

TRAINING GUIDE

FOR THE ADMINISTRATION OF XIAFLEX® FOR DUPUYTREN'S CONTRACTURE

This Training Guide 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, including tendon rupture and the potential risk of severe hypersensitivity events.¹

INDICATION

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

IMPORTANT SAFETY INFORMATION FOR XIAFLEX

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

Please see additional Important Safety Information throughout.

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Resources for Administration

XIAFLEX®
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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 finger(s) to bend or contract toward the palm of the hand, resulting in the inability to fully extend the affected finger(s) and a reduced range of motion.²

XIAFLEX[®] 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(s). The guide also includes special precautions for injection of a cord affecting the PIP joint of the fifth finger.¹

XIAFLEX[®] should be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture.¹

IMPORTANT SAFETY INFORMATION FOR XIAFLEX (cont)

- In the controlled and uncontrolled portions of clinical trials in Dupuytren's contracture, 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 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 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
- Other XIAFLEX-associated serious local adverse reactions in the controlled and uncontrolled portions of the clinical studies included pulley rupture, ligament injury, complex regional pain syndrome (CRPS), sensory abnormality of the hand, and skin laceration (tear). 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 premarketing trials (9%). Post-marketing cases of skin laceration requiring skin graft after finger extension procedures and local skin and soft-tissue necrosis, some requiring skin grafting, or other surgical interventions including finger amputation have been reported. Signs or symptoms that may reflect serious injury to the injected finger/hand should be promptly evaluated because surgical intervention may be required

DOSING OF XIAFLEX^{®1}

- XIAFLEX[®] should be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture.
- 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 into a palpable cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint. Each vial of XIAFLEX[®] and sterile diluent should only be used for a single injection.
- If 2 joints on the same hand are to be treated during a treatment visit, separate vials and syringes should be used for each reconstitution and injection.
- Approximately 24 to 72 hours after injection, perform a finger extension procedure if a contracture persists to facilitate cord disruption.
- Four weeks after the XIAFLEX[®] injection and finger extension procedure, 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 may be repeated (approximately 24 to 72 hours after injection).
- Injections and finger extension procedures may be administered up to 3 times per cord at approximately 4-week intervals.
- Perform up to 2 injections in the same hand according to the injection procedure during a treatment visit. Two palpable cords affecting 2 joints may be injected or one palpable cord affecting 2 joints in the same finger may be injected at 2 locations during a treatment visit. If the patient has other palpable cords with contractures of MP or PIP joints, these cords may be injected with XIAFLEX[®] at other treatment visits approximately 4 weeks apart.

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PREPARATION FOR ADMINISTRATION OF XIAFLEX®¹

This section summarizes the procedure for reconstitution of XIAFLEX®, supplied as a lyophilized powder.

Important Considerations

- Identify the joint contracture (ie, MP or PIP) that is associated with the palpable cord—the volume of sterile diluent required for the reconstitution is determined by the type of joint contracture.
- Prior to reconstitution, the vials of lyophilized XIAFLEX® powder and sterile diluent should be stored in a refrigerator at 2°C to 8°C (36°F 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 on the next page.
- Visually inspect the vial containing XIAFLEX®. The cake of lyophilized powder should be intact and white in color.
- If the cake has been eroded or is discolored, it should not be used and should be reported to Endo Pharmaceuticals Inc. by calling 1-800-462-3636.

1. XIAFLEX® is supplied in a single-use glass vial containing 0.9 milligrams of a sterile lyophilized powder for reconstitution. Also supplied is a single-use glass vial of sterile diluent. Before use, remove the vial(s) containing the lyophilized powder of XIAFLEX® and the vial(s) containing the diluent for reconstitution from the refrigerator and allow the vials to stand at room temperature for at least 15 minutes and no longer than 60 minutes. Visually inspect the vial(s) containing XIAFLEX®. The cake of lyophilized powder should be intact and white in color.



2. After removal of the flip-off cap from each vial, using aseptic technique swab the rubber stopper and surrounding surface of the vial(s) containing XIAFLEX® and the vial(s) containing the diluent for reconstitution with sterile alcohol (no other antiseptics should be used).



