

XIAFLEX®

(Zi-a-flex)

FOR DUPUYTREN'S CONTRACTURE

Collagenase clostridium histolyticum - 900 micrograms powder and diluent for solution for injection.

Consumer Medicine Information

What is in this leaflet

This leaflet answers some common questions about XIAFLEX.

It does not contain all the available information.

It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you having XIAFLEX against the benefits they expect it will have.

If you have any concerns about this injection, ask your doctor, nurse or pharmacist.

Keep this leaflet.

You may need to read it again.

What XIAFLEX is used for

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

Dupuytren's contracture is a disease that causes your finger(s) to bend inward. This bending is called a contracture and is caused by the abnormal formation of a cord(s) containing collagen under your skin.

For many people, a contracture causes significant difficulties with performing everyday tasks like driving, shaking hands, playing sports, opening jars, typing or holding objects.

How it works

XIAFLEX is injected directly into the palpable cord(s) by your doctor and works by breaking down the collagen in the cord(s) and thereby helps to remove the cause of your contracture so that your finger(s) can straighten.

The active substance is collagenase clostridium histolyticum, and is naturally produced by a bacterium named *Clostridium histolyticum*.

Before you are given XIAFLEX

Do not use XIAFLEX if:

1. You have an allergy to collagenase clostridium histolyticum or any of the ingredients listed at the end of this leaflet.

Please consult a doctor immediately if you experience any signs or symptoms of a serious allergic reaction:

- wide spread redness or rash,
 - swelling
 - tightness in the throat or difficulty breathing
 - chest pain.
2. You have taken anticoagulation medicine within the last 7 days.

One exception is the use of up to 150mg daily dose of acetylsalicylic acid (also called aspirin, a substance present in many medicines used to prevent blood clotting) which can be taken.

Do not use XIAFLEX in children under 18 years of age. There is not enough information at present to recommend use of XIAFLEX in children.

Do not use XIAFLEX after the expiry date printed on the pack.

Do not use XIAFLEX if the packaging is torn or shows signs of tampering.

If you are not sure whether you should have XIAFLEX, talk to your doctor or pharmacist.

Before you are given this medicine, tell your doctor:

- if you are pregnant or intend to become pregnant.

There is no experience in the use of XIAFLEX in pregnant women therefore the use of XIAFLEX is not recommended in pregnancy, and treatment should be postponed until after pregnancy.

- if you are breastfeeding
- if you have any allergies to any other medicines, any other substances, such as foods, preservatives or dyes
- if you have had an allergic reaction to a previous XIAFLEX injection
- if you have a history of problems with the normal clotting of your blood or if you are taking any medicines to help control the normal clotting of your blood (known as anticoagulation medicines)
- if you are taking or have recently taken anthracyclines/ anthraquinone derivatives such as doxorubicin and some tetracycline antibiotics such as doxycycline used to treat infections

If you have not told your doctor about any of the above, tell them before you start using XIAFLEX.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines, including any that you buy without a

prescription from your pharmacy, supermarket or health food shop.

Some medicines and XIAFLEX may interfere with each other.

Tell your doctor or pharmacist if you are using any medicine to thin your blood such as warfarin, clopidogrel or dabigatran. Some people refer to anticoagulation medicine as "blood thinners". If you are not sure, please check with your doctor or pharmacist.

XIAFLEX must not be given within 7 days of the last dose of your anticoagulation medicine, One exception is the use of up to 150mg daily dose of acetylsalicylic acid (also called aspirin, a substance present in many medicines used to prevent blood clotting) which can be taken.

Tell your doctor or pharmacist if you are taking or have recently taken anthracyclines/ anthraquinone derivatives such as doxorubicin, and some tetracycline antibiotics such as doxycycline used to treat infections. XIAFLEX should not be given within 14 days of receiving tetracycline antibiotics.

These medicines may be affected by XIAFLEX, or may affect how well it works. (You may need different amounts of these medicines, or you may need to take different medicines.) Your doctor or pharmacist will advise you and decide whether or not to give the Injection.

