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## EPAR summary for the public

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# Xiapex

collagenase *clostridium histolyticum*

This is a summary of the European public assessment report (EPAR) for Xiapex. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Xiapex.

## What is Xiapex?

Xiapex is a powder and solvent that are made up into a solution for injection. It contains the active substance collagenase *clostridium histolyticum*.

## What is Xiapex used for?

Xiapex is used to treat Dupuytren's contracture and Peyronie's disease in adults.

Dupuytren's contracture is a condition where one or more fingers are bent forwards toward the palm and cannot be fully straightened. It is caused by a thickening of the tissues under the skin of the palm that form 'cords' pulling down on the fingers. Xiapex is to be used in patients with cords in their palms that are thick enough to be felt through the skin.

Peyronie's disease is a condition in which men develop plaques of fibrous, scar-like tissue in their penis, causing it to become abnormally curved, and sometimes leading to pain or difficulty in sexual intercourse. Xiapex is used in patients with plaques that can be felt through the skin and in whom the abnormal curvature of the penis is at least 30 degrees at the start of therapy.

The medicine can only be obtained with a prescription.

## How is Xiapex used?

Xiapex must be given by a doctor trained in the use of the medicine and experienced in diagnosing and managing Dupuytren's contracture or male genital problems.



For Dupuytren's contracture, the doctor injects the appropriate dose of Xiapex directly into a cord in the patient's palm. Around 24 hours after the injection, the finger can then be straightened by the doctor, by performing a 'finger extension procedure' whereby it is stretched out for around 10 to 20 seconds to help disrupt the cord. Up to 2 cords or 2 affected joints in the same hand can be treated at a time. If injection and finger extension have not brought about a satisfactory response, the procedure may be repeated at monthly intervals up to a maximum of 3 injections per cord.

For patients with Peyronie's disease, Xiapex is given for up to 4 treatment cycles each lasting about 6 weeks. In each cycle, the dose of Xiapex is injected into the plaque causing the deformity followed by a second injection given 1 to 3 days after the first. A 'penile modeling procedure' is then performed by the doctor after a further 1 to 3 days to gently stretch and bend the plaque in the opposite direction to the abnormal curvature. Patients should subsequently continue modeling procedures daily at home as instructed for the rest of the cycle.

For more information on the use of Xiapex, including instructions on finger extension and penile modeling procedures, see the summary of product characteristics (also part of the EPAR).

### **How does Xiapex work?**

The cords in the palm of patients with Dupuytren's contracture and the plaques in Peyronie's disease are made of fibres of a protein called collagen. Xiapex contains a mixture of two 'collagenases', enzymes that break up collagen. When injected into a cord or a plaque, the collagenases break up the collagen fibres. This weakens and disrupts the cord or plaque.

The collagenases in Xiapex are extracted from the bacterium *Clostridium histolyticum*.

### **How has Xiapex been studied?**

Xiapex was compared with placebo (a dummy treatment) in two main studies involving a total of 374 adult patients with Dupuytren's contracture. The patients were treated with three injections and their hands were examined three months after the last injection to see how much the finger joints could be straightened out. The main measure of effectiveness was the proportion of patients whose main affected joint could be straightened so that it was bent forwards by no more than 5 degrees.

For Peyronie's disease, Xiapex was compared with placebo in two further studies involving 832 men. Patients received up to 4 treatment cycles, each involving two injections and subsequent modeling procedures, and the effects were measured on follow-up after 1 year. The main measures of effectiveness were the reduction in the abnormal curvature of the penis and the extent to which the condition was bothersome to the patient.

### **What benefit has Xiapex shown during the studies?**

Xiapex was shown to be more effective at treating Dupuytren's contracture than placebo. Among patients who completed the first study, 64% (130 out of 203) of those receiving Xiapex could straighten their fingers to an angle of 5 degrees or less compared with 7% (7 out of 103) of patients receiving placebo. In the second study the figures were 44% (20 out of 45) for the Xiapex group and 5% (1 out of 21) for the placebo group.

Xiapex was also more effective than placebo in treating Peyronie's disease, producing a 38% and 31% improvement in abnormal curvature in the two studies, compared with 21% and 15% respectively for placebo. There was also a greater improvement with Xiapex than placebo in patient-reported scores of how bothersome the condition was after treatment.

## **What is the risk associated with Xiapex?**

The most common side effects seen with Xiapex were local injection site reactions such as swelling, bruising, bleeding and pain. Injection site reactions were very common, occurring in the vast majority of patients. These reactions were mostly mild to moderate in severity and generally subsided within one to two weeks. Xiapex must not be used to treat Peyronie's disease if the plaque affects the urethra (the tube that carries urine and semen to the outside). For the full list of all side effects and restrictions with Xiapex, see the package leaflet.

## **Why has Xiapex been approved?**

The CHMP decided that Xiapex's benefits are greater than its risks and recommended that it be given marketing authorisation.

## **What measures are being taken to ensure the safe and effective use of Xiapex?**

A risk management plan has been developed to ensure that Xiapex is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Xiapex, including the appropriate precautions to be followed by healthcare professionals and patients.

The company that markets Xiapex must also ensure that all doctors expected to use the medicine are properly trained on the use of the medicine and experienced in diagnosing and managing Dupuytren's contracture or Peyronie's disease. The company must carry out an educational programme for doctors on the correct use and the potential side effects associated with the medicine.

## **Other information about Xiapex**

The European Commission granted a marketing authorisation valid throughout the European Union for Xiapex on 28 February 2011.

The full EPAR for Xiapex can be found on the Agency's website [ema.europa.eu/Find\\_medicine/Human\\_medicines/European\\_Public\\_Assessment\\_Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports). For more information about treatment with Xiapex, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 11-2015.