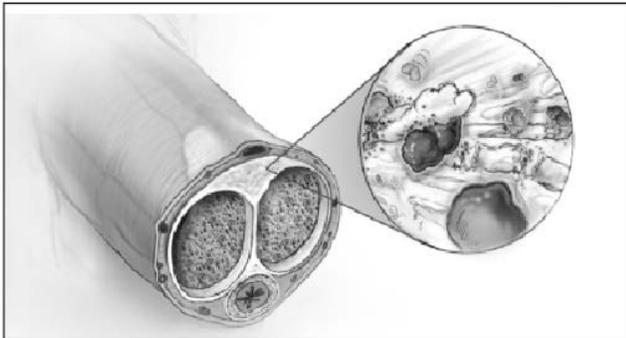


**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
Mechanism of Action

### VO:

Xiaflex contains two different types of purified collagenase clostridium histolyticum in a defined mass ratio. [\[Ref: PI/p.19/§11/¶1\]](#)

### Frame 5

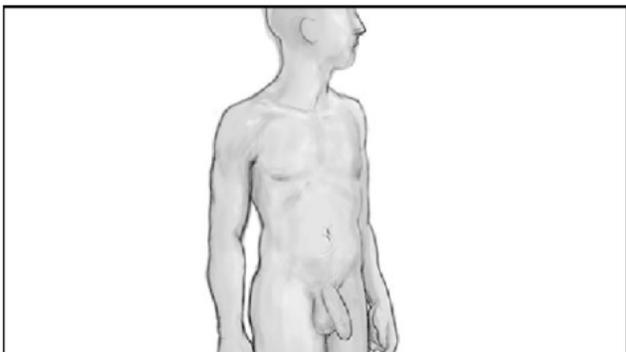


**VISUAL:** Animation illustrates enzymatic disruption of the collagen found in Peyronie's plaque

### VO:

Injection of Xiaflex into a Peyronie's plaque, which is composed mostly of collagen, may result in enzymatic disruption of the collagen found in Peyronie's plaque. [\[Ref: PI/p.20/§12.1/¶3, lines 1-3\]](#)

### Frame 6



**VISUAL:** Transition to full male figure

### VO:

Following this disruption of the collagen-containing plaque, penile curvature deformity may improve and Patient-Reported Bother may be reduced. [\[Ref: PI/p.20/12.1/¶3/lines 2-4\]](#)

**PREPARATION FOR ADMINISTRATION**

**Frame 7**



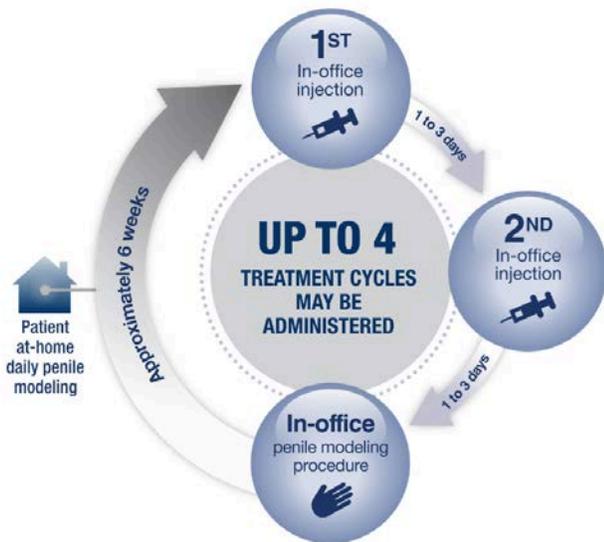
**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
Treatment Overview

**VO:**

Xiaflex should be administered by a healthcare provider experienced in the treatment of male urological diseases who has completed the required training. [Ref: PI/p.6/§2.2/¶1]

Xiaflex, supplied as a lyophilized powder, must be reconstituted with the provided diluent prior to use. [Ref: PI/p.7/§2.2/¶2/lines 1-2] The dose of Xiaflex is 0.58 mg per injection administered into a Peyronie’s plaque. If more than one plaque is present, inject into the plaque causing the curvature deformity. [Ref: PI/p.7/§2.2/¶2/lines 2-4]

**Frame 8**



**VISUAL:** Treatment cycle diagram; Treatment Cycle 1 circles are highlighted in dark blue to match the VO

**ON-SCREEN COPY:** One Xiaflex Treatment Cycle

Treatment Cycle 1; 1st in-office injection procedure → 1 to 3 days → 2nd in-office injection procedure → 1 to 3 days → In-office penile modeling procedure  
approximately 6 weeks; At-home penile modeling

**VO:**

A treatment course consists of a maximum of four treatment cycles. Each treatment cycle consists of two Xiaflex injection procedures and one in-office penile modeling procedure. The second Xiaflex injection procedure occurs one to three days after the first. The in-office penile modeling procedure is performed one to three days after the second injection of the treatment cycle. [Ref: PI/p.7/§2.2/¶3/lines 1-5] It is necessary to identify the treatment area prior to each treatment cycle.

[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a/line 1] Healthcare providers must counsel patients on the risks of penile fractures or other serious injuries of the penis and how to perform the at-home penile modeling activities as appropriate. After the third office visit of each treatment cycle, the patient performs approximately six weeks of daily, at-home penile modeling activities. [Ref: PI/p.9/§2.2/Penile Modeling for PD/¶2]

Up to four treatment cycles (for a total of eight injection procedures and four modeling procedures) may be administered per plaque causing the curvature deformity. If the curvature deformity is less than 15 degrees

## PREPARATION FOR ADMINISTRATION

activities→Treatment Cycle 2; approximately 6 weeks; At-home penile modeling activities→Treatment Cycle 3; approximately 6 weeks; At-home penile modeling activities→Treatment Cycle 4; approximately 6 weeks; At-home penile modeling activities

Up to 4 treatment cycles may be administered

If the curvature deformity is less than 15 degrees after the 1st, 2nd or 3rd Treatment Cycle, or if you determine that further treatment is not clinically indicated, then subsequent treatment cycles should not be administered.

The safety of more than one treatment course of Xiaflex is not known.

after the first, second or third treatment cycle, or if you determine that further treatment is not clinically indicated, then the subsequent treatment cycles should not be administered. The safety of more than one treatment course of Xiaflex is not known. [\[Ref: PI/p.7/§2.2/¶1-3\]](#)

### Frame 9



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
Preparation for Administration

### VO:

In this section, we will explain the procedure for reconstitution of the lyophilized powder of Xiaflex.

### Frame 10



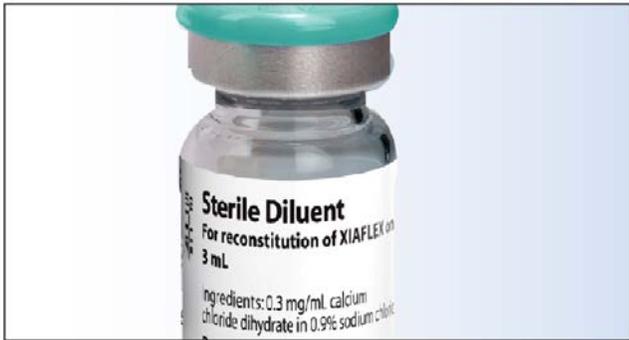
**VISUAL:** Xiaflex vial

### VO:

Xiaflex, supplied as a lyophilized powder, must be reconstituted with the provided diluent prior to use. Xiaflex is supplied in single-use glass vials containing 0.9 mg of collagenase clostridium histolyticum as a sterile, lyophilized powder for reconstitution. [\[Ref: PI/p.10/§3\]](#)

## PREPARATION FOR ADMINISTRATION

### Frame 11



**VISUAL:** Close-up of sterile diluent vial

### VO:

Sterile diluent for reconstitution is provided in the package in a single-use glass vial containing 3 mL of 0.3 mg/mL calcium chloride dihydrate in 0.9% sodium chloride. Xiaflex must be reconstituted with the provided diluent prior to use. [\[Ref: PI/p.10/§3\]](#)

### Frame 12



**VISUAL:** Xiaflex vial; Sterile diluent vial; temperature gauge illustrating 2°C to 8°C and 36°F to 46°F

**ON-SCREEN COPY:** Prior to Reconstitution  
Store in refrigerator

### VO:

The vials of lyophilized Xiaflex powder and sterile diluent should be stored in a refrigerator at two to eight degrees Celsius or thirty-six to forty-six degrees Fahrenheit. Do not freeze. [\[Ref: PI/p.31/§16/¶1\]](#)

### Frame 13



**VISUAL:** Xiaflex vial; Sterile diluent vial

### VO:

Before use, remove the vial containing the lyophilized powder of Xiaflex and the vial containing the diluent for reconstitution from the refrigerator and check the labels on both the diluent vial and the lyophilized powder vial to make sure they have not expired. Allow the two vials to stand at room temperature for at least fifteen minutes and no longer than sixty minutes [\[Ref: PI/p.7/§2.2/bullet a, lines 1-4\]](#)

## PREPARATION FOR ADMINISTRATION

**ON-SCREEN COPY:** After refrigeration, let the vial containing Xiaflex and the vial containing diluent stand at room temperature for at least 15 minutes before use  
No longer than 60 minutes

### Frame 14



**VISUAL:** Two Xiaflex vials one intact, one eroded

**ON-SCREEN COPY:** INTACT; ERODED  
If eroded, call 1-877-663-0412

### VO:

Visually inspect the vial containing Xiaflex. The cake of lyophilized powder should be intact and white in color. If the cake has been eroded, it should not be used, and should be reported to Auxilium by calling 1-877-663-0412.

