Medical Policy Bulletin

Title:

Collagenase clostridium histolyticum (Xiaflex®), collagenase clostridium histolyticum-aaes (Qwo™)

Policy #:

MA08.128

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)

Dupuytren's Contracture with a Palpable Cord

Collagenase clostridium histolyticum (Xiaflex) injection is considered medically necessary and, therefore, covered for the treatment of adult individuals with a diagnosis of Dupuytren's contracture with a palpable cord when all of the following criteria are met:

- The individual has a finger flexion contracture with a palpable cord in a metacarpophalangeal joint or a proximal interphalangeal joint.
- The contracture is at least 20 degrees.
- The individual had a positive tabletop test, defined as the inability to simultaneously place the affected finger(s) and palm flat against a table.

Peyronie's Disease

Collagenase clostridium histolyticum (Xiaflex) injection is considered medically necessary and, therefore, covered for the treatment of adult individuals with a diagnosis of Peyronie's disease when all of the following criteria are met:

- The individual has a palpable plaque inside the penis.
- The individual has curvature deformity of at least 30 degrees.

- The is individual is experiencing pain or sexual dysfunction.

BENEFIT CONTRACT EXCLUSION

The use of collagenase clostridium histolyticum (Qwo) for the treatment of buttocks cellulite is not covered by the Company because it is considered a cosmetic service. Services that are cosmetic are a benefit contract exclusion for all products of the Company. Therefore, it is not eligible for reimbursement consideration.

The use of collagenase clostridium histolyticum (Xiaflex) for the treatment of buttocks cellulite is not covered by the Company because it is considered a cosmetic service. Services that are cosmetic are a benefit contract exclusion for all products of the Company. Therefore, it is not eligible for reimbursement consideration.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for collagenase clostridium histolyticum (Xiaflex) not identified in this policy are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM

Collagenase clostridium histolyticum (Xiaflex), due to the risks of corporal rupture (penile fracture) or another serious penile injury in the treatment of Peyronie's disease, is available only through the Risk Evaluation and Mitigation Strategy (REMS) Program.Required components of the collagenase clostridium histolyticum (Xiaflex) REMS Program include the following:

- Prescribers must be certified with the program by enrolling and completing training in the administration of collagenase clostridium histolyticum (Xiaflex) treatment for Peyronie's disease.
- Healthcare sites must be certified with the program and ensure that collagenase clostridium histolyticum (Xiaflex) is only dispensed for use by certified prescribers.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, collagenase clostridium histolyticum (Xiaflex) is covered under the medical benefits of the Company’s Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Collagenase clostridium histolyticum (Xiaflex) was approved by the FDA on February 10, 2010, for the treatment of adult individuals with Dupuytren’s contracture with a palpable cord; additionally, it was approved by the FDA on December 6, 2013, for the treatment of adult male individuals with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees. Collagenase clostridium histolyticum (Qwo) was approved by the FDA on July 6, 2020, for the treatment of adult female individuals with moderate to severe cellulite in the buttocks

PEDIATRIC USE

The safety and effectiveness of histolyticum (Xiaflex) have not been established in pediatric individuals less than 18 years of age.

DOSING GUIDELINES

Dupuytren's Contracture with a Palpable Cord

The dose of collagenase clostridium histolyticum (Xiaflex) is 0.58 mg per injection administered into a palpable cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint. Four weeks after the clostridium histolyticum (Xiaflex) injection and finger extension procedure, if an MP or PIP contracture remains, the cord may be re-injected with a single dose of 0.58 mg of clostridium histolyticum (Xiaflex) and the finger extension procedure may be repeated (approximately 24 to 72 hours after injection). Injections and finger extension procedures may be administered up to 3 times per cord at approximately four-week intervals.

