

PACKAGE LEAFLET: INFORMATION FOR THE USER

Xiapex 0.9 mg powder and solvent for solution for injection collagenase clostridium histolyticum

Read all of this leaflet carefully before you are given this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you and must only be administered by your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Xiapex is and what it is used for
2. Before you are given Xiapex
3. How Xiapex is administered
4. Possible side effects
5. How to store Xiapex
6. Further information

1. WHAT XIAPEX IS AND WHAT IT IS USED FOR

Xiapex 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 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.

The active substance is collagenase *clostridium histolyticum*, and is naturally produced by a bacterium named *Clostridium histolyticum*. Xiapex is injected into this cord by your doctor and works by breaking down the collagen in the cord and thereby helps to remove the cause of your contracture so that your finger(s) can straighten.

2. BEFORE YOU ARE GIVEN XIAPEX

You must not be given Xiapex

If you are allergic (hypersensitive) to collagenase *clostridium histolyticum* or any of the other ingredients of Xiapex (see section 6 'further information' for a full list of ingredients).

Take special care with Xiapex

This medicine must only be injected into the collagen cord in your hand by your doctor. 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 to be treated is attached to the skin, you are at higher risk of the skin splitting or tearing during the finger extension procedure following the injection of Xiapex.

No evidence of an increased risk of serious allergic reactions or the development of a musculoskeletal syndrome upon repeated use of Xiapex has been demonstrated. However the potential for such adverse reactions to occur cannot be excluded. The symptoms of musculoskeletal syndrome could be joint or muscle pain, shoulder stiffness, hand swelling, fibrosis of the palms, and thickening or nodule forming of tendons. If you notice such symptoms you should inform your doctor.

Before you are given this medicine, make sure your doctor knows:

- 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 currently taking any anticoagulation medicines, you must not receive Xiapex within 7 days of last dose of your anticoagulation medicine. One exception is the use of up to 150 mg daily dose of acetylsalicylic acid (a substance present in many medicines used to prevent blood clotting) which can be taken.

Children

Xiapex has not been tested in children, therefore the use in children aged 0-18 years is not recommended.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines to help control the normal clotting of your blood (known as anticoagulation medicines), anthraquinone derivatives, some antibiotics (tetracyclines and anthracyclines/anthraquinolones) used to treat infections and those medicines obtained without a prescription.

Pregnancy and breast-feeding

Please tell your doctor if you are pregnant or if you are planning to become pregnant. There is no experience in the use of Xiapex in pregnant women therefore the use of Xiapex is not recommended in pregnancy, and treatment should be postponed until after pregnancy.

Xiapex can be used during breast-feeding.

Driving and using machines

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 Xiapex. 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.

Important information about some of the ingredients of Xiapex

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially 'sodium-free'.

3. HOW XIAPEX IS ADMINISTERED

Your doctor will perform all injections of Xiapex.

The recommended dose of your prescribed medicine is 0.58 mg.

The total volume of the injection depends on the joint being treated. Your doctor will carefully select an area where the collagen cord is best accessible and will proceed with the injection into the cord.

After the injection, your doctor will place a dressing on your hand. You must limit motion of the treated finger for a day and it is not uncommon for the finger 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 by self manipulation at any time. Elevate the injected hand as much as possible until the day after the finger extension procedure.

Your doctor will ask you to return the day after your injection to attempt to extend your finger 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.

If your finger is still not able to straighten during a follow-up visit with your doctor, you may need additional treatments with Xiapex 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. Only one cord must be treated at a time. If the disease has resulted in multiple contractures, treatment of each cord must be undertaken in a sequential order, as determined by your doctor.

Be sure to ask your doctor when you can resume normal activities after treatment with Xiapex. It is recommended to avoid strenuous activities of your finger 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.

If you receive more Xiapex than you should

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 listed in section 4 “Possible Side Effects” of this Package Leaflet.

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

Clinical study experience with Xiapex is currently limited to up to 3 injections per cord and up to a total of 8 injections in the hands.

4. POSSIBLE SIDE EFFECTS

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

Please consult a doctor immediately if you experience any signs or symptoms of a serious allergic reaction, e.g., wide spread redness or rash, swelling, tightness in the throat or difficulty breathing. **You must not be given Xiapex** if you know that you have had a serious allergic reaction to collagenase or any of the other ingredients.

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

The following side effects have been seen with Xiapex:

Very common side effects: affects more than 1 user in 10:

- reactions at the injection site like bleeding, pain, swelling, tenderness and bruising
- itching in the hand
- 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

Common side effects: affects 1 to 10 users in 100:

- reactions at the injection site like pain, warmth, swelling, presence of a blister, redness of skin and/or skin rash
- skin wound at the site of injection
- painful glands near the elbows or under the arm
- joint swelling and pain
- burning sensation, partial loss of sensitivity, feeling of “pins and needles” or numbness
- dizziness, headache, nausea
- increased perspiration

Uncommon side effects: affects 1 to 10 users in 1000:

- rupture of a tendon, ligament injury
- low blood platelet count
- swelling of the eyelid
- allergic reaction
- chronic pain
- discomfort, injury, paralysis of the limb
- tremor/shaking
- fainting
- vomiting, diarrhoea, upper abdominal pain
- rash, eczema
- stiffness, creaking of the joints
- muscle spasm, muscle weakness, musculoskeletal stiffness or discomfort
- feeling of pain in the groin, shoulder, chest wall, or neck
- swelling
- fever, general pain, discomfort, tiredness, feeling hot, malaise, flu-like illness
- reactions at the site of injection including peeling of the skin, skin discoloration, infection, pain, skin tightness, numbness, irritation or nodules, scab, wound
- increased liver enzymes
- agitation, disorientation, irritability, restlessness, difficulty sleeping
- shortness of breath, hyperventilation

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE XIAPEX

Keep out of the reach and sight of children.

Your doctor must not use Xiapex after the expiry date which is stated on the carton and vial label after EXP. The expiry date refers to the last day of that month.

Xiapex has to be stored in a refrigerator at 2°C-8°C and should not be frozen.

After reconstitution, immediate use of the medicine is recommended. Reconstituted Xiapex 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 Xiapex if the reconstituted solution is discolored or contains particles. The solution must be clear, colourless with no lumps or flakes or particles.

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

6. FURTHER INFORMATION

What Xiapex contains

The active substance is collagenase *clostridium histolyticum*. Each vial of Xiapex contains 0.9 mg of collagenase *clostridium histolyticum*. The other ingredients are sucrose, trometamol and hydrochloric acid.

The solvent contains calcium chloride dihydrate, sodium chloride and water for injections.

What Xiapex looks like and contents of the pack

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

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

Xiapex is supplied in a single use pack containing 1 vial of Xiapex powder and 1 vial of 3 ml solvent.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ, United Kingdom.

Manufacturer

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Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu/>.