*[Ref: PI/p.7/§2.2/bullet a, lines 4-5]*

### Frame 15



**VISUAL:** Gloved hands remove flip-off cap from Xiaflex vial

### VO:

After removing the flip-off cap from each vial, using aseptic technique, swab the rubber stopper and surrounding surface of the vial containing Xiaflex and the vial containing the diluent for reconstitution with sterile alcohol.

*[Ref: PI/p.8/§2.2/bullet b]*

## PREPARATION FOR ADMINISTRATION

Frame 16

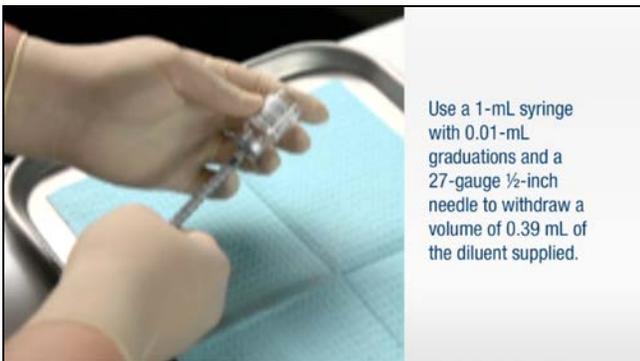


**VISUAL:** Gloved hands remove flip-off cap from diluent vial

**VO:**

No other antiseptics should be used. [\[Ref: PI/p.8/§2.2/bullet b\]](#) Use only the supplied diluent for reconstitution. The diluent contains calcium, which is required for the activity of Xiaflex. [\[Ref: PI/p.8/§2.2/bullet c\]](#)

Frame 17



**VISUAL:** Gloved hands hold 1-mL syringe with 0.01-mL graduations and a 27-gauge ½-inch needle to withdraw diluent

**ON-SCREEN COPY:** Use a 1-mL syringe with 0.01-mL graduations and a 27-gauge ½-inch needle to withdraw a volume of 0.39 mL of the **diluent supplied**

**VO:**

Using a 1-mL syringe with 0.01-mL graduations with a twenty-seven-gauge one-half-inch needle, which is not supplied, withdraw a volume of 0.39 mL of the **diluent supplied**. [\[Ref: PI/p.8/§2.2/bullet d\]](#)

## PREPARATION FOR ADMINISTRATION

### Frame 18



**VISUAL:** Gloved hands hold 1-mL syringe and inject diluent slowly into sides of Xiaflex vial

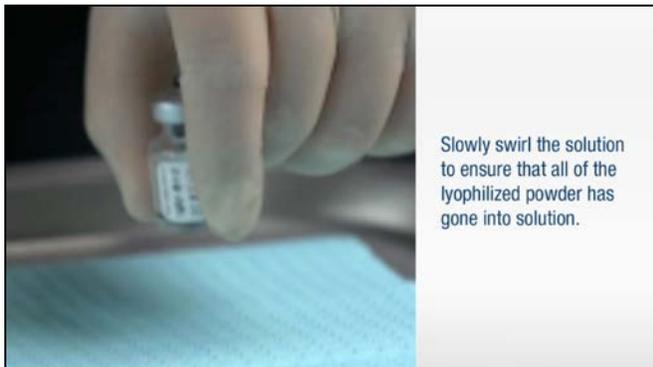
**ON-SCREEN COPY:** Inject the diluent slowly into the sides of the Xiaflex vial. Do not invert the vial or shake the solution

### VO:

Inject the diluent slowly into the sides of the vial containing the lyophilized powder of Xiaflex.

*[Ref: PI/p.8/§2.2/bullet e/lines 1-2]*

### Frame 19



**VISUAL:** Gloved hands slowly swirl the solution

**ON-SCREEN COPY:** Slowly swirl the solution to ensure that all of the lyophilized powder has gone into solution

### VO:

Do not invert the vial or shake the solution. Slowly swirl the solution to ensure that all of the lyophilized powder has gone into solution. Do not use if opaque particles, discoloration, or other foreign particles are present. *[Ref: PI/p.8/§2.2/bullet e/lines 2-3]*

## PREPARATION FOR ADMINISTRATION

### Frame 20



**VISUAL:** Gloved hand holds vial of reconstituted Xialflex solution

### VO:

The Xialflex solution is now ready for injection.

### Frame 21



**VISUAL:** Vial with reconstituted Xialflex; clock illustrating 15-minute duration; clock animates to 60 minutes, illustrating the VO “and no longer than 60 minutes”

**ON-SCREEN COPY:** Reconstituted Xialflex  
After refrigeration, let stand at room temperature for 15 minutes before use

### VO:

The reconstituted Xialflex solution can be kept at room temperature of twenty to twenty-five degrees Celsius, or sixty-eight to seventy-seven degrees Fahrenheit, for up to one hour; or refrigerated at two to eight degrees Celsius, or thirty-six to forty-six degrees Fahrenheit, for up to four hours prior to administration. If the reconstituted Xialflex solution is refrigerated, allow this solution to return to room temperature for approximately fifteen minutes before use and no longer than sixty minutes.

[\[Ref: PI/p.8/§2.2/bullet f\]](#)

## PREPARATION FOR ADMINISTRATION

### Frame 22



**VISUAL:** Gloved hand discards syringe

### VO:

As a final step, discard the syringe, needle and diluent used for reconstitution using medical waste disposal procedures. [\[Ref: PI/p.8/§2.2/bullet g\]](#)

### Frame 23



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum

Self-Test Questions

### VO:

This completes the section on Xiaflex preparation for administration. To confirm understanding of the key points of this section, please answer the following self-test questions. After answering these questions correctly, you may continue to the next section.

## INJECTION PROCEDURE

<p><b>Frame 24</b></p>  <p><b>ON-SCREEN COPY:</b> Xiaflex® collagenase clostridium histolyticum Self-Test Questions</p>	<p><b>VO:</b> Self-Test Questions</p>
<p><b>Frame 25</b> <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO <b>ON-SCREEN COPY:</b> Before use, for how long should the vials containing Xiaflex and the diluent be left to stand at room temperature? a) 5 to 10 minutes b) At least 15 but no more than 60 minutes c) 60 to 90 minutes d) At least 2 hours</p>	<p><b>VO:</b> Before use, for how long should the vials containing Xiaflex and the diluent be left to stand at room temperature? a) Five to ten minutes b) At least fifteen but no more than sixty minutes c) Sixty to ninety minutes d) At least two hours</p>
<p><b>Frame 25A</b> <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> Before use, for how long should the vials containing Xiaflex and the diluent be left to stand at room temperature? a) 5 to 10 minutes <b>b) At least 15 but no more than 60 minutes</b> c) 60 to 90 minutes d) At least 2 hours</p>	<p><b>VO:</b> <b>b) At least fifteen but no more than sixty minutes</b> [<i>Ref: PI/p.8/§2.2/bullet f</i>]</p>
<p><b>Frame 26</b> <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO <b>ON-SCREEN COPY:</b> The amount of diluent that should be used for reconstituting the lyophilized powder of Xiaflex is: a) 0.15 mL</p>	<p><b>VO:</b> The amount of diluent that should be used for reconstituting the lyophilized powder of Xiaflex is: a) 0.15 mL b) 0.25 mL c) 0.31 mL</p>

## INJECTION PROCEDURE

<p>b) 0.25 mL c) 0.31 mL d) 0.39 mL</p>	<p>d) 0.39 mL</p>
<p><b>Frame 26A</b> <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The amount of diluent that should be used for reconstituting the lyophilized powder of Xiaflex is: a) 0.15 mL b) 0.25 mL c) 0.31 mL <b>d) 0.39 mL</b></p>	<p><b>VO:</b> <b>d) 0.39 mL</b> [<i>Ref: PI/p.8/§2.2/bullet d</i>]</p>
<p><b>Frame 27</b> <b>VISUAL:</b> Question appears on screen and answers appear sequentially, corresponding to VO <b>ON-SCREEN COPY:</b> The reconstituted Xiaflex solution can be kept at room temperature for up to 1 hour or refrigerated for up to: a) 2 hours b) 3 hours c) 4 hours d) 5 hours</p>	<p><b>VO:</b> The reconstituted Xiaflex solution can be kept at room temperature for up to 1 hour or refrigerated for up to: a) Two hours b) Three hours c) Four hours d) Five hours</p>
<p><b>Frame 27A</b> <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The reconstituted Xiaflex solution can be kept at room temperature for up to 1 hour or refrigerated for up to: a) 2 hours b) 3 hours <b>c) 4 hours</b> d) 5 hours</p>	<p><b>VO:</b> <b>c) four hours</b> [<i>Ref: PI/p.8/§2.2/bullet f</i>]</p>

## INJECTION PROCEDURE

### Frame 28



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum

Identifying the Treatment Area and Injecting  
Xiaflex

### VO:

We will now discuss the proper procedures for identifying the treatment area and injecting the reconstituted Xiaflex (collagenase clostridium histolyticum) solution into the Peyronie's plaque.