3. 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 that contains 0.01-mL graduations with a 27-gauge, ½-inch needle (not supplied), withdraw a volume of the diluent supplied, as follows:

Volumes Needed for Reconstitution	Cords Affecting an MP Joint	Cords Affecting a PIP Joint
Volume of sterile diluent for reconstitution	0.39 mL	0.31 mL

5. Inject the diluent slowly into the sides of the vial containing the lyophilized powder of XIAFLEX®. Do not invert the vial or shake the solution.
6. Slowly swirl the solution to ensure that all of the lyophilized powder has gone into solution. Do not shake the solution because it can denature the proteins.



IMPORTANT SAFETY INFORMATION FOR XIAFLEX (cont)

- In the controlled portions of the clinical trials in Dupuytren's contracture, 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 in patients with Dupuytren's contracture
- 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 allergic reactions following XIAFLEX injections

Please see additional Important Safety Information throughout.

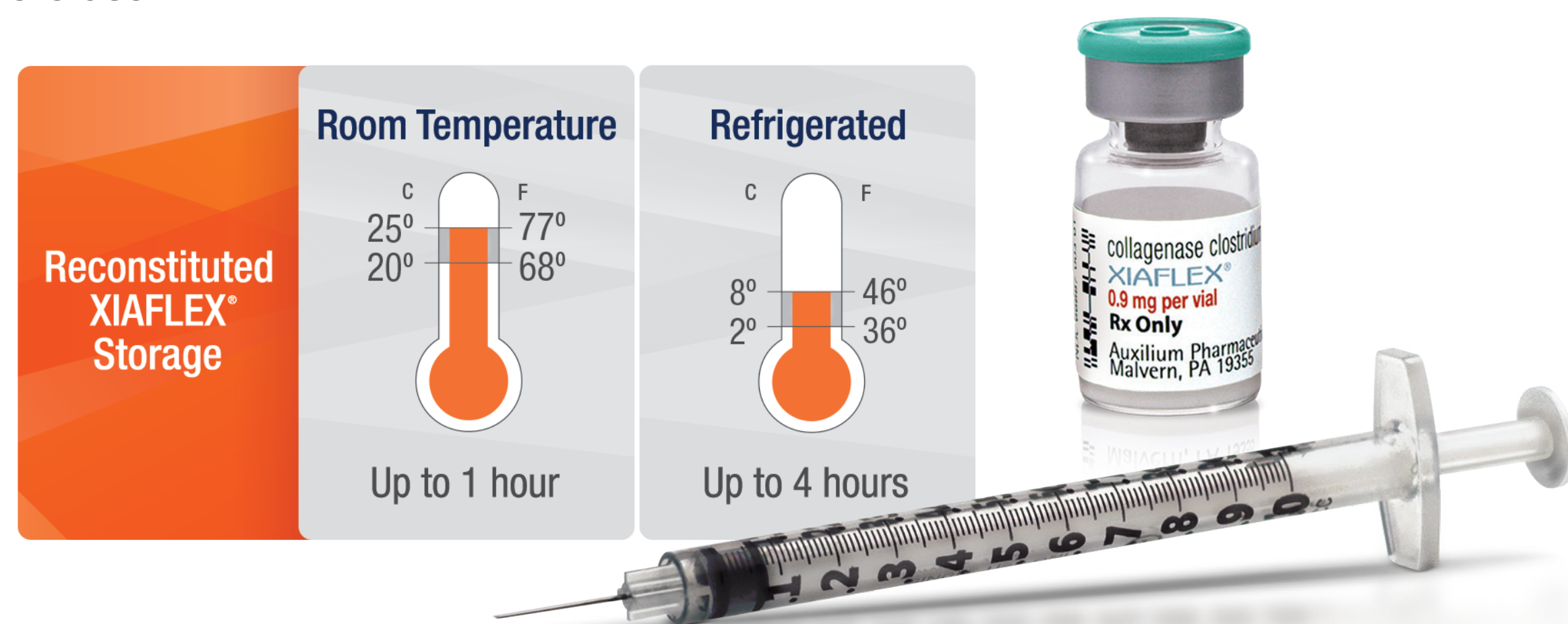
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PREPARATION FOR ADMINISTRATION OF XIAFLEX® (cont)¹

- Each vial of XIAFLEX® and sterile diluent should only be used for a single injection. If administering 2 injections in the same hand during a treatment visit, use a new syringe to reconstitute a second vial of XIAFLEX® with a second vial of diluent. Keep in mind that the second joint could require a different reconstitution volume based on the joint type.
- The solution is now ready for injection. 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 this solution to return to room temperature for approximately 15 minutes before use.



