



IMPORTANT DRUG WARNING

Dear Healthcare Provider,

The purpose of this letter is to inform you of updated important safety information about XIAFLEX[®] (collagenase clostridium histolyticum), a biologic medication indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. XIAFLEX is administered by intra-lesional injection into a palpable Dupuytren's cord by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for XIAFLEX to ensure that the benefits of XIAFLEX outweigh its risks of tendon rupture and other serious adverse reactions of the injected extremity, and its potential risk of serious hypersensitivity reactions (including the potential for anaphylaxis).

New Important Safety Information

The Prescribing Information for XIAFLEX was recently revised to incorporate new information regarding

- The safety of administering two concurrent injections into the same hand
- Extending the timing of the finger extension procedure to approximately 24 to 72 hours.
- Risk of skin lacerations



Contraindication

- XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

Tendon Rupture or Other Serious Injury to the Injected Extremity

- Injection of XIAFLEX into collagen-containing structures, such as tendons or ligaments of the hand, may result in damage to those structures and possible permanent injury, such as tendon rupture, ligament damage, or skin laceration.
- Out of 1,082 XIAFLEX-treated patients in the XIAFLEX clinical studies, serious adverse events of the injected extremity occurred in 11 (1%) patients, including 3 (0.3%) patients who had flexor tendon ruptures and other events of the injected extremity (pulley rupture, ligament injury, recurrence of complex regional pain syndrome, tendonitis, sensory abnormality of the hand). The incidence of XIAFLEX-associated serious adverse events of the injected extremity, including tendon ruptures, in clinical practice may be different than the incidence seen in the clinical studies.
- To reduce the risk of serious injury to the injected extremity, XIAFLEX should be injected only into a palpable Dupuytren's cord with a metacarpophalangeal (MP) or proximal interphalangeal (PIP) joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting XIAFLEX into a Dupuytren's cord affecting a PIP joint of the fifth finger, special precautions should be taken.
- In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared with subjects treated with up to three single injections in the placebo-controlled studies (9%). Cases of skin laceration



requiring skin graft after finger extension procedures have been reported post-marketing.

Hypersensitivity Reactions, Including Anaphylaxis

- Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture.
- Healthcare providers should be prepared to address severe hypersensitivity reactions (including anaphylaxis) following XIAFLEX injections.
- In the controlled portions of the XIAFLEX clinical trials, a greater proportion of XIAFLEX-treated patients (15%) compared with placebo-treated patients (1%) had mild allergic reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections.

Healthcare Provider Action

- Review training materials (procedure training video, training guide) on the proper preparation and injection of XIAFLEX, and on the finger extension procedures to facilitate cord disruption as described in the FDA-approved Prescribing Information, and the special precautions and potential risk with injection of a cord affecting the PIP joint of the fifth finger.

Patient Counseling

- Counsel and communicate with patients about the potential risks associated with XIAFLEX before treatment.

Medication Guide

- The Medication Guide contains information that can be used to facilitate discussions about the potential risks of XIAFLEX. Provide a copy to each patient before each injection.



Reporting Adverse Events

To report any adverse events with the use of XIAFLEX contact:

- Auxilium Drug Information Center at 1-877-663-0412; or
- FDA MedWatch program by phone at 1-800-FDA-1088 or online at www.fda.gov/medwatch/report.htm

Training materials are available at www.XIAFLEXREMS.com or by calling 1-877-XIAFLEX (1-877-942-3539).

Read the accompanying FDA-approved Prescribing Information for XIAFLEX for a complete understanding of the benefits and risks of XIAFLEX in the treatment of adult patients with Dupuytren's contracture with a palpable cord.

Sincerely,

Auxilium Pharmaceuticals, Inc.
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