

MEDICATION GUIDE
XIAFLEX® (Zī a flex)
(collagenase clostridium histolyticum)
For injection, for intralesional use

XIAFLEX is approved for two uses: Dupuytren's contracture and Peyronie's disease. Information is provided separately for each use. Use for treating Dupuytren's contracture is described first, followed by use for treating.

Read this Medication Guide before you receive XIAFLEX for the treatment of Dupuytren's contracture and each time you get an injection. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about XIAFLEX for the treatment of Dupuytren's contracture?

XIAFLEX may cause serious side effects, including:

- 1. Tendon rupture or ligament damage.** Receiving an injection of XIAFLEX may cause damage to a tendon or ligament in your hand and cause it to break or weaken. This could require surgery to fix the damaged tendon or ligament. Call your healthcare provider right away if you have trouble bending your injected finger (towards the wrist) after the swelling goes down or you have problems using your treated hand after your follow-up visit.
- 2. Nerve injury or other serious injury of the hand.** After finger procedures, some people developed tears in the skin (lacerations), and local skin and soft-tissue necrosis (death of skin cells). Some lacerations and necrosis required skin grafting, or other surgery including amputation. Call your healthcare provider right away if you get numbness, tingling, increased pain, or tears in the skin (laceration) in your treated finger or hand after your injection or after your follow-up visit.
- 3. Hypersensitivity reactions, including anaphylaxis.** Severe allergic reactions can happen in people who receive XIAFLEX, because it contains foreign proteins.
Call your healthcare provider right away if you have any of these symptoms of an allergic reaction after an injection of XIAFLEX:
 - hives
 - chest pain
 - swollen face
 - low blood pressure
 - breathing trouble
 - dizziness or fainting
- 4. Fainting:** Fainting or near fainting can happen in people who receive XIAFLEX, especially following finger procedures.
If you have dizziness or feel faint after receiving XIAFLEX, lie down until the symptoms go away.

What is XIAFLEX?

XIAFLEX is a prescription medicine used to treat adults with Dupuytren's contracture when a "cord" can be felt. It is not known if XIAFLEX is safe and effective in children under the age of 18.

Who should not receive XIAFLEX?

Do not receive XIAFLEX if you:

- are allergic to collagenase clostridium histolyticum, or any of the ingredients in XIAFLEX, or to any other collagenase product. See the end of this Medication Guide for a complete List of Ingredients in XIAFLEX.

Talk to your healthcare provider before receiving this medicine if you have any of these conditions.

What should I tell my healthcare provider before receiving XIAFLEX?

Before receiving XIAFLEX, tell your healthcare provider if you:

- have had an allergic reaction to a XIAFLEX injection in the past
- have a bleeding problem
- have received XIAFLEX to treat another condition
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if XIAFLEX will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if XIAFLEX passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you receive XIAFLEX.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Using XIAFLEX with certain other medicines can cause serious side effects.

Especially tell your healthcare provider if you take:

- medicines to thin your blood (anticoagulants). 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.

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How will I receive XIAFLEX?

- XIAFLEX should be injected into a cord by a healthcare provider who is experienced in injection procedures of the hand and treating people with Dupuytren's contracture. If you have more than 1 contracture, your healthcare provider may give you 2 injections in 1 of your hands during your visit.
- Your healthcare provider will inject XIAFLEX into the cord that is causing your finger to bend.
- After an injection of XIAFLEX, your affected hand will be wrapped with a bandage. You should limit moving and using the treated finger after the injection.
 - Do not bend or straighten the fingers of the injected hand until your healthcare provider says it is okay. This will help to keep the medicine from leaking out of the cord.
 - Do not try to straighten the treated finger yourself.
 - Keep the injected hand elevated until bedtime.
- **Call your healthcare provider right away if you have:**
 - signs of infection after your injection, such as fever, chills, increased redness, or swelling
 - numbness or tingling in the treated finger
 - trouble bending the injected finger after the swelling goes down
- Return to your healthcare provider's office as directed 1 to 3 days after your injection. During this first follow-up visit, if you still have the cord, your healthcare provider may try to extend the treated finger to "break" the cord and try to straighten your finger.
- Your healthcare provider will provide you with a splint to wear on the treated finger. Wear the splint as instructed by your healthcare provider at bedtime to keep your finger straight.
- Do finger exercises each day, as instructed by your healthcare provider.
- Follow your healthcare provider's instructions about when you can start doing your normal activities with the injected hand.

What are the possible side effects of XIAFLEX?