Prior to administering Xiaflex and as part of every treatment-related visit, use the Patient Counseling Tool to discuss important information with each patient.

### Frame 29



**VISUAL:** Gloved hand identifies the treatment area and induces an erection

### VO:

Prior to each treatment cycle, identify the treatment area as follows: Induce a penile erection. A single intracavernosal injection of ten micrograms or twenty micrograms of alprostadil may be used for this purpose. Apply antiseptic at the site of injection and allow the skin to dry prior to the intracavernosal injection. [\[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a, sub-bullet 1\]](#)

### Frame 30



**VISUAL:** Gloved hands locate the plaque at point of maximum concavity and mark the focal point with a surgical marker

### VO:

Locate the plaque at the point of maximum concavity, or focal point, in the bend of the penis. [\[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a, sub-bullet 2\]](#)

Mark the point with a surgical marker. This indicates the target area in the plaque for Xiaflex deposition. [\[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a, sub-bullet 3\]](#)

## INJECTION PROCEDURE

Frame 31



**VISUAL:** Gloved hand holds up vial for inspection

**VO:**

The reconstituted Xiaflex solution should be clear. Inspect the solution visually for particulate matter and discoloration prior to administration. If the solution contains particulates, is cloudy, or is discolored, do not inject the reconstituted solution. [\[Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet a\]](#)

Frame 32



**VISUAL:** Gloved hands apply antiseptic

**VO:**

Apply antiseptic at the site of the injection and allow the skin to dry. If desired, administer suitable local anesthetic. [\[Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullets b,c\]](#)

Frame 33



**VISUAL:** Gloved hands with hubless 0.01-mL syringe withdraw fluid

**VO:**

Using a new hubless syringe containing 0.01-mL graduations with a permanently fixed twenty-seven-gauge half-inch needle, which is not supplied, withdraw a volume of 0.25 mL of **reconstituted solution containing 0.58 mg of Xiaflex**. There will be reconstituted solution remaining in the vial. [\[Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet d\]](#)

## INJECTION PROCEDURE

Frame 34

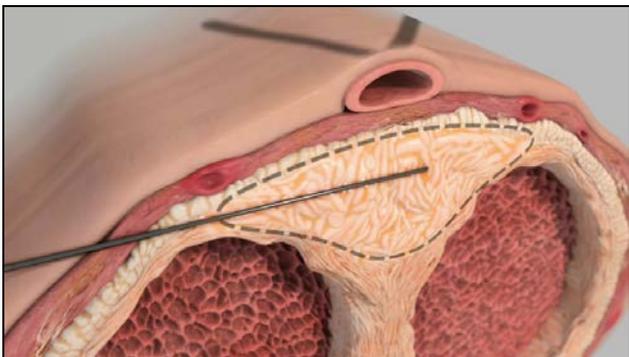


**VISUAL:** Gloved hands orient the needle so that it enters the plaque from the side

**VO:**

The penis should be in a flaccid state before injecting Xiaflex. Place the needle tip on the side of the target plaque in alignment with the point of maximal concavity. Orient the needle so that it enters the plaque from the side, NOT downward or perpendicularly toward the body of the corpora cavernosum. [\[Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet e\]](#)

Frame 35



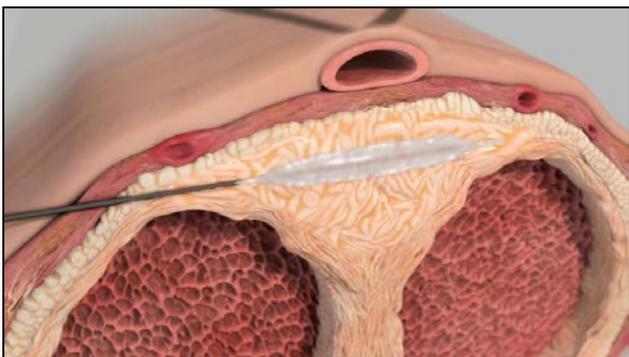
**VISUAL:** Cut to needle insertion animation

**ON-SCREEN COPY:** Image not to scale

**VO:**

Insert and advance the needle transversely through the width of the plaque, toward the opposite side of the plaque and without passing completely through it. Proper needle position is confirmed by carefully noting resistance to minimal depression of the syringe plunger. [\[Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet f\]](#)

Frame 36



**VO:**

With the tip of the needle placed within the plaque, initiate the injection, maintaining steady pressure to slowly inject the drug into the plaque. Withdraw the needle slowly so as to deposit the full dose along the needle track within the plaque. For plaques that are only a few millimeters in width, the distance of withdrawal of the syringe may be very minimal. The goal is always to deposit the full dose entirely within the plaque. [\[Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet g\]](#)

## INJECTION PROCEDURE

<p><b>VISUAL:</b> Needle withdrawal animation; arrow indicates direction</p> <p><b>ON-SCREEN COPY:</b> Image not to scale</p>	
<p><b>Frame 37</b></p>  <p><b>VISUAL:</b> A gloved hand applies pressure at the injection site</p>	<p><b>VO:</b> Upon complete withdrawal of the needle, apply gentle pressure at the injection site. Apply a dressing as necessary. <a href="#">[Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet h]</a></p> <p>Discard the unused portion of the reconstituted solution and diluent after each injection. Do not store, pool, or use any vials containing unused reconstituted solution or diluent. <a href="#">[Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet i]</a></p>
<p><b>Frame 38</b></p>  <p><b>VISUAL:</b> Gloved hand holds penis in place; copy and x's appear, indicating injection sites 2-3 mm apart</p> <p><b>ON-SCREEN COPY:</b> 2-3 mm apart, but still within the plaque</p>	<p><b>VO:</b> The second injection of each treatment cycle should be made approximately two to three millimeters apart from the first injection and within the plaque. <a href="#">[Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet j]</a></p>

## INJECTION PROCEDURE

### Frame 39

**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum

At each patient visit, counsel the patient as appropriate on the following:

- The risks of corporal rupture (penile fracture) and other serious injury to the penis
- That their penis may appear bruised and/or swollen
- That they may have mild-to-moderate penile pain that can be relieved by taking over-the-counter pain medications
- To promptly contact their physician if, at any time, they have any of these symptoms:
  - A popping sound or sensation in an erect penis
  - Sudden loss of the ability to maintain an erection
  - Severe purple bruising and swelling of the penis
  - Difficulty urinating or blood in the urine,
  - Severe pain in the penis
- These symptoms may be accompanied by a popping or cracking sound from the penis
- To return to their healthcare provider's office when directed for further injection(s) and/or penile modeling procedure(s)
- **To wait two weeks after the second injection of each treatment cycle before resuming sexual activity, provided pain and swelling have subsided**

### VO:

At each patient visit, counsel the patient as appropriate on the following:

- The risks of corporal rupture (penile fracture) and other serious injury to the penis
- That their penis may appear bruised and/or swollen [\[Ref: PI/p.32/§17.2/bullet 2\]](#)
- That they may have mild-to-moderate penile pain that can be relieved by taking over-the-counter pain medications [\[Ref: PI/p.32/§17.2/bullet 3\]](#)
- To promptly contact their physician if, at any time, they have any of these symptoms:
  - a popping sound or sensation in an erect penis
  - sudden loss of the ability to maintain an erection
  - severe purple bruising and swelling of the penis
  - difficulty urinating or blood in the urine,
  - severe pain in the penis

These symptoms may indicate penile fracture, and may require surgery [\[Ref: PI/p.32/§17.2/bullet 4\]](#)

- To return to their healthcare provider's office when directed for further injection(s) and/or penile modeling procedure(s) [\[Ref: PI/p.32/§17.2/bullet 5\]](#)
- To wait two weeks after the second injection of each treatment cycle before resuming sexual activity, provided pain and swelling have subsided [\[Ref: PI/p.32/§17.2/bullet 6\]](#)

## INJECTION PROCEDURE

### Frame 40

**XIAFLEX**<sup>®</sup>  
collagenase clostridium histolyticum

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Self-Test Questions

**ON-SCREEN COPY:** Xiaflex<sup>®</sup>  
collagenase clostridium histolyticum

Self-Test Questions

### VO:

This completes the section on identifying the treatment area and injecting Xiaflex. To confirm understanding of the key points of this section, please answer the following self-test questions. After answering these questions, you may continue to the next section.

