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RMX-00068

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.

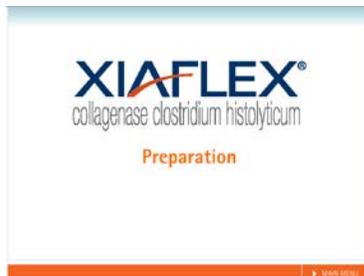


NARRATIVE

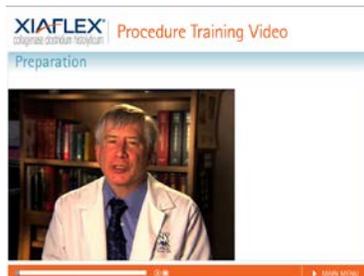
VISUAL

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 2nd or 3rd 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.

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.

Panel #1



Panel #2



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

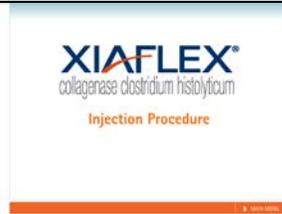
Preparation Questions

- 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. 0.39 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

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.

Panel #2

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]

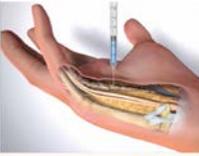
Narrator: This completes the section on the proper injection procedure for the XIAFLEX injection. To confirm understanding of the key points in this section, please answer the following self-test questions.

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

XIAFLEX
Chondroitin Sulfate Polysulfate

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 Details](#)

XIAFLEX
Chondroitin Sulfate Polysulfate

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

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XIAFLEX
Chondroitin Sulfate Polysulfate

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 Details](#)

XIAFLEX
Chondroitin Sulfate Polysulfate

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

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

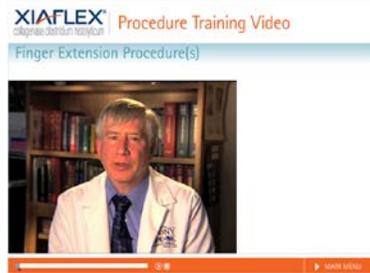
[TRANSITION SLIDE]



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 100mg/200mg

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 100mg/200mg

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 100mg/200mg

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



▶ VIEW MENU

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



▶ VIEW MENU

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



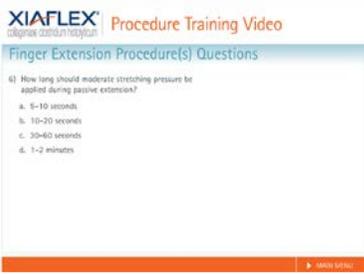
▶ VIEW MENU

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.



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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
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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
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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

XIAFLEX
Cilagener 200mg/100mg/ml

Procedure Training Video

Summary

INJECTION PROCEDURE

- Withdraw and inject the appropriate volume of reconstituted XIAFLEX.
 - For a cord affecting an MP joint, use 0.25 mL.

Cord to be Treated	Volume Required for Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

▶ VIEW VIDEO

Panel #5

XIAFLEX
Cilagener 200mg/100mg/ml

Procedure Training Video

Summary

INJECTION PROCEDURE

- Withdraw and inject the appropriate volume of reconstituted XIAFLEX.
 - For a cord affecting an MP joint, use 0.25 mL.
 - For a cord affecting a PIP joint, use 0.20 mL.

Cord to be Treated	Volume Required for Reconstitution	Volume to Inject to Patient
MP joints	0.25 mL	0.25 mL
PIP joints	0.20 mL	0.20 mL

▶ VIEW VIDEO

Panel #6

XIAFLEX
Cilagener 200mg/100mg/ml

Procedure Training Video

Summary

INJECTION PROCEDURE

- Withdraw and inject the appropriate volume of reconstituted XIAFLEX.
 - For a cord affecting an MP joint, use 0.25 mL.
 - For a cord affecting a PIP joint, use 0.20 mL.

Locations cord affecting the fourth finger:

Base of 4th joint

Proximal PIP joint

Distal PIP joint

Distal MP joint

▶ VIEW VIDEO

Panel #7

XIAFLEX
Cilagener 200mg/100mg/ml

Procedure Training Video

Summary

INJECTION PROCEDURE

- Withdraw and inject the appropriate volume of reconstituted XIAFLEX.
 - For a cord affecting an MP joint, use 0.25 mL.
 - For a cord affecting a PIP joint, use 0.20 mL.
 - When injecting a cord affecting a PIP joint of the fifth finger:
 - Needle insertion should not be more than 2 to 3 mm in depth.
 - Needle tip may not be more than 4 mm distal to the palmar digital crease.

Palmar digital crease of fifth finger

Image courtesy of T. Thomas D. Reagin

▶ VIEW VIDEO

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 #11Panel #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[®]
collagenase clostridium histolyticum

Indication and
Important Safety Information

▶ NEXT MENU

XIAFLEX[®]
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Indication

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

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XIAFLEX[®]
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 was given to XIAFLEX administration), local tissue. Therefore, use with caution in patients with osteoporosis. Discard any remaining product following recommended instructions for use.

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, numbness, tingling, skin reaction, pain in softening, tenderness, injection site swelling, pruritus, lymphadenopathy, skin laceration, lymph node pain, tenderness, and edema.

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

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

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 benzoyl peroxide). Following XIAFLEX treatment.

▶ VIEW VIDEO

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The Prescribing Information and the Mitigation Plan will be included in the product packaging and also can be found at www.xiaflex.com. For additional information, visit 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).

▶ VIEW VIDEO

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CONTACT US



XIAFLEX® 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 single use.

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

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

To report adverse events, please contact one of the following:
• National Drug Information Center at 1-877-852-2413
• FDA MedWatch reporting system by telephone 1-800-858-1088, fax 1-800-438-1916,
or via <http://www.accessdata.fda.gov/druginfocenter/medwatch/>, or by mail using the average postcard Medication Voluntary Reporting Form 2008.

Please send us:
• Full Safety Information and Adverse Event Reporting Program
• Initial Drug Information
• Initial Patient Form
• Product Name
• NDC/lot
• Patient Name

Web center

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