MEDICAL POLICY

Excellus

SUBJECT: COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX) FOR FIBROPROLIFERATIVE DISORDERS	EFFECTIVE DATE: 06/17/10 REVISED DATE: 08/18/11, 01/19/12, 12/20/12, 12/19/13
POLICY NUMBER: 5.01.15 CATEGORY: Technology Assessment	PAGE: 1 OF: 4

- ***If the member's subscriber contract excludes coverage for a specific service it is not covered under that contract. In such cases, medical policy criteria are not applied.***
- ***Medical policies apply to commercial and Medicaid products only when a contract benefit for the specific service exists.***
- ***Medical policies only apply to Medicare products when a contract benefit exists and where there are no National or Local Medicare coverage decisions for the specific service.***

POLICY STATEMENT:

I. Based upon our criteria and assessment of peer-reviewed literature, up to three injections of collagenase clostridium (e.g., Xiaflex) has been medically proven effective and therefore can be considered as a **medically appropriate** treatment option in the management of adults with Dupuytren's contracture in either the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joint when there is a palpable palmer cord.

II. Based upon our criteria and assessment of peer-reviewed literature, injectable collagenase clostridium (e.g., Xiaflex) has not been medically proven to be effective and is considered **investigational** for all other indications, including, but not limited to, Peyronie's disease and adhesive capsulitis of the shoulder.

POLICY GUIDELINES:

I. Collagenase clostridium is administered at four-week intervals for a total of three injections (0.58 mg) per cord. Each injection is followed by manual manipulation of the affected joint.

II. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION:

Fibroproliferative disorders, characterized by excessive collagen deposits, can affect the musculoskeletal system causing pain, limiting joint range of motion and negatively impacting quality of life. Examples of these fibrotic tissue disorders include Dupuytren's contracture, adhesive capsulitis and Peyronie's disease.

Collagenases, enzymes that digest native collagen and lead to the disruption of contracted cords, are being investigated as a non-surgical treatment for fibroproliferative disorders. Injection of collagenase clostridium histolyticum, a bacterial collagenase, is intended to provide a non-operative treatment option and is usually an office-based procedure. Its use in the treatment of Dupuytren's contracture has been the most widely studied. Therapy consists of up to three injections into a palpable cord, at 4-week intervals followed by manual manipulation of the affected joint to attempt rupture of the cord.

RATIONALE:

In February 2010, the FDA approved Auxilium Pharmaceutical Inc.'s biologics license application for clostridium collagenase histolyticum (Xiaflex) for treatment of adult patients with Dupuytren's contracture with a palpable cord. The FDA labeling for Xiaflex states that up to 3 injections at 4-week intervals may be given into a palpable Dupuytren's cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint.

While the evidence of long-term recurrence rates is not yet available, the outcomes from clinical trials thus far suggest that injectable collagenase clostridium provides short-term release of contracture in patients with Dupuytren's disease. Longer-term studies and comparative studies to surgical intervention are still needed to determine the overall safety and effectiveness of this therapy.

On December 6, 2013, the FDA approved collagenase clostridium histolyticum (CCH, Xiaflex) as treatment for men with Peyronie's disease who have a penile curvature of at least thirty degrees. According to the FDA, CCH will be available only through a Risk Evaluation and Mitigation Strategy (REMS), a stipulation the FDA places on approved therapies when a risk of potentially serious adverse effects exists, in this case, penile fracture and other serious injuries to the penis. This mirrors the REMS requirement that accompanied the FDA approval for Dupuytren's contracture in 2010. The REMS for CCH requires healthcare professionals to complete a training program for administration of CCH to patients with Peyronie's disease. Per the manufacture's web site, the dose of CCH is 0.58 mg per injection administered into a Peyronie's plaque. Up to eight injections (four treatment cycles) may be administered in the course of treatment. Also, a penile modeling procedure is recommended after every treatment cycle of two injections in an effort to further disrupt the plaque.

In 2013, Gelbard and colleagues published the results of 2 double-blind, placebo-controlled RCTs, IMPRESS (Investigation for Maximal Peyronie's Reduction Efficacy and Safety Studies) I and II, which examined the clinical efficacy and safety of collagenase injections in subjects with Peyronie disease. These RCTs were sponsored by the manufacturer (Auxilium Pharmaceuticals), the findings of which were submitted to the FDA in support of their biologics license application. These 2 studies examined collagenase injections in 417 and 415 participants, respectively, through a maximum of 4 treatment cycles, each separated by 6 weeks (for up to 8 injections of 0.58 mg collagenase). Men were stratified by baseline penile curvature (30 to 60 vs. 61 to 90 degrees) and randomized to collagenase injections or placebo in a 2:1 ratio. The primary outcomes were the percent change in the penile curvature abnormality and the change in the Peyronie's Disease Questionnaire (PDQ, developed by the manufacturer) symptoms bother score from baseline to 52 weeks. Data from the IMPRESS I and II studies were combined. Participants treated with collagenase injections showed a mean percent improvement in penile curvature abnormality of 34%, compared to 18% improvement in penile curvature in the placebo group; this change in curvature and the percent improvement in the collagenase group were significantly greater than in the placebo group (each $p < 0.0001$). The mean change in the PDQ symptom bother domain score was significantly improved in the collagenase group vs. the placebo group (-2.8 ± 3.8 vs. -1.8 ± 3.5, $p = 0.0037$). The most frequently reported complications ($\geq 45\%$) in the collagenase-treated group included penile ecchymosis, penile swelling and penile pain. Six participants experienced treatment-related serious adverse events, including corporeal rupture in 3 cases and penile hematoma in the other 3 cases. The 3 corporeal ruptures and one hematoma were successfully repaired surgically. Of the 2 remaining penile hematomas, one case was successfully resolved without intervention and the other resolved with aspiration.

Five studies, including 2 manufacturer-sponsored double-blind, placebo-controlled randomized trials, have demonstrated short-term improvement in patients with Peyronie's disease. Larger trials directly comparing outcomes with current treatment options are required.

Use of this biologic material for treatment of conditions (e.g., adhesive capsulitis) other than Dupuytren's and Peyronie's disease is an off-label application.

No studies including patients with adhesive capsulitis were identified in the literature search.

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

CPT:	20527	Injection, enzyme (e.g., collagenase), palmer fascial cord (e.g., Dupuytren's contracture)

	26341	Manipulation, palmer fascial cord (e.g., Dupuytren's contracture), post enzyme injection (e.g., collagenase)

HCPCS:	J0775	Injection, collagenase clostridium histolyticum, 0.1mg
ICD9:	607.85 **(E/I)**	Peyronie's disease
	726.0 **(E/I)**	Adhesive capsulitis of shoulder
	728.6	Contracture of palmar fascia (Dupuytren's contracture)
ICD10:	M72.0	Palmer fascial fibromatosis (Dupuytren)
	M75.00-M75.02 **(E/I)**	Adhesive capsulitis (code range)
	N48.6 **(E/I)**	Induratio penis plastic (Peyronie's disease)

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* key article

KEY WORDS:

Collagenase clostridium injection, collagenase injection, Dupuytren's contracture, Peyronie's disease, Xiaflex

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination (LCD) for Drugs and Biologicals and an accompanying Article specifically addressing collagenase clostridium histolyticum. Please refer to the following LCD websites for Medicare Members:

http://apps.ngsmedicare.com/lcd/LCD_L25820.htm

http://apps.ngsmedicare.com/sia/ARTICLE_A49949.htm