XIAFLEX may cause serious side effects, including:

- **See "What is the most important information I should know about XIAFLEX for the treatment of Dupuytren's contracture?"**
- increased chance of bleeding. Bleeding or bruising at the injection site can happen in people who receive XIAFLEX. Talk to your healthcare provider if you have a problem with your blood clotting. XIAFLEX may not be right for you.

The most common side effects with XIAFLEX for the treatment of Dupuytren's contracture include:

- swelling of the injection site or the hand
- bruising or bleeding at the injection site
- pain or tenderness of the injection site or the hand
- swelling of the lymph nodes (glands) in the elbow or armpit (axilla)
- itching
- breaks in the skin
- redness or warmth of the skin
- pain in the armpit

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects with XIAFLEX. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of XIAFLEX.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about XIAFLEX. If you would like more information, talk to your healthcare provider. You can ask your healthcare provider or pharmacist for information about XIAFLEX that is written for health professionals.

For more information, go to www.XIAFLEX.com or call 1-800-462-3636.

What are the ingredients in XIAFLEX?

Active ingredient: collagenase clostridium histolyticum

Inactive ingredients: hydrochloric acid, sucrose, and tromethamine. The diluent contains: calcium chloride dihydrate in 0.9% sodium chloride

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:

Endo Biologics Limited
Dublin, Ireland D15 TX2V

US License No. 1816

US Patent Nos. 7,811,560 and 6,022,539

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XIAFLEX® (Zī a flex)
(collagenase clostridium histolyticum)
For injection, for intralesional use

XIAFLEX is approved for two uses: Dupuytren's contracture and Peyronie's disease. Information is provided separately for each use. Use for treating **Dupuytren's contracture** is described on the previous pages, and use for treating Peyronie's disease is described below.

Read this Medication Guide before you receive XIAFLEX for the treatment of Peyronie's disease and each time you get an injection. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment.

Your healthcare provider will also talk to you about receiving XIAFLEX for the treatment of Peyronie's disease using the "**What You Need to Know About XIAFLEX Treatment for Peyronie's Disease: A Patient Guide**". You can ask your healthcare provider for a copy of the Patient Guide.

What is the most important information I should know about XIAFLEX for the treatment of Peyronie's Disease?

XIAFLEX can cause serious side effects, including:

1. **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 a corporal rupture.
 - After treatment with XIAFLEX, 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. If a hematoma appears, you may also develop skin and soft tissue necrosis (death of skin cells) which could require surgery.

Symptoms of corporal rupture or other serious injury to your penis may include:

- a popping sound or sensation in an erect penis
- sudden loss of the ability to maintain an erection
- pain in your penis
- purple bruising and swelling of your penis
- difficulty urinating or blood in the urine

Call your healthcare provider right away if you have any of the symptoms of corporal rupture or serious injury to the penis listed above.

Do not have sex or any other sexual activity between the first and second injections of a treatment cycle.

Do not have sex or have any other sexual activity for at least 4 weeks after the second injection of a treatment cycle with XIAFLEX and after any pain and swelling has gone away.

XIAFLEX for the treatment of Peyronie's disease is only available through a restricted program called the XIAFLEX Risk Evaluation and Mitigation Strategy (REMS) Program. For more information about the XIAFLEX REMS Program go to www.XIAFLEXREMS.com or call 1-877-313-1235.

2. **Hypersensitivity reactions, including anaphylaxis.** Severe allergic reactions can happen in people who receive XIAFLEX, because it contains foreign proteins.
Call your healthcare provider right away if you have any of these symptoms of an allergic reaction after an injection of XIAFLEX:

- hives
- chest pain
- swollen face
- low blood pressure
- breathing trouble
- dizziness or fainting

3. **Back pain reactions.** After receiving an injection of XIAFLEX for Peyronie's disease, you may suddenly feel back pain, including severe lower back pain moving to your legs, feet, chest and arms. The back pain may also include spasms and make it hard to walk. These symptoms usually go away in 15 minutes or less but may last longer.

Tell your healthcare provider right away if you have sudden back pain, chest pain, or have a hard time walking after an injection.

4. **Fainting:** Fainting or near fainting can happen in people who receive XIAFLEX, especially if they have severe penile pain.

If you have dizziness or feel faint after receiving XIAFLEX, lie down until the symptoms go away.

What is XIAFLEX?

XIAFLEX is a prescription medicine used to treat adult men with Peyronie's disease who have a "plaque" that can be felt and a curve in their penis greater than 30 degrees when treatment is started.

It is not known if XIAFLEX is safe and effective in children under the age of 18.

Who should not receive XIAFLEX?

