Molina Clinical Policy
Xiaflex for Dupuytren's Contracture
Policy No. 259

Last Approval: 6/9/2021
Next Review Due By: June 2022

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Dupuytren contracture (DC) is a progressive, nonmalignant fibroproliferative disorder that affects the palmar and digital fascia of the hand and results in contracture deformities. It is characterized by the abnormal production of collagen nodules, which often develop into cords that connect the dermis to the palmar fascia, causing affected joints to bend or flex toward the palm in a constant state of contracture that limits finger movement and hand function. The joints commonly affected by DC are the metacarpophalangeal joints and the proximal interphalangeal joints, the fourth and fifth digits (ring and pinky). The exact etiology is unknown. The condition is more common in men, usually presenting in patients over the age of 50. Other potential risk factors include manual labor with vibration exposure, prior hand trauma, alcoholism, smoking, diabetes mellitus, hyperlipidemia, Peyronie disease, and complex regional pain syndrome (Hindocha et al.). Diagnosis is made clinically by thorough history and physical examination. Imaging (i.e., ultrasound, MRI, or CT scan) is usually not indicated unless diagnosis is uncertain or required to help rule out other pathology. The symptoms of DC are generally not painful unless aggravated by forceful activities that put pressure on the nodule. As the condition progresses, the cords of fibrous tissue form in the palm and run into the fingers or thumb, eventually, pulling into a permanently flexed position. The aggressive form of the disease can be debilitating, limiting the ability to perform everyday activities.

Treatment for DC is not curative, and the goals of treatment are to improve flexibility of the fingers and to evaluate the need for surgery or other interventions. Non-surgical and surgical options are available for management of DC and the choice of therapy mostly depends on the severity of disease, degree of deformity, limitations in function, and provider preference. Non-surgical options in the early stages include physical or occupational therapy, triamcinolone acetonide injections, collagenase injections, needle fasciotomy (needle aponeurotomy), and radiation therapy. Surgery is treatment of choice for advanced stages of disease and usually considered when disease is functionally symptomatic, or contracture is progressing. Surgical procedures include open excision (limited or total fasciectomy), open or percutaneous division (fasciotomy), or percutaneous puncture (needle aponeurotomy) of the culprit cord(s). There is no formal consensus though it is generally accepted that surgical procedures are reserved for patients with contractures >30 to 40 degrees at the metacarpophalangeal (MCP) or >20 degrees at the proximal interphalangeal (PIP) joint have been suggested as indications for surgery (Feldman et al. 2017; UTD 2021)

Xiaflex (collagenase clostridium histolyticum; CCH) is a bacterial collagenase injected into the Dupuytren's cord with the goal of weakening and disrupting the cord, which results in contracture reduction and range of motion improvement. Xiaflex contains purified collagenase clostridium histolyticum, consisting of two microbial collagenases, Collagenase AUX-1 and Collagenase AUX-II, which are isolated and purified from the fermentation of Clostridium histolyticum bacteria. Collagenases are proteinases that hydrolyze collagen in its native triple helical conformation under physiological conditions, resulting in lysis of collagen deposits. Xiaflex is the first FDA-approved non-surgical option for the treatment of adult patients with DC with a palpable cord. Xiaflex is indicated for the treatment of DC with a palpable cord, a condition involving the connective tissue in the hands that leads to abnormal curvature/contracture of the fingers.

COVERAGE POLICY

Xiaflex (collagenase clostridium histolyticum) for the treatment of the treatment of adults with Dupuytren's contracture **may be considered medically necessary** when **ALL** of the following clinical criteria are met:

1. Diagnosis of Dupuytren's contracture with a palpable cord; **AND**

2. A positive "tabletop test" (defined as the inability to simultaneously place the affected finger and palm flat against a tabletop); **AND**

3. Documentation of **ONE** of the following:
   a. Flexion contracture > 20 degrees at the metacarpophalangeal (MP) joint
   b. Flexion contracture > 20 degrees at the proximal interphalangeal (PIP) joint

Informational Note: Patients in clinical trials must have had a finger flexion contracture with a palpable cord of at least one finger (other than the thumb) of 20° to 100° in a metacarpophalangeal joint or 20° to 80° in a proximal interphalangeal (PIP) joint.