**INJECTION PROCEDURE—SELF-TEST**

<p><b>Frame 41</b></p> <div style="border: 1px solid black; padding: 10px; text-align: center;">  <p style="color: orange; margin-top: 20px;">Self-Test Questions</p> </div> <p><b>ON-SCREEN COPY:</b> Xiaflex® collagenase clostridium histolyticum</p> <p>Self-Test Questions</p>	<p><b>VO:</b></p> <p><b>SELF-TEST QUESTIONS</b></p>
<p><b>Frame 42</b></p> <p><b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO</p> <p><b>ON-SCREEN COPY:</b> The proper site of injection for Xiaflex is:</p> <ul style="list-style-type: none"> <li>a) Laterally into the distal two-thirds of the penis</li> <li>b) At the point of minimal concavity in the bend of the penis</li> <li>c) At the point of maximal concavity in the bend of the penis</li> <li>d) 2 mm from the base of the erect penis</li> </ul>	<p><b>VO:</b></p> <p>The proper site of injection for Xiaflex is:</p> <ul style="list-style-type: none"> <li>a) Laterally into the distal two-thirds of the penis</li> <li>b) At the point of minimal concavity in the bend of the penis</li> <li>c) At the point of maximal concavity in the bend of the penis</li> <li>d) Two millimeters from the base of the erect penis</li> </ul>
<p><b>Frame 42A</b></p> <p><b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The proper site of injection for Xiaflex is:</p> <ul style="list-style-type: none"> <li>a) Laterally into the distal two-thirds of the penis</li> <li>b) At the point of minimal concavity in the bend of the penis</li> <li><b>c) At the point of maximal concavity in the bend of the penis</b></li> <li>d) 2 mm from the base of the erect penis</li> </ul>	<p><b>VO:</b></p> <p><b>c) At the point of maximal concavity in the bend of the penis</b> <i>[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a, sub-bullet 2]</i></p>
<p><b>Frame 43</b></p> <p><b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO</p> <p><b>ON-SCREEN COPY:</b> The amount of reconstituted Xiaflex that should be injected into the Peyronie’s plaque is:</p> <ul style="list-style-type: none"> <li>a) 0.20 mL</li> <li>b) 0.25 mL</li> <li>c) 0.31 mL</li> </ul>	<p><b>VO:</b></p> <p>The amount of reconstituted Xiaflex that should be injected into the Peyronie’s plaque is:</p> <ul style="list-style-type: none"> <li>a) 0.20 mL</li> <li>b) 0.25 mL</li> <li>c) 0.31 mL</li> <li>d) 0.39 mL</li> </ul>

**INJECTION PROCEDURE—SELF-TEST**

<p>d) 0.39 mL</p>	
<p><b>Frame 43A</b>  <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The amount of reconstituted Xiaflex that should be injected into the Peyronie’s plaque is:  a) 0.20 mL  <b>b) 0.25 mL</b>  c) 0.31 mL  d) 0.39 mL</p>	<p><b>VO:</b>  <b>b) 0.25 mL</b> [Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet d]</p>
<p><b>Frame 44</b>  <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO  <b>ON-SCREEN COPY:</b> The penis should be _____ when marking the treatment area and _____ when injecting Xiaflex.  a) Erect; erect  b) Flaccid; flaccid  c) Erect; flaccid  d) Flaccid; erect</p>	<p><b>VO:</b>  When marking the treatment area the penis should be (a) flaccid or (b) erect.   When injecting Xiaflex the penis should be: (a) flaccid or (b) erect.</p>
<p><b>Frame 44A</b>  <b>VISUAL:</b> Answers disappear and the correct answers are inserted into the question and highlighted.  <b>ON-SCREEN COPY:</b> The penis should be <u>erect</u> when marking the treatment area and <u>flaccid</u> when injecting Xiaflex.</p>	<p><b>VO:</b>  The penis should be <b>erect</b> when marking the treatment area and <b>flaccid</b> when injecting Xiaflex.  [Ref: PI/p.8/§2.2/ID of Tx Area for PD/bullet a/sub-bullet 1]  [Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet e/line 1]</p>
<p><b>ALT FRAME 44</b>  <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO  <b>ON-SCREEN COPY:</b> When marking the treatment area should the penis be (a) flaccid or (b) erect?</p>	<p><b>VO:</b>  When marking the treatment area should the penis be (a) flaccid or (b) erect?</p>

**INJECTION PROCEDURE—SELF-TEST**

<p><b>ALT FRAME 44A</b>  <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b>  When marking the treatment area should the penis be  (a) flaccid or <b>(b) erect</b></p>	<p><b>VO:</b>  When marking the treatment area the penis should be <b>erect</b>. [Ref: PI/p.8/§2.2/ID of Tx Area for PD/bullet a/sub-bullet 1]</p>
<p><b>ALT FRAME 44B</b>  <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO  <b>ON-SCREEN COPY:</b> When injecting Xiaflex should the penis be:  (a) flaccid or (b) erect?</p>	<p><b>VO:</b>  When injecting Xiaflex should the penis be:  (a) flaccid or (b) erect?</p>
<p><b>ALT FRAME 44C</b>  <b>VISUAL:</b> Answers disappear and the correct answers are inserted into the question and highlighted.  <b>ON-SCREEN COPY:</b> When injecting Xiaflex should the penis be:  <b>(a) flaccid</b> or (b) erect?</p>	<p><b>VO:</b>  When injecting Xiaflex should the penis be:  <b>flaccid</b> [Ref: PI/ p.8/§2.2/Inj Procedure for PD/bullet e/line 1]</p>
<p><b>Frame 45</b>  <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO  <b>ON-SCREEN COPY:</b> The needle needs to be inserted _____ the plaque  a) Perpendicular to  b) Transversely through the width of  c) Parallel to  d) Adjacent to, but not within</p>	<p><b>VO:</b>  The needle needs to be inserted <i>in which direction into</i> the plaque?  a) Perpendicular to  b) Transversely through the width of  c) Parallel to  d) Adjacent to, but not within</p>
<p><b>Frame 45A</b>  <b>VISUAL:</b> Answers disappear and the correct answer is inserted into the question and highlighted.  <b>ON-SCREEN COPY:</b> The needle needs to be inserted <b><u>transversely through the width of</u></b> the plaque</p>	<p><b>VO:</b>  The needle needs to be inserted <b>transversely through the width of</b> the plaque? [Ref: PI/ p.9/§2.2/Inj Procedure for PD/bullet f/lines 1-2]</p>

## INJECTION PROCEDURE—SELF-TEST

<p><b>Frame 46</b> <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO <b>ON-SCREEN COPY:</b> The goal of injection is always to deposit the full dose of drug: a) Entirely within the plaque b) Mostly within the plaque c) Entirely outside of the plaque d) Both inside and outside of the plaque</p>	<p><b>VO:</b> The goal of injection is always to deposit the full dose of drug... a) Entirely within the plaque b) Mostly within the plaque c) Entirely outside of the plaque d) Both inside and outside of the plaque</p>
<p><b>Frame 46A</b> <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The goal of injection is always to deposit the full dose of drug: <b>a) Entirely within the plaque</b> b) Mostly within the plaque c) Entirely outside of the plaque d) Both inside and outside of the plaque</p>	<p><b>VO:</b> The goal of injection is always to deposit the full dose of drug <b>entirely within the plaque</b> <i>[Ref: PI/p.9/\$2.2/Inj Procedure for PD/bullet g/lines 5-6]</i></p>

## PENILE MODELING (IN-OFFICE AND AT-HOME)

### Frame 47



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
Penile Modeling (In-Office and At-Home)

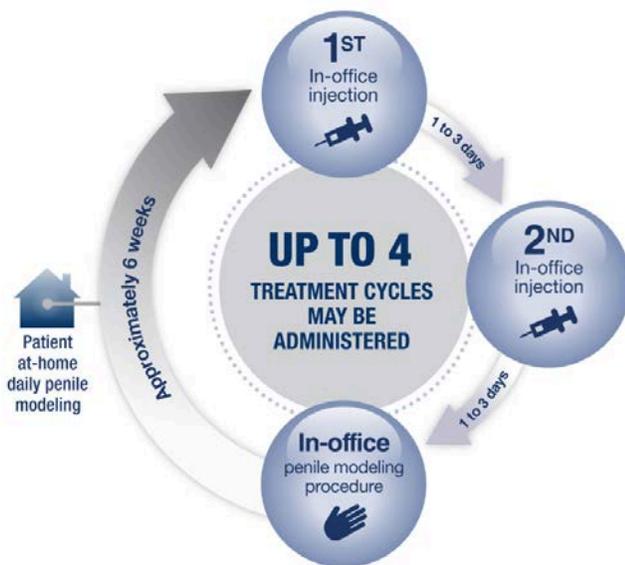
### VO:

In conjunction with Xiaflex, penile modeling helps improve curvature deformity and straighten the penile shaft. In this section, we will review the in-office penile modeling procedure that is performed one to three days following the second injection of Xiaflex in each treatment cycle. [Ref: PI/ p.9/§2.2/Penile Modeling Procedure/¶ 1] We will also review the at-home penile modeling activities that patients should be instructed to do daily.

[Ref: PI/ p.9/§2.2/Penile Modeling for PD/¶ 2]

Prior to administering Xiaflex and as part of every treatment-related visit, use the Patient Counseling Tool to discuss important information with each patient.

