DECLARATION OF COMPLETION

XIAPEX®
collagenase clostridium histolyticum

Mr Michael Fraser

IN RECOGNITION OF COMPLETING THE XIAPEX TRAINING PROGRAMME FOR PEYRONIES DISEASE

Training completed on 24th August 2015

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Pioneer in Rare Diseases

▼XIAPEX® Abbreviated Prescribing Information (Peyronie's Disease):
(See XIAPEX Summary of Product Characteristics for full Prescribing Information)
Presentation: Powder and solvent for solution for injection. The vial of powder contains 0.9 mg collagenase *clostridium histolyticum*. The powder is a white lyophilised powder and the solvent is a clear colourless solution.
Indications: The treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.
Dosage: Xiapex must be administered by a physician appropriately trained in the correct administration of the product and experienced in the diagnosis and treatment of male urological diseases. The recommended dose of Xiapex is 0.58 mg per injection administered into a Peyronie's plaque. The volume of reconstituted Xiapex to be administered into the plaque is 0.25 ml. If more than one plaque is present, only the plaque causing the curvature deformity should be injected. A treatment course consists of a maximum of 4 treatment cycles. Each treatment cycle consists of two Xiapex injections and one penile modelling procedure. The second Xiapex injection is administered 1 to 3 days after the first injection. A penile modelling procedure is performed 1 to 3 days after the second injection of each treatment cycle. The interval between treatment cycles is approximately six weeks.
Contraindications: Hypersensitivity to the active substance or to any of the excipients. Treatment of Peyronie's plaques that involve the penile urethra due to potential risk to this structure
Warnings and Precautions: *Allergic reactions* - Following Xiapex injection, severe allergic reaction could occur, and patients should be observed for 30 minutes before leaving the clinic in order to monitor for any signs or symptoms of a serious allergic reaction, e.g. wide spread redness or rash, swelling, tightness in the throat or difficulty breathing. Patients should be instructed to consult a doctor immediately if they experience any of these signs or symptoms. Emergency medication for treatment of potential allergic reactions should be available. An anaphylactic reaction was reported in a post-marketing clinical study in a patient who had previous exposure to Xiapex for the treatment of Dupuytren's contracture, demonstrating that severe reactions including anaphylaxis can occur following Xiapex injections. *Corporal rupture* was reported as a serious adverse event after Xiapex injection in 5 out of 1044 patients (0.5%) in the controlled and uncontrolled clinical trials in Peyronie's disease. In other Xiapex-treated patients (9 of 1044; 0.9%), a combination of penile ecchymoses or haematoma, sudden penile detumescence, and/or a penile "popping" sound or sensation was reported, and in these cases, a diagnosis of corporal rupture cannot be excluded. Severe penile haematoma was also reported as an adverse reaction in 39 of 1044 patients (3.7%) in the controlled and uncontrolled clinical studies in Peyronie's disease. Signs or symptoms that may reflect serious injury to the penis should be promptly evaluated in order to assess for corporal rupture or severe penile haematoma. *Use in patients with coagulation disorders* – Xiapex must be used in caution in patients with coagulation disorders or those taking anticoagulants. Use of Xiapex in patients who have received anticoagulants (with the exception of up to 150 mg acetylsalicylic acids daily) within 7 days prior to receiving an injection of Xiapex is not recommended. *Immunogenicity* - As with any non-human protein medicinal product, patients may develop antibodies to the therapeutic protein. Since the enzymes in Xiapex have some sequence homology with human matrix metalloproteinases (MMPs), antidrug antibodies could theoretically interfere with human MMPs. No safety concerns related to the inhibition of endogenous MMPs have been observed, in particular no adverse events indicating the development or exacerbation of autoimmune diseases or the development of a musculoskeletal syndrome but the potential for it to occur cannot be excluded. If this syndrome were to develop, it would occur progressively and is characterised by one or more of the following signs and symptoms: arthralgia, myalgia, joint stiffness, stiffness of the shoulders, hand oedema, palmar fibrosis and thickening or nodules forming in the tendons. *Special penile conditions/diseases not studied in clinical trials* - Xiapex treatment in patients having a calcified plaque that could have interfered with the injection technique, chordee in the presence or absence of hypospadias, thrombosis of the dorsal penile artery and/or vein, infiltration by a benign or malignant mass resulting in penile curvature, infiltration by an infectious agent, such as in lymphogranuloma venereum, ventral curvature from any cause and isolated hourglass deformity of the penis has not been studied and treatment in these patients should be avoided. *Long-term safety* - Long-term safety of Xiapex is not fully characterised. The impact of treatment with Xiapex on subsequent surgery, if needed, is not known.
Drug Interactions: Use of Xiapex in patients who have received tetracycline antibiotics e.g. doxycycline, within 14 days prior to receiving an injection of Xiapex is not recommended.
Pregnancy & Lactation: Peyronie's disease occurs exclusively in adult male patients and hence there is no relevant information for use in females.
Driving and operating machinery: Minor influences on the ability to drive and use machines include dizziness, paresthesia, hypoesthesia, and headache that have also been reported following injection of Xiapex. Patients must be instructed to avoid potentially hazardous tasks such as driving or using machines until it is safe to do so or as advised by the physician.
Side Effects: Most adverse reactions were local events of the penis and groin and the majority of these events were of mild or moderate severity, and most (79%) resolved within 14 days of the injection. The adverse reaction profile was similar after each injection, regardless of the number of injections administered. The most frequently reported adverse drug reactions (> 25%) during the Xiapex clinical studies (832 male patients, 551 patients received Xiapex) were penile haematoma, penile swelling and penile pain. A popping noise or popping sensation in the penis, sometimes described as "snapping" or "cracking"and sometimes accompanied by detumescence, haematoma and/or pain, were reported in 73/551 (13.2%) Xiapex-treated patients and 1/281 (0.3%) placebo-treated patients, in Studies 1 and 2 combined. In the controlled and uncontrolled clinical studies of Xiapex in Peyronie's disease corporal rupture and other serious penile injury were reported uncommonly. **Very common** (≥1/10): Penile haematoma, swelling, pain, ecchymosis. **Common** (≥1/100 to <1/10): Blood blister, Skin discolouration, Penile blister, Pruritus genital, Painful erection, Erectile dysfunction, Dyspareunia, Penile erythema. Injection site vesicles, pruritus, Localised oedema, Nodule Suprapubic pain, Procedural pain.
Overdose: Overdose is expected to be associated with increased local injection site reactions. Symptomatic care and routine supportive care should be provided. Consult the summary of product charactistics for full details.Consult the summary of product charactistics for full details.
Legal Category: POM.
Marketing Authorisation Holder: Swedish Orphan Biovitrum AB (publ), SE-112 76 Stockholm, Sweden
Package Quantities, Marketing Authorisation Numbers and Basic NHS Price: XIAPEX 0.9mg powder and solvent for solution for injection, EU/1/11/671/001, £650.00.
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Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to SOBI Ltd by email: drugsafety@sobi.com