AND

4. Member has not received ANY of the following treatments:
   a. A surgical treatment (e.g., fasciectomy, fasciotomy) on the selected primary joint within 90 days before the first injection requested; **AND**
   b. An anticoagulation medication (except for up to 150 mg/day of aspirin) within 7 days before the first injection

AND

3. Functional impairment as a result of the contracture

CONTINUATION OF THERAPY

1. Reauthorization request is for treatment of a previously treated cord following recurrence:

   NOTE: Continuation of therapy criteria is for the same treated cord. If the condition developed in a different cord, a new request must be submitted and meet all 'Initial Coverage' criteria.

AND

2. Continued need for treatment has been formally assessed and documented

AND

3. Member received less than 3 injections total in affected cord (at approximately 4-week intervals)

AND

4. Member followed up within 24 hours following an injection for finger extension procedure if a contracture persists (in order to qualify for additional injections)

AND

5. Injection may be repeated up to a **maximum of 3 sessions** per cord (at 4-week intervals) if reduction in contracture of the selected primary joint (MP or PIP) is NOT within 0 to 5 degrees of normal full extension.

   NOTE: If there is no improvement after the 2nd second injection, the 3rd injection will NOT be authorized.

AND

5. Unacceptable adverse events, complications, or toxicity to previous Xiaflex injection(s)

LIMITATIONS AND EXCLUSIONS

The following are considered **contraindications/exclusions** based on insufficient evidence:

1. Hypersensitivity to Xiaflex (CCH) or to collagenase used in any other therapeutic application or application method
2. Greater than 3 injections per cord
3. Surgery on the primary joint within the past 90 days
4. No improvement* after the 2nd injection (*Improvement is defined as a reduction in contracture of the selected primary joint (MP or PIP) within 0° to 5° of normal full extension)
5. Concomitant use of anticoagulants (with the exception of low-dose aspirin) and in patients with coagulation disorders

The following are considered conditions for **discontinuation of treatment** and re-treatment may not be authorized:

1. Unacceptable adverse events, complications, or toxicity
2. Persistent and uncorrectable problems with adherence to treatment
3. Limited response to treatment as evidenced by physical findings and/or clinical symptoms

The following are considered **experimental, investigational and unproven** based on insufficient evidence:

1. Any indications other than those listed above

PRESCRIBER REQUIREMENTS: Prescribed and administered by a board-certified healthcare provider experienced in injection procedures of the hand and in the treatment of DC (e.g., board-certified hand surgeon, orthopedic surgeon, rheumatologist, or plastic surgeon)
AND
Prescriber has completed the required REMS training for use of Xiaflex in the treatment of DC

AGE RESTRICTIONS: 18 years of age or older

DOSING CONSIDERATIONS: 0.58 mg intralesionally per cord affecting a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint

- If a contracture persists, finger extension procedure should be performed 24 to 72 hours following injection to facilitate cord disruption. If MP or PIP contracture remains, may reinject cord with a single dose of 0.58 mg 4 weeks following initial injection; injections and finger extension procedures may be administered up to 3 times per cord separated by approximately 4-week intervals.

DURATION AND QUANTITY LIMITATIONS

1. Initial authorization: ONE injection
2. Reauthorization: Up to TWO additional injections per cord (at approximately 4-week intervals) for a total of THREE injections per each affected cord.
3. Total authorization: Maximum of THREE injections per cord **AND** ONE injection per 30 days for a total duration of therapy of 3 months (12 weeks)

ADMINISTRATION:

1. Xiaflex is considered a provider-administered procedure performed in a physician's office by a healthcare provider experienced in injection procedures of the hand and in the treatment of patients with Dupuytren's contracture.
2. Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: Intralesional injection

DRUG CLASS: Connective Tissue Agent; Enzyme; Proteolytic Enzyme; Tissue Permeability Modifier

FDA-APPROVED USES:

- Dupuytren Contracture (DC): Treatment of adults with DC with a palpable cord.
- Peyronie Disease (PD): Treatment of adult men with PD with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy. ***This indication is not addressed in this policy. REFER to MCP-279.**

COMPENDIAL APPROVED OFF-LABELED USES: None

SUMMARY OF MEDICAL EVIDENCE

FDA approval of CCH for the management of Dupuytren contracture was based on the results of CORD I and CORD I Extension, multicenter, randomized, double-blind, placebo-controlled trials (n=374).