- Discard the syringe(s) and needle(s) used for reconstitution and the diluent vial(s).

IMPORTANT SAFETY INFORMATION FOR XIAFLEX (cont)

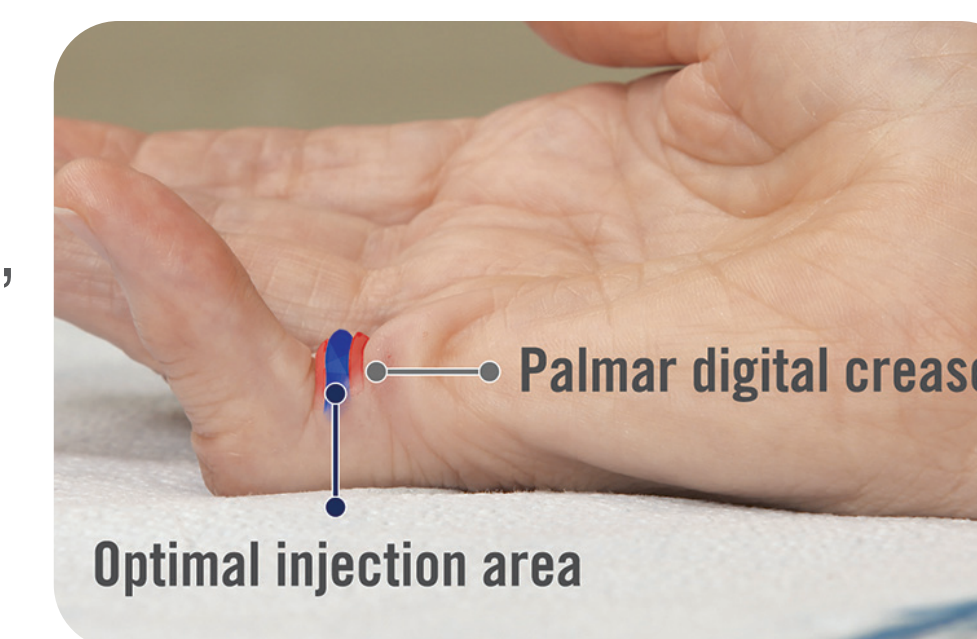
- In the XIAFLEX trials in Dupuytren's contracture, 70% and 38% of XIAFLEX-treated patients developed an ecchymosis/contusion or an injection site hemorrhage, respectively. Patients with abnormal coagulation (except for patients taking low-dose aspirin, eg, up to 150 mg per day) were excluded from participating in these studies. Therefore, the efficacy and safety of XIAFLEX in patients receiving anticoagulant medications (other than low-dose aspirin, eg, up to 150 mg per day) within 7 days prior to XIAFLEX administration is not known. In addition, it is recommended to avoid use of XIAFLEX in patients with coagulation disorders, including patients receiving concomitant anticoagulants (except for low-dose aspirin)
- In the XIAFLEX clinical trials for Dupuytren's contracture, the most common adverse reactions reported in ≥25% of patients treated with XIAFLEX and at an incidence greater than placebo were edema peripheral (eg, swelling of the injected hand), contusion, injection site hemorrhage, injection site reaction, and pain in the injected extremity. Post-marketing experience – Syncope and presyncope have been reported in patients treated with XIAFLEX for Dupuytren's contracture. In some cases, pain from injection and pain during finger extension procedures were identified as potential triggers for syncopal events
- XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method

This section summarizes the preparation of XIAFLEX® prior to injection.