Peyronie's Disease

The dose of collagenase clostridium histolyticum (Xiaflex) is 0.58 mg per injection administered into a Peyronie's plaque. If more than one plaque is present, an injection administered into the plaque causing the curvature deformity. Each treatment cycle consists of two clostridium histolyticum (Xiaflex) injection procedures and one penile modeling procedure. The second clostridium histolyticum (Xiaflex) injection procedure is performed one to three days after the first. The penile modeling procedure is performed one to three days after the second injection of the treatment cycle. The interval between treatment cycles is approximately six weeks. The treatment course consists of a maximum of eight injection procedures and four modeling procedures.

Description

Collagenase clostridium histolyticum (Xiaflex) and collagenase clostridium histolyticum-aaes (Qwo) each contains two forms of microbial collagenase (collagenase AUX-I and collagenase AUX-II), which are isolated and purified from the fermentation of Clostridium histolyticum bacteria.

Collagenase clostridium histolyticum is marketed under brand names Xiaflex and Qwo, each of which serves distinct populations. Xiaflex's approved indications include Peyronie's disease and Dupuytren's contracture, and Qwo is approved for the treatment of moderate-severe buttocks cellulite in adult women.

Xiaflex is composed of proteinases that hydrolyze collagen, leading to enzymatic disruption of contracted Dupuytren cord or Peyronie plaque, both of which are composed primarily of collagen, whereas Qwo enzymatically targets the fibrous connective tissue tethering the skin to the underlying fascia; disruption of these fibrous septae diminishes the "dimpling" effect and leads to improved cellulite appearance.

Dupuytren's contracture is a disease that causes a deformity of the palmar and digital fascia of the hand. Abnormal deposition of collagen initially causes nodules in the palm of the hand, which may lead to the formation of cords. With the progression of the disease, the cords gradually contract, leading to deformities of the fingers. Damage to a joint is typically painless but is associated with significant functional impairment. The exact etiology of Dupuytren's contracture is unknown, but some risk factors have been identified, including alcohol, smoking, diabetes, epilepsy, thyroid disorders, and trauma.

Peyronie's disease is an acquired penile condition caused by fibrosis of the tunica albuginea that consists of three connective tissue layers: an outer layer of mesothelium apposed to the basal lamina (tunica vaginalis), a middle layer of dense fibrous tissue, and an inner layer of loose connective tissue (tunica vascularis) with nerve fibers and abundant blood and lymphatic vessels. Peyronie's disease may cause pain, deformity, erectile dysfunction, and/or distress. Usually repeated minor trauma to the penis initiates a cascade involving extravascular protein deposition, fibrin trapping, and overexpression of cytokines, leading to collagen changes characteristic of the condition. Males around 50 years of age are most commonly affected. Most individuals with Peyronie's disease will have pain resolved over time without intervention, but curvature deformities are less likely to resolve without treatment.

Cellulite involves fibrous connective cords that tether the skin to the underlying muscle, with the fat lying between. As fat cells accumulate, they push up against the skin, while the long, tough cords pull down. This creates an uneven surface or dimpling.

On December 6, 2013, the FDA approved Collagenase clostridium histolyticum (Xiaflex) for the treatment of Peyronie's disease in male adult individuals. The efficacy of collagenase clostridium histolyticum (Xiaflex) was evaluated in two randomized, double-blind, placebo-controlled, multi-centered trials in 832 adult males with Peyronie's disease. At study entry, individuals had penile curvature deformity of at least 30 degrees in the stable phase of Peyronie's disease. Individuals were excluded if they had a ventral curvature deformity, an isolated hourglass deformity, or a calcified plaque that could have interfered with the injection technique. At baseline, penile pain was either not present or was mild in most individuals. Individuals were given up to four treatment cycles of Xiaflex or placebo. In each treatment cycle, two injections of collagenase clostridium histolyticum (Xiaflex) or two injections of placebo were administered one to three days apart. The primary endpoints were the percent change from baseline to week 52 in penile curvature deformity and the change from baseline to week 52 in the Bother domain score. The Bother domain score is a composite of the following individual-reported items: concern about erection pain, erection appearance, and the impact of Peyronie's disease on intercourse and on the frequency of intercourse. Collagenase clostridium histolyticum (Xiaflex) treatment significantly improved penile curvature deformity in individuals with Peyronie's disease compared with placebo. Collagenase clostridium histolyticum (Xiaflex) also significantly reduced individual-reported bother associated with Peyronie's disease compared with placebo. Serious adverse events were three cases of corporeal rupture requiring surgical repair and three cases of a penile hematoma.