Hurst et al. (2009) conducted a double-blind, placebo-controlled, multicenter trial of 308 subjects with Dupuytren's joint contractures of 20 degrees or more to receive up to 3 injections of CCH (n=204) or placebo (n=104) in the contracted collagen cord at 30-day intervals, with manipulation of the joints the day following injection. Joints were stratified according to joint type (MP or PIP) and the joints were manipulated one day after injection if necessary. The mean number of affected joints was 3. The proportion of patients who had undergone prior surgery for DC was 38%, with 8% having had surgery for contracture on the same finger as the primary treated joint. Findings included a reduction in contractures to less than 5º in 64% of collagenase-injected patients compared with 6.8% of patients treated with placebo. Patients with MCP involvement tended to improve to a greater extent, as did those patients with less severe flexion contractures. The mean range of motion in the treated joints also improved significantly (from 44 to 81 degrees versus 45 to 50 degrees). Response rates were better in patients with less severe contractures (Hurst et al. CORD I Study Group).

Study 2 enrolled 66 patients (n=66). The mean number of affected joints was 3.3. The proportion of patients who had undergone prior surgery for DC was 53%, with 18% having had surgery for contracture on the same finger as the primary treated joint. More collagenase-treated joints achieved a reduction in contracture and a greater increase in range of motion of the affected joints.

Peimer et al. (2015) analyzed the recurrence rate of DC 5 years after successful treatment with CCH (CORDLESS study) in a non-interventional follow-up in patients from previous CCH clinical studies. Successfully treated joints was defined as joint correction 5° contracture or less following CCH treatment (prospectively established definition of success by Hurst et al.). The aim of this study was to evaluate the long-term durability of CCH treatment across multiple studies that used this definition of success. Recurrence was defined as 20° or greater worsening (relative to day 30 after the last injection) with a palpable cord or any medical/surgical intervention to correct new/worsening contracture. The study enrolled patients (n=644) with a total of 1,081 treated joints evaluated annually for contracture and safety at 2, 3, 4, and 5 years after their first injection (0.58 mg) of CCH. A total of 1,081 treated joints with more than one follow-up were analyzed; of these, 623 joints (58%) were initially treated successfully (i.e., reduction of contracture to 0° to 5°). The follow-up study concluded that longer-term (>5 years) follow-up in 1,081 joints treated with collagenase demonstrated an overall recurrence rate of 47% in both metacarpophalangeal and proximal interphalangeal joints combined. This rate (47%) is comparable with the published recurrence rates after surgical treatments, with one reported long-term treatment-related adverse event. The recurrence rate was worse at the PIP joint (66%) than the MCP joint (39%), which parallels results seen with needle aponeurotomy and open surgery (Peimer et al. 2015).

SUPPLEMENTAL INFORMATION

Collagen: A fibrous protein found in connective tissue, bone, and cartilage.
Collagenase: An enzyme capable of causing the hydrolysis of collagen and gelatin
Contracture: Shortening of the tendon or muscle because of intrinsic or extrinsic conditions.
Fascia: A sheet of fibrous tissue that envelops the body beneath the skin; it also encloses muscles and groups of muscles and separates their several layers or groups.
Fasciectomy: Surgical removal of the fibrous tissue beneath the skin.
Fibroproliferative: Producing new fibrous tissue.
Metacarpophalangeal (MP) joint: Commonly referred to as the knuckle; attached to the proximal first phalanges.
Proximal interphalangeal (PIP) joint: The second joint of the finger.