### Frame 48



**VISUAL:** “In-office penile modeling procedure” is highlighted to correspond with VO

**ON-SCREEN COPY:** One Xiaflex Treatment Cycle

Treatment Cycle 1; 1st in-office injection procedure → 1 to 3 days → 2nd in-office injection procedure → 1 to 3 days → In-office penile modeling

### VO:

At a follow-up visit one to three days after the second injection of each treatment cycle, perform the in-office penile modeling procedure on the flaccid penis in order to stretch and elongate the treated plaque. [Ref: PI/ p.9/§2.2/Penile Modeling for PD/¶ 1]

## PENILE MODELING (IN-OFFICE AND AT-HOME)

procedure

approximately 6 weeks; At-home penile modeling activities→Treatment Cycle 2; approximately 6 weeks; At-home penile modeling activities→Treatment Cycle 3; approximately 6 weeks; At-home penile modeling activities→Treatment Cycle 4; approximately 6 weeks; At-home penile modeling activities

Up to 4 treatment cycles may be administered

If the curvature deformity is less than 15 degrees after the 1st, 2nd or 3rd Treatment Cycle, or if you determine that further treatment is not clinically indicated, then subsequent treatment cycles should not be administered.

The safety of more than one treatment course of Xiaflex is not known.

### Frame 49



**VISUAL:** Gloved hands grasp the plaque or indurated portion of the flaccid penis about 1 cm proximal and distal to the injection site.

### VO:

If desired, administer suitable local anesthetic.  
[\[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 1\]](#)

Wearing gloves, grasp the plaque or indurated portion of the flaccid penis about one centimeter proximal and distal to the injection site. Avoid direct pressure on the injection site.  
[\[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 2\]](#)

## SELF-TEST — PENILE MODELING (IN-OFFICE AND AT-HOME)

### Frame 50



**VISUAL:** Gloved hands apply firm, steady pressure to elongate and stretch the plaque, creating bending opposite to the patient's penile curvature

#### ON-SCREEN COPY:

- Use target plaque as fulcrum point
- Apply firm, steady pressure
- Gradually bend the shaft in the opposite direction of the curvature

#### VO:

Using the target plaque as a fulcrum point, use both hands to apply firm, steady pressure to elongate and stretch the plaque. The goal is to gradually create bending opposite to the patient's penile curvature, with stretching to the point of moderate resistance.

[\[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 3\]](#)

Hold pressure for thirty seconds then release.

[\[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 3\]](#)

### Frame 51



**VISUAL:** Gloved hands repeat the penile modeling technique

#### ON-SCREEN COPY:

- Rest for 30 seconds
- Repeat a total of 3 times
- Hold for 30 seconds each time

#### VO:

After a thirty-second rest period, repeat the penile modeling technique for a total of three modeling attempts at thirty seconds each.

[\[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 4\]](#)

### Frame 52

#### VO:

For the approximately six weeks following each treatment cycle, patients will need to perform the following penile modeling activities at home daily to help reduce penile curvature [\[Ref:](#)

[PI/p.9/§2.2/Penile Modeling for PD/¶12\]](#)

SELF-TEST — PENILE MODELING (IN-OFFICE AND AT-HOME)



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
At-home Penile Modeling Activities

**Frame 52A**



**VO:**  
There are two types of home penis activities. One is a stretching activity. The other is a straightening activity. Be sure to instruct patients on exactly when to start the activities and how long to continue performing them. [\[Ref: PI/p.9/§2.2/Penile Modeling for PD/¶2\]](#)

The stretching activity should be performed three times daily and when the penis is not erect. Instruct patients to grasp the tip of the penis with the fingers of one hand and hold the base of the penis with the fingers of the other. Then, **gently** pull the penis away from the body to its full length. Hold the stretch for thirty seconds. Then let go and allow the penis to return to its normal unstretched length. [\[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullet 2\]](#)

The penile straightening activity is performed a maximum of once per day on an erection unrelated to sexual activity. If the patient does not have a spontaneous erection, he should not attempt the penis straightening. Instruct patients to **gently** attempt to bend the shaft of the erect penis in the opposite direction of the curve, but not so forcefully as to produce significant pain or discomfort. Patients should hold the penis in this more straightened position for thirty seconds, then let go. [\[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullet 1\]](#)

**SELF-TEST — PENILE MODELING (IN-OFFICE AND AT-HOME)**

 <p><b>VISUAL:</b> Animation demonstrates at-home patient stretching (first of three images above) and straightening (second and third images above) activities.</p>	
<p><b>Frame 53</b></p> <p><b>ON-SCREEN COPY:</b> Provide instructions on at-home penile modeling activities:</p> <ul style="list-style-type: none"> <li>• On flaccid penis: Stretch 3 times daily for 30 seconds at a time</li> <li>• On erect penis: Gently straighten and hold for 30 seconds, once daily</li> </ul>	<p><b>VO:</b> In summary, penis stretching is performed on a non-erect penis, three times a day for thirty seconds each time. Penis straightening is performed no more than once a day on a spontaneous erection unrelated to sexual activity. Discuss with patients the best time to perform these activities. <i>[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullets 1-2]</i></p>
<p><b>Frame</b></p> <div data-bbox="168 1283 764 1602" style="border: 1px solid black; padding: 10px; text-align: center;">  <hr style="width: 30%; margin: 10px auto;"/> <p style="color: orange;">Self-Test Questions</p> </div> <p><b>54</b></p> <p><b>ON-SCREEN COPY:</b> Xiaflex® collagenase clostridium histolyticum Self-Test Questions</p>	<p><b>VO:</b> This completes the section on the Xiaflex penile modeling, both in-office and at-home. To confirm understanding of the key points of this section, please answer the following self-test questions. After answering these questions, you may continue to the next section.</p>
<p><b>Frame 55</b></p> <p><b>VISUAL:</b> Question appears on-screen and answers</p>	<p><b>VO:</b> How soon should the in-office penile modeling</p>

## SELF-TEST — PENILE MODELING (IN-OFFICE AND AT-HOME)

<p>appear sequentially, corresponding to VO</p> <p><b>ON-SCREEN COPY:</b> In-office penile modeling procedure should be performed _____ after the second injection of each treatment cycle:</p> <ul style="list-style-type: none"><li>a) Immediately</li><li>b) 15 to 60 minutes</li><li>c) 1 to 3 days</li><li>d) 5 to 7 days</li></ul>	<p>procedure be performed after the second injection of each treatment cycle:</p> <ul style="list-style-type: none"><li>a) Immediately</li><li>b) Fifteen to sixty minutes</li><li>c) One to three days</li><li>d) Five to seven days</li></ul>
<p><b>Frame 55A</b></p> <p><b>VISUAL:</b> The correct answer is highlighted.</p> <p><b>ON-SCREEN COPY:</b> In-office penile modeling procedure should be performed _____ after the second injection of each treatment cycle:</p> <ul style="list-style-type: none"><li>a) Immediately</li><li>b) 15 to 60 minutes</li><li><b>c) 1 to 3 days</b></li><li>d) 5 to 7 days</li></ul>	<p><b>VO:</b></p> <p>In-office penile modeling procedure should be performed <b>one to three days</b> after the second injection of each treatment cycle: <a href="#">[Ref: PI/p.9/§2.2/Penile Modeling for PD/¶1]</a></p>
<p><b>Frame 56</b></p> <p><b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO</p> <p><b>ON-SCREEN COPY:</b> When performing in-office penile modeling procedure, hold the pressure for 30 seconds and rest for 30 seconds for a total of:</p> <ul style="list-style-type: none"><li>a) 2 times</li><li>b) 3 times</li><li>c) 5 times</li><li>d) 10 times</li></ul>	<p><b>VO:</b></p> <p>When performing in-office penile modeling procedure, hold the pressure for thirty seconds and rest for thirty seconds for a total of:</p> <ul style="list-style-type: none"><li>a) Two times</li><li>b) Three times</li><li>c) Five times</li><li>d) Ten times</li></ul>
<p><b>Frame 56A</b></p> <p><b>VISUAL:</b> The correct answer is highlighted.</p> <p><b>ON-SCREEN COPY:</b> When performing in-office penile modeling procedure, hold the pressure for 30 seconds and rest for 30 seconds for a total of:</p> <ul style="list-style-type: none"><li>a) 2 times</li><li><b>b) 3 times</b></li><li>c) 5 times</li><li>d) 10 times</li></ul>	<p><b>VO:</b></p> <p>When performing in-office penile modeling procedure, hold the pressure for thirty seconds and rest for thirty seconds for a total of: <b>three times.</b> <a href="#">[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullets 3 and 4]</a></p>