Important Considerations

- Reconfirm the cord and site chosen for injection. It should be the area where the contracting cord is maximally separated from the underlying flexor tendons and where the skin is not adhered intimately to the cord.
- Before injecting, make sure any jewelry on the affected hand has been removed, then prepare the skin with an antiseptic and allow it to dry.
- Administration of a local anesthetic agent prior to injection of XIAFLEX® is not recommended because it may interfere with proper injection placement.

- 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. If particulate matter is detected, report it to Endo Pharmaceuticals Inc. by calling 1-800-462-3636.
- Administration of a local anesthetic agent prior to injection is not recommended, as it may interfere with proper placement of the XIAFLEX® injection.
- If injecting into a cord affecting the PIP joint of the fifth finger, care should be taken to inject as close to the palmar digital crease as possible (as far proximal to the digital PIP joint crease), and the needle insertion should not be more than 2 to 3 mm in depth. Tendon ruptures occurred after XIAFLEX® injections near the digital PIP joint crease (see WARNINGS AND PRECAUTIONS in the FDA-approved Prescribing Information).
- Reconfirm the cord(s) to be injected. The site chosen for each injection should be the area where the contracting cord is maximally separated from the underlying flexor tendons and where the skin is not intimately adhered to the cord.
- Apply an antiseptic at the site(s) of the injection(s) and allow the skin to dry.



Dupuytren's cord affecting the fourth finger



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INJECTION PROCEDURE FOR XIAFLEX®¹

This section outlines the procedure for injecting the reconstituted XIAFLEX® solution into the Dupuytren's cord.

Important Considerations

- 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.
- Patients should be informed that the injection may result in swelling, bruising, bleeding and/or pain at the injection site and surrounding tissue.

1. Using a new 1-mL hubless syringe that contains 0.01-mL graduations with a permanently fixed, 27-gauge, ½-inch needle (not supplied), withdraw a volume of **reconstituted solution (containing 0.58 mg of XIAFLEX®)** as follows:

Volumes Needed for Administration

Cords Affecting an MP Joint

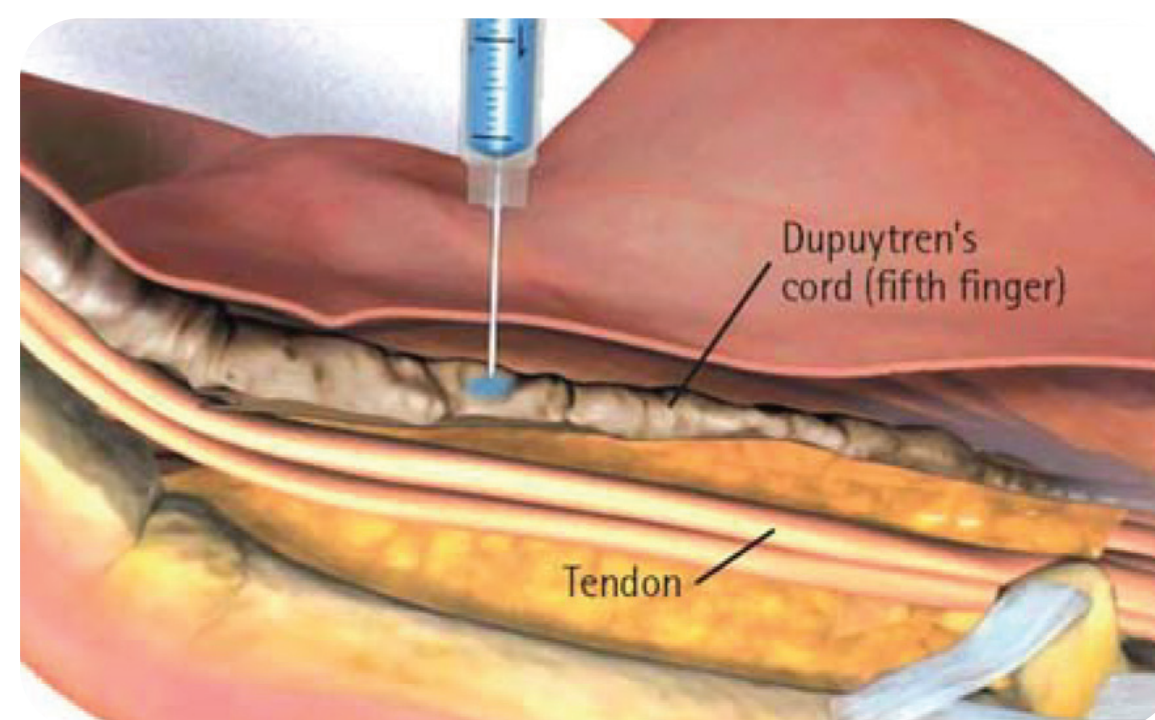
Cords Affecting a PIP Joint

Volume of reconstituted solution to be injected (containing 0.58 mg of XIAFLEX®)