On February 3, 2010, the FDA approved Collagenase clostridium histolyticum (Xiaflex) for the treatment of Dupuytren's contracture in adult individuals. The safety and efficacy of collagenase clostridium histolyticum (Xiaflex) in Dupuytren's contracture was evaluated in two randomized, double-blind, placebo-controlled, multi-centered trials in 374 adult individuals with Dupuytren's contracture. At study entry, individuals 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 (MP) joint or 20° to 80° in a proximal interphalangeal (PIP) joint and a positive “table top test" defined as the inability to simultaneously place the affected finger(s) and palm flat against a tabletop. The cord affecting the selected primary joint received up to 3 injections of 0.58 mg of collagenase clostridium histolyticum (Xiaflex) or placebo on days 0, 30, and 60. About 24 hours after each injection of study medication, if needed, the investigator manipulated the treated finger in an attempt to facilitate the rupture of the cord. The primary endpoint was the proportion of individuals who achieved a reduction in a contracture of the selected primary joint (MP or PIP) to within 0° to 5° of normal 30 days after the last injection. Both studies showed a statistically significant reduction in contracture in the Xiaflex group compared to the placebo group.

COSMETIC PROCEDURES

Cosmetic procedures are those provided to improve an individual's physical appearance, from which no significant improvement in physiologic function can be expected. Emotional and/or psychological improvement alone does not constitute an improvement in physiologic function.

Collagenase clostridium histolyticum-aaes (Qwo) is a prescription medication used to treat moderate-severe buttocks cellulite in adult women via subcutaneous injection. Specifically, Qwo enzymatically targets the fibrous connective tissue tethering the skin to the underlying fascia; disruption of these fibrous septae diminishes the "dimpling" effect and leads to improved cellulite appearance. Although Qwo is the same pharmaceutical substance as Xiaflex, it is not indicated for the treatment of Peyronie's disease or Dupuytren's contracture; it is approved solely for cosmetic usage.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to the evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issues by leading professional organizations and government entities.

References

American Academy of Dermatology (AAD). Position statement on the definitions of cosmetic and reconstructive surgery. [AAD Web site]. 08/07/2010. Available at: https://server.aad.org/Forms/Policies/Uploads/PS/PS-Definitions of Cosmetic & Reconstructive Surgery.pdf. Accessed March 8, 2022.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
M72.0 Palmar fascial fibromatosis [Dupuytren]

N48.6 Induration penis plastica

HCPCS Level II Code Number(s)

THE FOLLOWING CODE IS USED TO REPORT COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)

J0775 Injection, collagenase, clostridium histolyticum, 0.01 mg

THE FOLLOWING CODE IS USED TO REPORT COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (QWO) AND IS CONSIDERED COSMETIC AND THEREFORE IS A BENEFIT EXCLUSION

J0775 Injection, collagenase, clostridium histolyticum, 0.01 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.128:

03/28/2025	This policy has been reissued in accordance with the Company's annual review process.
05/07/2024	This policy has been reissued in accordance with the Company's annual review process.
03/08/2023	This policy has been reissued in accordance with the Company's annual review process.
04/06/2022	This policy has been reissued in accordance with the Company's annual review process.
07/28/2021	This policy has been reissued in accordance with the Company's annual review process.
11/30/2020	This new policy will become effective on 11/30/2020. The policy has been developed to communicate the Company's coverage position for collagenase clostridium histolyticum (Xiaflex) and (Qwo), as previously communicated through a Provider News Center article.

Version Effective Date:
11/30/2020
Version Issued Date:
11/30/2020
Version Reissued Date:
03/28/2025