## SUMMARY

<p><b>Frame 57</b> <b>VISUAL:</b> Question appears on-screen and answers appear sequentially, corresponding to VO <b>ON-SCREEN COPY:</b> The patient should be instructed to perform at-home penile <i>straightening</i> activity on a spontaneous <u>erection</u> unrelated to sexual activity no more than once daily for 30 seconds. The patient should also be instructed to perform the <i>stretching</i> activity on the <u>flaccid penis</u>:</p> <ul style="list-style-type: none"><li>a) At no time</li><li>b) Once daily for a total of 1 minute</li><li>c) 5 times daily for 30 seconds at a time</li><li>d) 3 times daily for 30 seconds at a time</li></ul>	<p><b>VO:</b> The patient should be instructed to perform at-home penile <i>straightening</i> activity on a spontaneous <u>erection</u> unrelated to sexual activity no more than once daily for thirty seconds. How often should the patient perform the <i>stretching</i> activity on the <u>flaccid penis</u>:</p> <ul style="list-style-type: none"><li>a) At no time</li><li>b) Once daily for a total of one minute</li><li>c) Five times daily for thirty seconds at a time</li><li>d) Three times daily for thirty seconds at a time</li></ul>
<p><b>Frame 57A</b> <b>VISUAL:</b> The correct answer is highlighted. <b>ON-SCREEN COPY:</b> The patient should be instructed to perform at-home penile <i>straightening</i> activity on an <u>erection</u> unrelated to sexual activity once daily for 30 seconds. The patient should also be instructed to perform the <i>stretching</i> activity on the <u>flaccid penis</u>:</p> <ul style="list-style-type: none"><li>a) At no time</li><li>b) Once daily for a total of 1 minute</li><li>c) 5 times daily for 30 seconds at a time</li><li><b>d) 3 times daily for 30 seconds at a time</b></li></ul>	<p><b>VO:</b> Instruct the patient to perform the <i>stretching</i> activity on the <u>flaccid penis</u> <b>three times daily for thirty seconds at a time.</b> <a href="#">[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullet 2]</a></p>
<p><b>Frame 58</b> <b>VISUAL:</b> Title screen with Xiaflex logo and copy below. <b>ON-SCREEN COPY:</b> Xiaflex® collagenase clostridium histolyticum Instructions for Using the Xiaflex Patient Counseling Document</p>	<p><b>VO:</b> Instructions for using the Xiaflex Patient Counseling Document.</p>

## SUMMARY

<p><b>Frame 59</b> <b>VISUAL:</b> Copy appears and scrolls as VO is heard <b>ON-SCREEN COPY:</b> Prior to initiating treatment with Xiaflex, and as part of each treatment-related visit, discuss the following information included in the Patient Counseling Document with each patient:</p> <ul style="list-style-type: none"><li>• The risks of corporal rupture (penile fracture) and other serious penile injury</li><li>• Precautions related to the patient’s role in reducing the risks of these adverse outcomes (for example, advising patients to wait two weeks until after the second injection of each treatment cycle before resuming sexual activity)</li><li>• Conditions under which patients should promptly contact their healthcare provider</li><li>• Clear instructions on at-home penile modeling activities</li><li>• Important information regarding the safe use of Xiaflex in treating Peyronie’s disease</li></ul> <p>The patient must be given a copy of the Patient Counseling Document to take home.</p> <p>In addition, provide a Medication Guide to each patient prior to each injection of Xiaflex.</p>	<p><b>VO:</b> Prior to initiating treatment with Xiaflex, and as part of each treatment-related visit, discuss the following information included in the Patient Counseling Tool with each patient:</p> <ul style="list-style-type: none"><li>• The risks of corporal rupture (penile fracture) and other serious penile injury</li><li>• Precautions related to the patient’s role in reducing the risk of these adverse outcomes (for example, advising patients to wait two weeks until after the second injection of each treatment cycle before resuming sexual activity)</li><li>• Conditions under which patients should promptly contact their healthcare provider</li><li>• Clear instructions on at-home penile modeling activities</li><li>• Important information regarding the safe use of Xiaflex in treating Peyronie’s disease</li></ul> <p>The patient must be given a copy of the Patient Counseling Document to take home.</p> <p>In addition, provide a Medication Guide to each patient prior to each injection of Xiaflex.</p>
<p><b>Frame 60</b> <b>VISUAL:</b> Scrolling copy stops and fades to new copy <b>ON-SCREEN COPY:</b> To obtain copies of the Patient Counseling Document:</p> <ul style="list-style-type: none"><li>• Visit <a href="http://www.XiaflexREMS.com">www.XiaflexREMS.com</a></li><li>• Call 1-877-XIAFLEX (1-877-942-3539)</li><li>• Or contact your Xiaflex sales representative</li></ul>	<p><b>VO:</b> To obtain copies of the Patient Counseling Document:</p> <ul style="list-style-type: none"><li>• Visit <a href="http://www.XiaflexREMS.com">www.XiaflexREMS.com</a></li><li>• Call 1-877-XIAFLEX (1-877-942-3539)</li><li>• Or contact your Xiaflex sales representative</li></ul>

## SUMMARY

<p><b>Frame 61</b></p> <div data-bbox="134 289 764 625" style="border: 1px solid black; padding: 10px; text-align: center;"><p><b>XIAFLEX</b><sup>®</sup> collagenase clostridium histolyticum</p><hr/><p>Summary</p></div> <p><b>ON-SCREEN COPY:</b> Xiaflex<sup>®</sup> collagenase clostridium histolyticum Summary</p>	<p><b>VO:</b></p> <p>Thank you for taking the time to review the REMS training video for using Xiaflex in treating Peyronie’s disease. Here are some key points to remember.</p>
<p><b>Frame 62</b></p> <p><b>ON-SCREEN COPY:</b></p> <p>Storage and handling</p> <ul style="list-style-type: none"><li>• Keep vials of Xiaflex and sterile diluent refrigerated between 2° and 8° C or 36° to 46° F</li><li>• Before use, allow vials to stand at room temperature for at least 15 minutes and no longer than 60 minutes</li><li>• Reconstituted solution can be kept at room temperature for up to 1 hour or refrigerated for up to 4 hours prior to administration. If refrigerated, allow to return to room temperature for 15 minutes before use</li></ul>	<p><b>VO:</b></p> <p><b>STORAGE AND HANDLING</b></p> <p>Prior to reconstitution, the vials of lyophilized powder of Xiaflex and sterile diluent should be stored in a refrigerator at two to eight degrees Celsius or thirty-six to forty-six degrees Fahrenheit. <a href="#">[Ref: PI/p.31/§16/¶1]</a></p> <ul style="list-style-type: none"><li>• Before preparing Xiaflex, allow vials to stand at room temperature for at least fifteen minutes and no longer than sixty minutes. <a href="#">[Ref: PI/p.7/§2.2/bullet a, lines 1-4]</a></li><li>• The reconstituted Xiaflex solution can be kept at room temperature of twenty to twenty-five degrees Celsius or sixty-eight to seventy-seven degrees Fahrenheit for up to one hour or refrigerated at two to eight degrees Celsius or thirty-six to forty-six degrees Fahrenheit for up to four hours prior to administration. <a href="#">[Ref: PI/p.8/§2.2/bullet f, lines 1-3]</a></li></ul>
<p><b>Frame 63</b></p>	<p><b>VO:</b></p> <p>If the reconstituted Xiaflex solution is refrigerated, allow this solution to return to room temperature for approximately fifteen minutes before use.</p> <p><a href="#">[Ref: PI/p.8/§2.2/bullet f, lines 3-5]</a></p>

## SUMMARY



**VISUAL:** Vial with reconstituted Xiaflex; clock illustrating 15-minute interval

**ON-SCREEN COPY:** Reconstituted Xiaflex

After refrigeration, let stand at room temperature for 15 minutes before use

### Frame 64



**VISUAL:** Gloved hands mark injection site with surgical marker.

**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum

Identifying the Treatment Area

- Induce an erection
- Locate the point of maximum concavity
- Mark the area with a marker

### VO:

#### Identifying the Treatment Area

After inducing an erection, locate the point of maximum concavity, or focal point in the bend of the penis, which is where the plaque and the curvature intersect. [\[Ref: PI/p.8/§2.2/ID of Tx Area for PD, bullet a, sub-bullets 1-2\]](#)

### Frame 65

### VO:

#### INJECTION PROCEDURE

Withdraw 0.25 mL of reconstituted Xiaflex solution. [\[Ref: PI/p. 8/§2.2/Inj Procedure for PD/bullet d\]](#)

The penis should be in a flaccid state before injecting Xiaflex. Place the needle tip on the side of the target plaque in alignment with

## SUMMARY



**VISUAL:** Two gloved hands inject penis with syringe; copy bullets appear, corresponding with VO

**ON-SCREEN COPY:** Injection Procedure

- Withdraw 0.25 mL of reconstituted Xiaflex solution
- Penis should be flaccid
- Place needle tip on the side of the plaque in alignment with the point of maximal concavity
- Insert and advance the needle transversely
- Confirm proper positioning by noting resistance in syringe plunger
- Deposit full dose within the plaque

the point of maximal concavity. Orient the needle so that it enters the plaque from the side, NOT downward or perpendicularly toward the body of the corpora cavernosum.

[\[Ref: PI/p. 8/§2.2/Inj Procedure for PD/bullet e\]](#)

Insert and advance the needle transversely through the width of the plaque, toward the opposite side of the plaque without passing completely through it. Proper needle position is confirmed by carefully noting resistance to minimal depression of the syringe plunger.

[\[Ref: PI/p. 9/§2.2/Inj Procedure for PD/bullet f\]](#)

Withdraw the needle slowly, so as to deposit the full dose along the needle track within the plaque. The goal is always to deposit the full dose entirely within the plaque. [\[Ref: PI/p. 9/§2.2/Inj Procedure for PD/bullet g\]](#)

**Frame 66**



**VISUAL:** Gloved hands bending penis opposite to penile curvature, with stretching to the point of moderate resistance.