0.25 mL

0.20 mL

2. With your non-dominant hand, secure the patient's hand to be treated while simultaneously applying tension to the cord. With your dominant hand, place the needle into the cord, using caution to keep the needle within the cord. Avoid having the needle tip pass completely through the cord to 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 (DIP) joint. 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 cord.



IMPORTANT SAFETY INFORMATION FOR XIAFLEX (cont)

- In the controlled and uncontrolled portions of clinical trials in Dupuytren's contracture, 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 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 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

3. If the needle is in the proper location, there will be some resistance noted during the injection procedure. After confirming that the needle is correctly placed in the cord, inject approximately one-third of the dose.
4. Next, withdraw the needle tip from the cord and reposition it in a slightly more distal location (approximately 2 to 3 mm) to the initial injection in the cord and inject another one-third of the dose.
5. Again withdraw the needle tip from the cord and reposition it a third time 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 not completely withdrawn from the skin when being repositioned in the cord (approximately 2 to 3 mm to each side of the initial injection).



6. When administering 2 injections in the same hand during a treatment visit, use a new syringe and separate vial of reconstituted solution for each injection. Repeat steps 1 through 5.
7. When administering 2 injections in the same hand during a treatment visit, begin with the affected finger in the most medial aspect of the hand and continue toward the lateral aspect (eg, fifth finger to index finger). When administering 2 injections in a cord affecting 2 joints in the same finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (eg, MP to PIP).
8. Wrap the patient's treated hand with a soft, bulky gauze dressing.
9. Instruct the patient to limit motion of the treated finger(s) and to keep the injected hand elevated until bedtime.
10. Instruct the patient not to attempt to disrupt the injected cord(s) by self-manipulation and to return to the healthcare provider's office the next day for follow-up and a finger extension procedure(s), if needed.
11. Discard the unused portion of the reconstituted solution and diluent after injection. Do not store, pool, or use any vials containing unused reconstituted solution or diluent.