How XIAFLEX is given

Your doctor will perform all injections of XIAFLEX. XIAFLEX should only be used by an approved practitioner

who will be able to display (or show you) such an authorisation.

This medicine must only be injected into the collagen cord in your hand by your doctor. Up to two cords or two affected joints in the same hand can be injected at the same time during a treatment 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.

Your doctor will take care to avoid injecting into tendons, nerves or blood vessels.

Incorrect injection into tendons, nerves or blood vessels may result in bleeding or damage and possible permanent injury to these structures.

If your cord(s) to be treated is attached to the skin, you are at higher risk of the skin splitting or tearing during the finger(s) extension procedure following the injection of XIAFLEX. This will usually be treated by applying a dressing. In severe cases a skin graft may be required.

How much is given

Each vial of XIAFLEX and sterile solvent for reconstitution should only be used for a single injection. If cords of two affected 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.

The recommended dose of your prescribed medicine is 0.58mg.

The total volume of the injection depends on the joint(s) being treated.

Your doctor will carefully select an area where the collagen cord(s) is best accessible and will proceed with the injection into the cord(s).

If you take too much (overdose)

As this product is administered to you by your doctor it is very unlikely that you will be given an incorrect dosage. In the unlikely event that your doctor administers a higher dosage than recommended, you may experience an increase in the severity of possible side effects especially reactions at the injection site listed under "Side Effects" in this Leaflet.

You can telephone your doctor or the Poisons Information Centre on 13 11 26 for advice on overdose management.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

Clinical study experience with XIAFLEX is currently limited to up to 3 injections per cord at approximately 4 weeks interval.

After having XIAFLEX

Things you must do

Be sure to ask your doctor when you can resume normal activities after treatment with XIAFLEX.

After the injection, your doctor will place a dressing on your hand. You must limit motion of the treated finger(s) for a day and it is not uncommon for the finger(s) to straighten on its own for some patients.

Until advised by your doctor, do not flex or extend the fingers of the injected hand.

Do not attempt to disrupt the injected cord(s) by self-manipulation at any time.

Elevate the injected hand as much as possible until bedtime.

Your doctor will ask you to return 24 to 72 hours after your injection to attempt to extend your finger(s) to straighten it.

Following extension of your finger, your doctor will fit you with a splint to wear at bedtime for up to 4 months.

It is recommended to avoid strenuous activities of your treated hand until instructed further by your doctor.

Your doctor may recommend you perform a series of finger flexion and extension exercises several times a day for several months when you are ready.

Keep follow-up appointments with your doctor.

If your finger(s) is/are still not able to straighten during a follow-up visit with your doctor, you may need additional treatments with XIAFLEX which may be administered approximately 4 weeks after the first treatment.

Injections and finger extension procedures may be administered up to 3 times per cord at approximately 4-week intervals.

If the disease has resulted in multiple contractures, additional cords maybe treated at other treatment visits approximately 4 weeks apart as determined by your doctor.

Tell your doctor immediately if:

- symptoms of infection (fever, chills, increased redness or swelling) appear
- symptoms of tendon rupture (trouble bending the finger after swelling goes down or altered sensation in the treated finger) appear.

Tell your doctor if symptoms of musculoskeletal syndrome (joint or muscle pain, joint stiffness, shoulder stiffness, hand swelling, fibrosis of the palms, and thickening or nodule forming of tendons) appear.

Serious allergic reactions and musculoskeletal syndrome are rare but serious side effects which require immediate medical attention.

Things to be careful of

Be careful driving or operating machinery until you know how XIAFLEX affects you.

Swelling and pain which may impair the use of the treated hand and dizziness, numbness or altered sensation, and headache have been reported as side effects immediately after injection of XIAFLEX.

You must avoid potentially hazardous tasks such as driving or using machines until it is safe to do so or as advised by your doctor.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well after having XIAFLEX.

Like all medicines, XIAFLEX can cause side effects, although not everybody gets them.