**ON-SCREEN COPY:**

- Create a reverse bend
- Stretch to point of moderate resistance
- Hold for 30 seconds

**IN-OFFICE PENILE MODELING**

**VO:**

**PENILE MODELING (IN-OFFICE AND AT-HOME)**

In-office penile modeling procedure should be performed one to three days after the second injection of each treatment cycle. [\[Ref: PI/p.9/§2.2/Penile Modeling Procedure/¶ 1\]](#)

Using the target plaque as a fulcrum point, use both hands to apply firm, steady pressure to elongate and stretch the plaque. The goal is to gradually create bending opposite to the patient's penile curvature, with stretching to the point of moderate resistance.

Hold pressure for thirty seconds and then release. [\[Ref: PI/p.9/§2.2/Penile Modeling Procedure/bullet 3\]](#)

After a thirty-second rest period, repeat the penile modeling technique for a total of three times at thirty seconds each.

## SUMMARY

	<p><a href="#">[Ref: PI/ p.9/§2.2/Penile Modeling Procedure/bullet 4]</a></p>
<p><b>Frame 67</b></p> <p><b>At-home penile modeling activities:</b></p> <div data-bbox="136 380 643 590"><p><b>Stretching</b></p><p>On flaccid penis: Stretch 3 times daily for 30 seconds at a time</p><p><b>Straightening</b></p><p>On erect penis: Gently straighten and hold for 30 seconds, once daily</p></div> <p><b>VISUAL:</b> Illustrations of stretching and straightening technique for at-home penile modeling</p> <p><b>ON-SCREEN COPY:</b> At-home penile modeling activity:</p> <ul style="list-style-type: none"><li>• On flaccid penis: Stretch 3 times daily for 30 seconds at a time</li><li>• On erect penis: Gently straighten and hold for 30 seconds once per day</li></ul>	<p>At-home penile modeling activities involve a gentle stretching and straightening of the penis.</p> <p><a href="#">[Ref: PI/p.9/§2.2/Penile Modeling for PD/¶12]</a></p> <p>The stretching activity should be performed three times daily and when the penis is not erect. Stretching should last for thirty seconds.</p> <p><a href="#">[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullet 2]</a></p> <p>The straightening activity is performed for thirty seconds, no more than once per day on a spontaneous erection unrelated to sexual activity. <a href="#">[Ref: PI/p.10/§2.2/Penile Modeling for PD/bullet 1]</a></p> <p>Remember, prior to initiating treatment and as part of each treatment-related visit, use the Xiaflex Patient Counseling Tool to discuss important information with each patient.</p>

## CONTACT US

### FRAME 68



**ON-SCREEN COPY:** Xiaflex®  
collagenase clostridium histolyticum  
Contact Us  
1-877-663-0412

### VO:

If you have product-related questions or to report adverse events, please contact the Auxilium Drug Information Call Center at 1-877-663-0412.

### FRAME 69



**ON-SCREEN COPY:** Auxilium  
Innovations for Life®  
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# What You Need to Know About XIAFLEX Treatment for Peyronie's Disease: A Patient Guide

**Patients:** Keep this guide for important safety information and instructions for your at-home activities.

**Healthcare Providers:** Review this guide with your patients and give them a copy.

XIAFLEX is a prescription medicine used to treat adult men with Peyronie's disease with an abnormally curved penis and a plaque that can be felt.

## What are the serious risks of XIAFLEX treatment?

**XIAFLEX can cause serious side effects including:**

- **Penile fracture (corporal rupture) or other serious injury to the penis**

### **Penile fracture (corporal rupture) or other serious injury to the penis**

Receiving an injection of XIAFLEX may cause damage to the tubes in your penis called the corpora. After treatment with XIAFLEX, one of these tubes may break during an erection. This is called a corporal rupture or penile fracture. This could require surgery to fix the damaged area. Damage to your penis might not get better after corporal rupture.

After treatment, blood vessels in your penis may also break, causing blood to collect under the skin (hematoma). This could require a procedure to drain the blood from under the skin.

**Do not have sex or any other sexual activity** for at least **2 weeks** after any XIAFLEX injection, and the pain and swelling have gone away, or until given permission by your healthcare provider.

## What symptoms do I need to look for?

**Call your healthcare provider right away if you have any of the following symptoms of penile fracture or other serious injury to the penis:**

- A popping sound or sensation in an erect penis
- Sudden loss of the ability to maintain an erection
- Severe purple bruising and swelling of your penis
- Difficulty urinating or blood in the urine
- Severe pain in your penis

**You may report side effects to the FDA at 1-800-FDA-1088 or to the Auxilium Drug Information Call Center at 1-877-663-0412.**

# How can I lower the risks associated with XIAFLEX?

## Before treatment:

- Tell your healthcare provider if you have ever had an allergic reaction to XIAFLEX.
- Tell your healthcare provider about all the medications you take, especially blood thinner medicines such as aspirin, clopidogrel bisulfate (PLAVIX), prasugrel hydrochloride (EFFIENT) or warfarin sodium (COUMADIN). If you are told to stop taking a blood thinner before your XIAFLEX injection, your healthcare provider should tell you when to restart the blood thinner.
- Tell your healthcare provider if you have any bleeding problems or if you have other medical conditions.

## After treatment:

- Within 24 hours after treatment, your penis may appear bruised and/or swollen and you may have mild-to-moderate penile pain. Ask your healthcare provider if over-the-counter medications are appropriate.
- Do not engage in sexual activity for at least 2 weeks following any injection of XIAFLEX, and the pain and swelling has gone away, or until given permission by your healthcare provider.
- Do the gentle stretching and straightening of your penis at home as shown below.
- Return to your healthcare provider's office when directed for further injection(s) and/or penile modeling procedures.

## What do I need to do at home?

For the 6 weeks after each treatment cycle, you will need to perform the following **gentle penis stretching and straightening** activities. Your doctor will tell you exactly when to start and how long to continue.

### 1) Penis Stretches (when penis is not erect)

- Grasp the tip of your penis with the fingers of one hand and hold the base of your penis with the fingers of your other hand (see diagram).
- **Gently** pull your penis away from your body to its full length.
- Hold the stretch for 30 seconds.
- Let go and allow your penis to return to its normal, unstretched length.
- Do this stretching three times each day, only when the penis is not erect.

Side View of Penis Stretching Activity



### 2) Penis Straightening (when penis is erect)

- If you have a spontaneous erection, not related to sexual activity, attempt to straighten your penis by **gently** bending the shaft in the opposite direction of the curve, but not so forcefully so as to produce significant pain or discomfort.
- Hold the penis in this more straightened position for 30 seconds, then let go.
- Do this straightening **only one time** each day. If you do not have a spontaneous erection, do not attempt the penis straightening activity.

Top View of Penis Straightening Activity



Healthcare Provider Enrollment Form for Peyronie's Disease

**INSTRUCTIONS:** Fax completed form to **XIAFLEX at 1-877-313-1236** or mail to XIAFLEX REMS program, PO Box 13185, La Jolla, CA 92039. You will receive confirmation of certification within 2 business days after your form is received by Auxilium. For questions regarding the XIAFLEX REMS program for Peyronie's disease, call 1-877-313-1235.

**Healthcare Provider responsibilities for the use of XIAFLEX in the treatment of Peyronie's disease.**

I understand that XIAFLEX is only available for the treatment of Peyronie's disease through the XIAFLEX REMS program.

I confirm that to be specially certified I have met all of the following requirements:

- I am a healthcare provider knowledgeable in the management of male urological diseases.
- I have read the Prescribing Information for XIAFLEX, including the risks associated with the use of XIAFLEX and how to properly administer XIAFLEX for Peyronie's disease.
- I have completed the XIAFLEX REMS training video and/or training guide for the treatment of Peyronie's disease.
- Prior to initiating treatment, and as part of each treatment-related visit, I 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.
- 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.
- I agree that I will make available to Auxilium, and/or a designated third party or the FDA, documentation to verify understanding of, and adherence to, the XIAFLEX REMS requirements.

I understand that this enrollment and certification only applies to me, and does not apply to any Healthcare Setting that employs me, or in which I may have an interest. Failure to enroll and become certified in the XIAFLEX REMS program for Peyronie's disease as a Healthcare Provider will result in my inability to receive shipments of XIAFLEX.

Healthcare Provider Name \_\_\_\_\_ Signature \_\_\_\_\_ Date \_\_\_\_\_

**HEALTHCARE PROVIDER INFORMATION**

First Name \_\_\_\_\_ MI \_\_\_\_\_ Last \_\_\_\_\_ Suffix \_\_\_\_\_ Degree \_\_\_\_\_  
Fax \_\_\_\_\_ Phone \_\_\_\_\_ Phone Type \_\_\_\_\_  MD  DO  PA  CNP  
Email \_\_\_\_\_ Preferred method of contact is:  Office  Mobile  Home  
 Email  Phone  Fax  Mail  
Provide as appropriate:  
NPI# \_\_\_\_\_ ME# \_\_\_\_\_ License # and State \_\_\_\_\_

Specialty:  General Surgeon  Plastic Surgeon  Urologist  Other (specify) \_\_\_\_\_

**PRACTICE INFORMATION**

Practice Name \_\_\_\_\_  
Address \_\_\_\_\_  
City \_\_\_\_\_ State \_\_\_\_\_ Zip \_\_\_\_\_

Primary Treatment Setting:  Inpatient  Outpatient/Clinic (not affiliated with hospital)  Outpatient/Clinic (affiliated with hospital)

# XIAFLEX<sup>TM</sup>

collagenase clostridium histolyticum

## REMS Program for Peyronie's Disease

NEW Enrollment

Enrollment Update

Program Use Only:  
Healthcare Setting Enrollment ID#

### Pharmacy/Healthcare Setting Enrollment Form for Peyronie's Disease

To enroll, the pharmacy or healthcare setting must designate an Authorized Representative to coordinate the setting's activities and assure compliance with the XIAFLEX REMS Program for Peyronie's disease.