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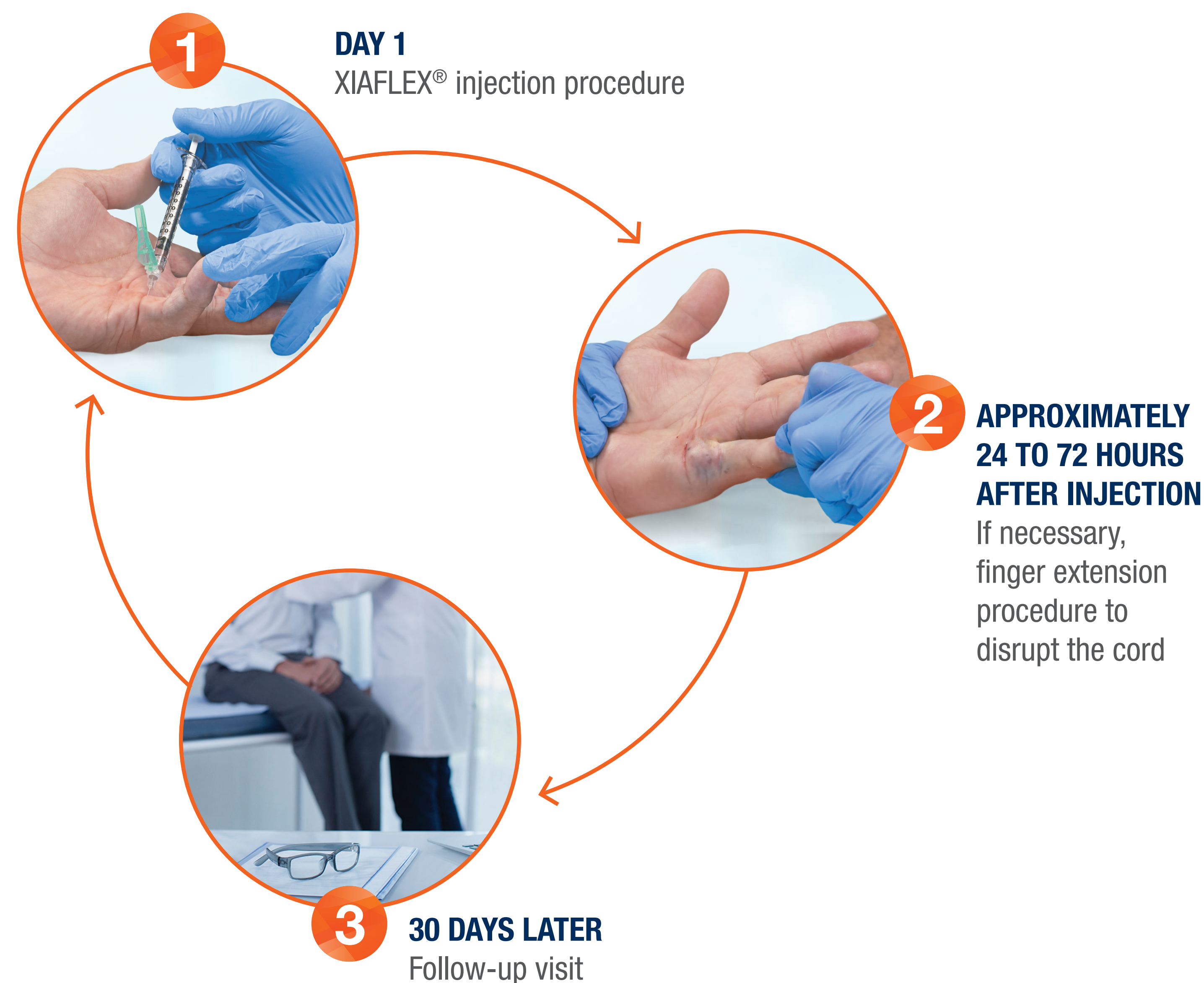
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FINGER EXTENSION PROCEDURE AFTER XIAFLEX® INJECTION¹

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

1. At the follow-up visit approximately 24 to 72 hours after the injection(s), if a contracture remains, perform a passive finger extension procedure on each treated joint (as described below) to facilitate cord disruption. If 2 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.
2. Local anesthesia may be used. Avoid direct pressure on the injection site as it will likely be tender. 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.
3. While the patient's wrist is in the flexed position, apply moderate stretching pressure to the injected cord by extending the finger for approximately 10 to 20 seconds. Do not jerk the finger to attempt to disrupt the cord, as this may contribute to tendon rupture. For cords affecting the PIP joint, perform the finger extension procedure when the MP joint is in the flexed position.
4. If the first finger extension procedure does not result in disruption of the cord, a second and third attempt can be performed at 5- to 10-minute intervals. However, no more than 3 attempts per joint are recommended to disrupt a cord.
5. If the cord has not been disrupted after 3 attempts, a follow-up visit may be scheduled in approximately 4 weeks. If, at that subsequent visit, the contracted cord persists, an additional XIAFLEX® injection with finger extension procedures may be performed.
6. Following the finger extension procedure(s), fit patient with a splint and provide instructions for use at bedtime for up to 4 months to maintain finger extension. Also, instruct the patient to perform finger extension and flexion exercises several times a day for several months. The patient may resume normal activities but should not perform strenuous activities with the injected hand until given permission to do so.



IMPORTANT SAFETY INFORMATION FOR XIAFLEX (cont)

- Other XIAFLEX-associated serious local adverse reactions in the controlled and uncontrolled portions of the clinical studies included pulley rupture, ligament injury, complex regional pain syndrome (CRPS), sensory abnormality of the hand, and skin laceration (tear). 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 premarketing trials (9%). Post-marketing cases of skin laceration requiring skin graft after finger extension procedures and local skin and soft-tissue necrosis, some requiring skin grafting, or other surgical interventions including finger amputation have been reported. Signs or symptoms that may reflect serious injury to the injected finger/hand should be promptly evaluated because surgical intervention may be required.
- In the controlled portions of the clinical trials in Dupuytren's contracture, 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 in patients with Dupuytren's contracture.

