



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Collagenase clostridium histolyticum (Xiaflex™)

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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers collagenase clostridium histolyticum (Xiaflex™) as medically necessary for the treatment of a symptomatic Dupuytren's contracture in adults as an alternative to surgical treatment when there is both a palpable cord and a functional impairment as manifested by a metacarpophalangeal (MCP) joint or proximal interphalangeal (PIP) joint contracture exceeding 30 degrees.

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to collagenase clostridium histolyticum (Xiaflex™) therapy for the condition being addressed.

FDA Approved Indications

Xiaflex is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.

FDA Recommended Dosing

Xiaflex should be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture. The dose of Xiaflex is 0.58 mg per injection into a palpable cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint.

Drug Availability

Xiaflex is available in single-use, glass vials containing 0.9 mg of collagenase clostridium histolyticum as a sterile, lyophilized powder. Sterile diluent for reconstitution is available in single-use, glass vials containing 3 mL of 0.3 mg/mL calcium chloride dihydrate in 0.9% sodium chloride.

General Background

Pharmacology / Pharmacokinetics

Xiaflex contains two collagenases, AUX-I and AUX II, which are isolated from fermentation products of *Clostridium histolyticum* bacteria. The cords formed in Dupuytren contracture are made of collagen, which make them susceptible to collagenase. The pharmacokinetic properties of Xiaflex™ are not well described. In single-dose studies, plasma concentrations were not measurable within 30 days of local injection.

Clinical Efficacy

No trials comparing Xiaflex to other treatments or to surgery have been reported. There are no data evaluating Xiaflex for surgery prevention. In three randomized, double-blind trials, more patients evaluated 30 days after the last of up to 3 treatments achieved a reduction in joint contracture to within 5 degrees of normal with Xiaflex 0.58 mg (44.4% to 91%) compared with placebo (0% to 6.8%, $p < 0.001$). In the largest trial, the median time to reach the primary endpoint was 56 days. In two trials, more patients achieved $\geq 50\%$ improvement from baseline in the primary contracture with Xiaflex (77.8% to 84.7%) compared to placebo (11.7% to 14.3%, $p < 0.001$). In one unpublished, long-term follow-up study, the nominal 2-year recurrence rate was 19.3% (119/619 joints).

No trials comparing Xiaflex to other treatments have been reported. There are also no data evaluating the efficacy of Xiaflex for preventing surgery. The efficacy of Xiaflex in Dupuytren contracture was demonstrated in three phase III, randomized, double-blind, placebo-controlled, multi-dose trials. FDA considered two of these trials, CORD-I and CORD-II, which were multicenter trials, as pivotal trials, and the third which was a single-center trial as supportive. CORD-I and the single-center trial are published. CORD-II is not published; data for this trial are available from the product label and from the FDA reports. The primary endpoint in these three trials was a reduction in joint contracture to within 5 degrees of normal 30 days after the last of up to 3 injections administered at 1-month intervals. In three trials, more patients achieved the primary endpoint with Xiaflex 0.58 mg (44.4% to 91%) compared with placebo (0% to 6.8%, $p < 0.001$). After the first injection, more patients achieved reduction in contracture to within 5 degrees of normal with Xiaflex (26.7% to 70%) compared with placebo (0% to 4.8%, $p = 0.001$ in two trials, p -value not reported in one trial). In two trials, more patients achieved $\geq 50\%$ improvement from baseline in the primary contracture with Xiaflex (77.8% to 84.7%) compared to placebo (11.7% to 14.3%, $p < 0.001$).

Recurrence was defined as an increase in contracture to 20 degrees or more in the presence of a palpable cord, in a contracture that had previously been successfully treated. One trial reported 5 recurrences in 54 successfully treated joints in patients followed for 24 months. Pooled data from 5 trials reported contracture recurrence in 30 of 830 cases (4% of cases) that had been successfully treated with Xiaflex; the mean follow-up period after treatment was 7.4 months. Of the cases that recurred, approximately one fourth of these recurred within 3 months and one-half recurred between 3 and 6 months of successful treatment. One unpublished, long-term follow-up study (data from manufacturer) followed 634 patients (1065 joints) who had completed one of the phase 3 trials. The mean follow-up time from initial Xiaflex treatment was 2.1 years. Eighty-one percent of the successfully treated joints (499/619 joints) had not suffered recurrence of contracture at 2 years. The nominal 2-year recurrence rate was 19.3% (119/619 joints).

Adverse Drug Reactions / Interactions

In controlled trials, 98% of patients treated with Xiaflex experienced an adverse reaction compared to 51% treated with placebo. Common adverse reactions include peripheral edema, contusion, injection site hemorrhage, injection site reaction, and pain in the treated extremity. Serious effects that may occur with Xiaflex include allergic reactions, tendon rupture, or other serious injuries to the treated extremity. Flexor tendon rupture occurred in 0.3% of all treated patients. No pharmacokinetic drug interactions have been described regarding Xiaflex. The efficacy and safety of Xiaflex have not been evaluated in patients receiving anticoagulants within seven days of Xiaflex administration with the exception of patients taking low-dose aspirin (≤ 150 mg daily). Use Xiaflex with caution in patients who are anticoagulated or who have coagulation disorders.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

HCPCS Codes	Description
J0775	Injection, collagenase clostridium histolyticum, 0.01 mg

ICD-9-CM Diagnosis Codes	Description
728.6	Contracture of palmar fascia

Associated Covered Codes:

CPT®* Codes	Description
20550	Injection(s); single tendon sheath or ligament, aponeurosis (e.g. plantar "fascia")
26340	Manipulation, finger joint, under anesthesia, each joint
29130	Application of finger splint, static

Associated code not covered when used to report finger joint manipulation performed on the day following the injection of this drug:

CPT®* Codes	Description
26989	Unlisted procedure, hands or fingers

*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.

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