Do not receive XIAFLEX if you:

- have been told by your healthcare provider that the Peyronie's plaque to be treated involves the "tube" that your urine passes through (urethra).
- are allergic to collagenase clostridium histolyticum, or any of the ingredients in XIAFLEX, or to any other collagenase product. See the end of this Medication Guide for a complete List of Ingredients in XIAFLEX.

Talk to your healthcare provider before receiving this medicine if you have any of these conditions.

What should I tell my healthcare provider before receiving XIAFLEX?

Before receiving XIAFLEX, tell your healthcare provider if you:

- have had an allergic reaction to a XIAFLEX injection in the past
- have a bleeding problem
- have received XIAFLEX to treat another condition
- have any other medical conditions

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Using XIAFLEX with certain other medicines can cause serious side effects.

Especially tell your healthcare provider if you take:

- medicines to thin your blood (anticoagulants). If you are told to stop taking a blood thinner before your XIAFLEX injection, your healthcare provider should tell you when to start taking the blood thinner again.

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How will I receive XIAFLEX?

- XIAFLEX should be injected into the plaque by a healthcare provider who is trained and experienced in treating adult men with Peyronie's disease.
- Your healthcare provider will inject XIAFLEX into the plaque that is causing your penis to curve.
- XIAFLEX is given as part of a treatment cycle. In each treatment cycle, you will receive an injection of XIAFLEX, followed by a second injection 1 to 3 days later.
- After each injection of XIAFLEX, your penis may be wrapped with a bandage. Your healthcare provider will tell you when to take the bandage off.
- 1 to 3 days after your second injection of XIAFLEX in a treatment cycle, you will need to return to your healthcare provider's office for a manual procedure that will stretch and help straighten your penis. Your healthcare provider will tell you when to come back for this.
- Your healthcare provider will show you how to gently stretch your penis the right way. See "How to gently stretch your penis."
- You should gently stretch your penis 3 times a day for 6 weeks after each treatment cycle. **You should only gently stretch your penis when you do not have an erection.**
- Your healthcare provider will show you how to gently straighten your penis the right way. See "How to gently straighten your penis."
- You should gently straighten your penis 1 time a day for 6 weeks after each treatment cycle. **You should only gently straighten your penis if you have an erection that happens without any sexual activity (spontaneous erection).**
- **Do not use a vacuum erection device during your treatment with XIAFLEX.**
- Your healthcare provider will tell you when you can resume sexual activity after each treatment cycle.
- Your healthcare provider will also tell you when to come back if more treatment cycles are needed.

Tell your healthcare provider right away if you have trouble stretching or straightening your penis, or if you have pain or other concerns.

How to gently stretch your penis:

Gently stretch your penis 3 times a day. Only stretch your penis if your penis is not hard (erect).

- With 1 hand, hold the tip of your penis with your fingers. With your other hand, hold the base of your penis with your fingers (See Figure A)
- Gently pull your penis away from your body to its full length and hold the stretch for 30 seconds.
- Let go of the tip of your penis and let your penis return to its normal length.



(Figure A)

How to gently straighten your penis:

Gently straighten your penis 1 time a day. Only straighten your penis if you have an erection that happens without any sexual activity (spontaneous erection). Bending your penis should not cause any pain or discomfort.

- With 1 hand hold your penis. With your other hand, gently bend your penis in the opposite direction of the curve (See Figure B). Hold the penis in this more straightened position for 30 seconds, then let go.



(Figure B)

What should I avoid while receiving XIAFLEX?

Avoid situations that may cause you to strain your stomach (abdominal) muscles, such as straining during bowel movements.

What are the possible side effects of XIAFLEX?

XIAFLEX can cause serious side effects, including:

See “What is the most important information I should know about XIAFLEX for the treatment of Peyronie’s Disease?”

- **increased chance of bleeding.** Bleeding or bruising at the injection site can happen in people who receive XIAFLEX. Talk to your healthcare provider if you have a problem with your blood clotting. XIAFLEX may not be right for you.

The most common side effects with XIAFLEX for the treatment of Peyronie’s disease include:

- a small collection of blood under the skin at the injection site (hematoma)
- swelling at the injection site or along your penis
- pain or tenderness at the injection site, along your penis and above your penis
- penis bruising
- itching of your penis or scrotum (genitals)
- painful erection
- erection problems (erectile dysfunction)
- changes in the color of the skin of your penis
- blisters at the injection site
- pain with sex
- a lump at the injection site (nodule)

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects with XIAFLEX. For more information, ask your healthcare provider or pharmacist.

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