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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 degrees to 5 degrees after up to 3 injections.¹

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

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

IMPORTANT SAFETY INFORMATION FOR XIAFLEX

- 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 in Dupuytren's contracture, 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 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 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
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- 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 allergic reactions following XIAFLEX injections
- In the XIAFLEX trials in Dupuytren's contracture, 70% and 38% of XIAFLEX-treated patients developed an ecchymosis/contusion or an injection site hemorrhage, respectively. Patients with abnormal coagulation (except for patients taking low-dose aspirin, eg, up to 150 mg per day) were excluded from participating in these studies. Therefore, the efficacy and safety of XIAFLEX in patients receiving anticoagulant medications (other than low-dose aspirin, eg, up to 150 mg per day) within 7 days prior to XIAFLEX administration is not known. In addition, it is recommended to avoid use of XIAFLEX in patients with coagulation disorders, including patients receiving concomitant anticoagulants (except for low-dose aspirin)
- In the XIAFLEX clinical trials for Dupuytren's contracture, the most common adverse reactions reported in $\geq 25\%$ of patients treated with XIAFLEX and at an incidence greater than placebo were edema peripheral (eg, swelling of the injected hand), contusion, injection site hemorrhage, injection site reaction, and pain in the injected extremity. Post-marketing experience – Syncope and presyncope have been reported in patients treated with XIAFLEX for Dupuytren's contracture. In some cases, pain from injection and pain during finger extension procedures were identified as potential triggers for syncopal events

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FREQUENTLY ASKED QUESTIONS

1. What are the risks of XIAFLEX® use in the treatment of Dupuytren's contracture?

In the controlled and uncontrolled portions of clinical trials in Dupuytren's contracture, 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 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, 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.¹

Because XIAFLEX® contains foreign proteins, severe allergic reactions to XIAFLEX® can occur. Anaphylaxis was reported in a post-marketing clinical study 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.¹

2. 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.¹

3. Were there any allergic reactions to XIAFLEX®?

Anaphylaxis was reported in a post-marketing clinical study 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.¹

In the controlled portions of the clinical trials in Dupuytren's contracture, 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 in patients with Dupuytren's contracture.¹

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

You should read the full 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 affecting the PIP joint of the fifth finger, and other serious adverse events of the injected extremity. Secondly, provide a Medication Guide 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 full Prescribing Information, including the Medication Guide, will be included in the product packaging and can also be found at XIAFLEX.com. For additional information, visit 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: the Endo Medical Information Call Center at 1-800-462-3636 or the FDA MedWatch reporting system by telephone (1-800-FDA-1088), fax (1-800-FDA-0178), or online (www.fda.gov/medwatch).

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ACCESS TO XIAFLEX® FOR THE TREATMENT OF DUPUYTREN'S CONTRACTURE WITH A PALPABLE CORD

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

Upon completion of this training, the enrollment process consists of 2 steps:

1. Complete, sign, and fax or mail the Healthcare Provider Enrollment Form to be able to order XIAFLEX®.
2. Complete, sign, and fax or mail the Site Enrollment Form to register site(s) for shipping.

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 Endo Medical Information Call Center at 1-800-462-3636. To report adverse events, please contact either of the following:

- Endo Medical Information Call Center at 1-800-462-3636
- FDA MedWatch reporting system by telephone (1-800-FDA-1088), fax (1-800-FDA-0178), online (www.fda.gov/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

Visit XIAFLEX.com/XTRA

to access and complete the Managed Distribution Enrollment Forms.

IMPORTANT SAFETY INFORMATION FOR XIAFLEX

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

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References: 1. XIAFLEX® [package insert]. Malvern, PA: Endo Pharmaceuticals Inc. 2. Feldman G, Rozen N, Rubin G. Dupuytren's contracture: current treatment methods. *Isr Med Assoc J.* 2017;19(10):648-650.

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