**INSTRUCTIONS:** Fax completed form to **XIAFLEX at 1-877-313-1236** or mail to XIAFLEX REMS program, PO Box 13185, La Jolla, CA 92039. You will receive an enrollment confirmation within 2 business days after your form is received by Auxilium. For questions regarding the XIAFLEX REMS program for Peyronie's disease call 1-877-313-1235.

#### AUTHORIZED REPRESENTATIVE RESPONSIBILITIES

I understand that XIAFLEX is only available through the XIAFLEX REMS program for Peyronie's disease.

I am the Authorized Representative designated by my pharmacy or healthcare setting to coordinate the activities of the XIAFLEX REMS. I agree to comply with the following program requirements:

- Ensure that the staff responsible for dispensing and administering XIAFLEX at this healthcare setting is aware of my responsibilities as the Authorized Representative.
- Prior to dispensing XIAFLEX, confirm that the Healthcare Provider treating Peyronie's disease is specially certified in the XIAFLEX REMS program for Peyronie's disease.
- Maintain a current list of Healthcare Providers affiliated with my healthcare setting who are specially certified. The current affiliated Healthcare Providers of this healthcare setting include the individuals listed below. I will maintain this list by adding or removing affiliated Healthcare Providers as appropriate.
- Agree not to loan, sell or transfer XIAFLEX to another pharmacy, healthcare setting, prescriber, institution or distributor.
- Make available to Auxilium, and/or a designated third party or the FDA, documentation to verify understanding of, and adherence to, the requirements of the XIAFLEX REMS.

I understand that this enrollment only applies to me as the designated Authorized Representative of this pharmacy or healthcare setting. I will complete a separate enrollment form for each pharmacy or healthcare setting (unique ship-to site address) for which my designation and responsibilities extend. Failure to enroll a pharmacy or healthcare setting in the XIAFLEX REMS program for Peyronie's disease will result in the inability to receive shipments of XIAFLEX.

HCP First and Last Name      Healthcare Provider Enrollment ID#

For additional Affiliated Healthcare Setting Providers please continue on page 2.

Authorized Representative (Please Print)

Signature

Date

#### AUTHORIZED REPRESENTATIVE

Salutation:  Dr  Mr  Ms  Mrs

First Name

MI

Last

Suffix

Fax

Phone

Phone Type

Main  Direct  Mobile

Email

Preferred method of contact is:

Email  Phone  Fax  Mail

Role:  Office Staff  Clinician/Healthcare Provider  Office Administration  Other (Specify)

# XIAFLEX<sup>™</sup>

collagenase clostridium histolyticum

## REMS Program for Peyronie's Disease

Program Use Only:  
Healthcare Setting Enrollment ID#

### Pharmacy/Healthcare Setting Enrollment Form for Peyronie's Disease

To enroll, the pharmacy or healthcare setting must designate an Authorized Representative to coordinate the setting's activities and assure compliance with the XIAFLEX REMS Program for Peyronie's disease.

**INSTRUCTIONS:** Fax completed form to **XIAFLEX at 1-877-313-1236** or mail to XIAFLEX REMS program, PO Box 13185, La Jolla, CA 92039. You will receive an enrollment confirmation within 2 business days after your form is received by Auxilium. For questions regarding XIAFLEX REMS program for Peyronie's disease call 1-877-313-1235.

### AFFILIATED HEALTHCARE SETTING HEALTHCARE PROVIDERS

HCP First and Last Name	Healthcare Provider Enrollment ID#
HCP First and Last Name	Healthcare Provider Enrollment ID#
HCP First and Last Name	Healthcare Provider Enrollment ID#
HCP First and Last Name	Healthcare Provider Enrollment ID#
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HCP First and Last Name	Healthcare Provider Enrollment ID#
HCP First and Last Name	Healthcare Provider Enrollment ID#
HCP First and Last Name	Healthcare Provider Enrollment ID#



[Medication Guide](#)

[Full Prescribing Information](#)

[Important Safety Information](#)

## **XIAFLEX REMS (Risk Evaluation and Mitigation Strategy)**

A REMS is a strategy to manage known or potential serious risks associated with a drug and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. Auxilium has worked with the FDA to develop materials to communicate to healthcare providers and patients, the potential serious risks associated with use of XIAFLEX.

### **XIAFLEX is approved for two indications:**

- the treatment of adult patients with Dupuytren's contracture with a palpable cord
- the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy

**Each indication has separate REMS requirements and educational materials.** Follow the links below to learn more about the XIAFLEX REMS for each indication.

[XIAFLEX for Dupuytren's Contracture](#)

[XIAFLEX for Peyronie's disease](#)



[Medication Guide](#)

[Full Prescribing Information](#)

[Important Safety Information](#)

## **Risk Evaluation and Mitigation Strategy**

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug and is required by the Food and Drug Administration to ensure that the benefits of the drug outweigh its risks. In order for Auxilium to communicate certain risks to ensure that XIAFLEX is injected properly, Auxilium has worked with the FDA to develop materials to communicate the risks of tendon rupture and hypersensitivity reactions. The REMS program is designed to inform health care providers about the potential risks with XIAFLEX. To learn more about serious risks of XIAFLEX, read the Full Prescribing Information, including the Medication Guide, and important safety information by clicking above, and discuss it with your patients.

The goals of the XIAFLEX REMS for 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.

To access training materials on how to properly administer XIAFLEX for Dupuytren’s contracture click here:

- [Procedure Training Video](#)
- [Training Guide for the Administration of XIAFLEX \(pdf\)](#)

Please see the [Dear Healthcare Provider Letter](#) for more information about XIAFLEX for Dupuytren’s contracture.

XIAFLEX for the treatment of Dupuytren’s contracture is available only through a managed distribution program. The XIAFLEX managed distribution program requires Healthcare Providers and Healthcare Settings that intend to use XIAFLEX for treatment of Dupuytren’s contracture to complete an enrollment process. To enroll as a Healthcare Provider and/or a Healthcare Setting click the link below:

**XIAFLEX Enrollment for  
Dupuytren’s Contracture**





Healthcare Provider Certification	Healthcare Setting Certification	Patient Counseling Tool
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## XIAFLEX REMS for Peyronie's Disease

A REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a strategy to manage known or potential serious risks associated with a drug and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. Auxilium has worked with the FDA to develop the XIAFLEX REMS Program.

### XIAFLEX REMS Program Overview

XIAFLEX is available for the treatment of Peyronie's disease only through the XIAFLEX REMS Program. The XIAFLEX REMS Program requirements include:

- **Training** for healthcare providers on the risks of corporal rupture and other serious injuries to the penis, and how to properly administer XIAFLEX
- **Certification** in the XIAFLEX REMS Program by completing training and enrollment in the program
- **Patient Counseling** about the risks of corporal rupture and other serious injuries to the penis and the importance of patient adherence to post-injection instructions. Healthcare Providers must give patients the Patient Counseling Tool, "*What You Need to Know About XIAFLEX Treatment for Peyronie's Disease: A Patient Guide*", after each XIAFLEX injection.
- **Restricted distribution** through specially certified healthcare settings (e.g., pharmacies, practitioners, hospitals or outpatient settings)

## **Healthcare Provider Certification**

To become certified in the XIAFLEX REMS Program, healthcare providers must read the prescribing information, take the training below (video or guide) and complete the Enrollment Form.

- **[Prescribing Information](#)**
- **[Training Video for the Administration of XIAFLEX for Peyronie's Disease](#)**
- **[Training Guide for the Administration of XIAFLEX for Peyronie's Disease \(pdf\)](#)**
- **[Patient Counseling Tool, "What You Need to Know About XIAFLEX Treatment for Peyronie's Disease: A Patient Guide"](#)**
- **[Healthcare Provider Enrollment Form for Peyronie's Disease](#)**

## **Pharmacy/Healthcare Setting Certification**

To become certified in the XIAFLEX REMS Program, pharmacies and healthcare settings must complete the Pharmacy/Healthcare Setting Enrollment Form.

- **[Pharmacy/Healthcare Setting Enrollment Form for Peyronie's Disease](#)**

### **XIAFLEX is approved for two indications:**

- the treatment of adult patients with Dupuytren's contracture with a palpable cord
- the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy

**[For information on XIAFLEX treatment for Dupuytren's contracture please click on this link:](#)**

- **[XIAFLEX REMS for Dupuytren's contracture](#)**