Most of the side effects that occurred in the clinical studies were mild or moderate in severity and were localised to the hand treated.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor or pharmacist if you notice any of the following and they worry you:

Very common:

- reactions at the injection site like bleeding, pain, swelling, tenderness and bruising
- itching in the hand or skin
- feeling of pain in the hand, wrist or arm
- swollen or enlarged glands near the elbow or under the arm
- swelling in the hand or arm
- blood blister
- skin wound at the site of injection.

Common side effects:

- reactions at the injection site like itching, presence of a blister
- skin discolouration, possible bruising
- painful glands near the elbows or under the arm
- joint swelling and pain
- muscle pain or stiffness
- burning sensation, partial loss of sensitivity, feeling of "pins and needles" or numbness
- dizziness, headache, nausea.

These are the more common side effects of XIAFLEX. Mostly these are mild and short-lived.

Do not be alarmed by this list of possible side effects.

You may not experience any of them.

This is not a complete list of all possible side-effects. Others may occur in some people and there may be some side-effects not yet known.

You may experience serious side effects which need urgent medical attention. Serious side effects are rare.

If any of the following happen, tell your doctor immediately or go to Accident and Emergency at your nearest hospital:

- sudden signs of allergy such as:
 - widespread redness or rash
 - swelling of the face, lips, throat or other parts of the body
 - tightness in the chest, shortness of breath or difficulty breathing.

Contact your doctor if you have trouble bending the injected finger(s) after the swelling has subsided as it may be a symptom of tendon rupture.

These are very serious side effects. You may need urgent medical attention or hospitalisation.

As with any non-human protein medical product, the potential long term risk of autoimmune disease cannot be excluded.

All of these side effects are rare.

Other side effects not listed above may occur in some patients. Tell your doctor or pharmacist if you notice anything that is making you feel unwell.

Storing XIAFLEX

XIAFLEX is usually stored in the doctor's surgery or clinic, or at the pharmacy. However, if you need to store XIAFLEX at home:

- **Keep out of the reach and sight of children.**
- **Keep XIAFLEX in the original pack until it is time for it to be given.**
- **Keep it in the refrigerator, between 2°C and 8°C. Do not freeze XIAFLEX.**

After reconstitution, the medicine can be used immediately. Alternatively, reconstituted XIAFLEX can be kept at ambient room temperature (20°C-25°C) for up to one hour or refrigerated at 2°C-8°C for up to 4 hours prior to administration. If refrigerated, the reconstituted solution must be allowed to return to ambient room temperature (20°C-25°C) for approximately 15 minutes before use.

Your doctor must not use XIAFLEX if the reconstituted solution is discoloured or contains particles.

The reconstituted solution must be clear, colourless with no lumps or flakes or particles.

Your doctor will take care of storing, handling and disposing of XIAFLEX. Medicines must not be disposed of via wastewater or household waste. These measures will help to protect the environment.

Product description

What it looks like

XIAFLEX is supplied as a white powder in a 3 mL clear glass vial with rubber stopper, aluminium seal and flip-off plastic cap.

The 3 mL diluent that is used to dissolve the powder is supplied as a clear liquid in a 5 mL clear glass vial with rubber stopper, aluminium seal and flip-off plastic cap.

XIAFLEX is supplied in a single use pack containing 1 vial of XIAFLEX powder and 1 vial of 3 mL diluent.

Ingredients

Each vial of XIAFLEX 900 micrograms Powder contains:

Active ingredients:

collagenase clostridium histolyticum

Inactive ingredients:

sucrose, trometamol, hydrochloric acid.

Each vial of Diluent contains:

Ingredients

calcium chloride, sodium chloride, water for injection

Manufacturer/Distributor/ Supplier

XIAFLEX is supplied in Australia by Actelion
Pharmaceuticals Australia Pty Ltd.

Suite 6/13b Narabang Way

BELROSE NSW 2085

Australian Registration Number:

XIAFLEX - AUST R 199584

XIAFLEX is supplied in New Zealand by

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This leaflet was prepared in November 2017.