CODING & BILLING INFORMATION

CPT	Description

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

AVAILABLE DOSAGE FORMS:
Single-use glass vials containing 0.9 mg of collagenase clostridium histolyticum as a sterile, lyophilized powder for reconstitution

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/9/2021 MCPC	Policy reviewed and revised. Updated references. No changes to medical necessity criteria. Minor revisions, including clarification and addition of language, however no change to intent. • In initial authorization criteria section, clarification of prescriber specialty criterion with the following 'healthcare provider experienced in injection procedures of the hand and in the treatment of DC' • In the 'Reauthorization/Continuation of Therapy' section, clarification to criterion #1 (intent did not change; clarification to align with the 'Administration/Quantity Limit and Authorization' section): Reauthorization request is for treatment of a previously treated cord following recurrence: Continued need for treatment has been formally assessed and documented; AND Member received less than 3 injections total in affected cord (at approximately 4-week intervals); AND If the condition developed in a different cord, a new request must be submitted and meet all 'Initial Coverage' criteria.
Q3 2020 P&T	Policy reviewed and updated, no changes in coverage criteria, updated references.
Q4 2019 P&T	Policy reviewed and updated, no changes in coverage criteria, updated references.
7/10/2018 MCPC	Policy reviewed and updated, no changes in coverage criteria, updated references.
9/19/2017 MCPC	Policy reviewed and updated, no changes in coverage criteria, updated references.
12/15/2016 MCPC	Policy reviewed and updated, no changes in coverage criteria, updated references.
10/13/2015 MCPC	New policy. Internal Peer Review. MCPC Chair, Sr. Medical Director of Policy.

REFERENCES

Government Agency
Centers for Medicare & Medicaid Services (CMS). Medicare Coverage Database. National Coverage Determination (NCD) Search. Accessed at: CMS ; CMS NCD

Prescribing Information and Drug Compendia

Xiaflex (collagenase clostridium histolyticum) [prescribing information]. Malvern, PA: Endo Pharmaceuticals Inc; April 2021.

American Hospital Formulary Service (AHFS). Drug Information 2021. [STAT!Ref Web site]. Accessed April 2021. Available at: http://online.statref.com. [via subscription only].

Drug Facts and Comparisons. Facts and Comparisons eAnswers [online]. Clinical Drug Information LLC, 2021. Accessed April 2021. Available from Wolters Kluwer Health, Inc. [via subscription]

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology.com. Accessed April 2021. [via subscription]

Peer Reviewed Publications

Feldman G, Rozen N, Rubin G. Dupuytren's Contracture: Current Treatment Methods. *Isr Med Assoc J*. 2017 Oct. 19 (10):648-650.

Hurst LC, Badalamente MA, Hentz VR, et al.; CORD I Study Group. Injectable collagenase clostridium histolyticum for Dupuytren's contracture. N Engl J Med. 2009; 361(10):968-979.

Hindocha S, et al. Epidemiological evaluation of Dupuytren's disease incidence and prevalence rates in relation to etiology. *Hand (N Y)*. 2009 Sep. 4(3):256-69. Available at: Link. Accessed on May 2021.

Mafi R, Hindocha S, Khan W. Recent Surgical and Medical Advances in the Treatment of Dupuytren's Disease - A Systematic Review of the Literature. Open Orthop J. 2012;6:77-82 Available at: Link Accessed on May 2021.

Peimer CA, Blazar P, Coleman S, et al. Dupuytren Contracture Recurrence Following Treatment with Collagenase Clostridium histolyticum (CORDLESS [Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study]): 5-Year Data. J Hand Surg Am. 2015 Aug;40(8):1597-605. doi: 10.1016/j.jhsa.2015.04.036. Epub 2015 Jun 18. PMID: 26096221.

National and Specialty Organizations

American Academy of Orthopedic Surgeons (AAOS). Dupuytren's Contracture. Available at: http://orthoinfo.aaos.org/topic.cfm?topic=A00008. Accessed on May 2020.

Other Peer Reviewed and Professional Organization Publications (used in the development of this policy)

UpToDate. Retrieved from www.uptodate.com [Registration and login required]

- Dupuytren's Contracture. Topic last updated: Mar 20, 2020. Topic 7753 Version 18.0. Accessed May 2021

DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T114104, Dupuytren Disease; [updated 2018 Nov 30, cited May 2021]. Available from https://www.dynamed.com/topics/dmp~AN~T114104. [via subscription]

APPENDIX

Reserved for State specific information *(to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*