

DR.010.D Xiaflex® (Collagenase clostridium histolyticum)

Original Implementation Date : 08/01/2021
Version [D] Date : 09/18/2025
PARP Approved Date: 09/01/2026
Last Reviewed Date: 09/16/2026

Thank you for being a valued provider for members in one or more of our health plans: Jefferson Health Plans Medicare Advantage, Jefferson Health Plans Individual and Family Plans, Jefferson Health Plans CHIP, and/or Jefferson Health Plans EverWell (our Medicaid plan).

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans lines of business.

POLICY STATEMENT

The plan considers Xiaflex® (Collagenase clostridium histolyticum) medically necessary for its FDA approved indications when the prior authorization criteria listed in this policy are met.

OFF-LABEL USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off-label use Medical Directors will review scientific literature and local practice patterns.

FDA APPROVED INDICATIONS

Xiaflex® is a combination of bacterial collagenases indicated for the treatment of:

- Adult (≥ 18 -years-old) patients with Dupuytren's contracture with palpable cord.

- Adult (≥ 18 -years-old) men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

1. Patient is an adult (18 years or older) who has documentation of a diagnosis of Dupuytren's contracture with palpable cord; **AND**
 - a. Patient has functional impairment with **both**:
 - i. Positive "table-top" test (inability to simultaneously place affected finger and palm flat on a flat surface)
 - ii. Metacarpophalangeal (MCP) contracture of at least 20 degrees or proximal interphalangeal (PIP) contracture of at least 20 degrees **AND**
 - b. Medication is prescribed by or in consultation with a physician who is a hand specialist or experienced in injection procedures of the hand **AND**
 - c. Patient will receive comprehensive treatment based on standards of care for Dupuytren's contracture (e.g., finger extension after injection) **AND**
 - d. Prescribed Xiaflex® is requested for a maximum of 2 injections per hand (0.58 mg per injection site), for a maximum of 3 treatment cycles 4 weeks apart.

IF ALL CRITERIA MET, APPROVE FOR 5 MONTHS

2. Patient is an adult male (18 years of age or older) who has documentation of a diagnosis of **Peyronie's Disease** with at curvature of ≥ 30 degrees and palpable plaque; **AND**
 - a. Patient does not have any contraindications to the requested drug for the treatment of Peyronie's disease, such as a history of hypersensitivity to Xiaflex® or to collagenase used in other therapeutic applications or have Peyronie's plaque that involves the penile urethra **AND**
 - b. The member has intact erectile function (with or without medication) **AND**

- c. The medication is prescribed by or in consultation with a urologist or physician who is experienced in the treatment of male urological diseases **AND**
- d. The patient will receive comprehensive treatment based on standards of care for Peyronie's Disease (i.e., penile modeling activities after injection) **AND**
- e. The prescriber and healthcare site are certified with the Xiaflex® REMS program if prescribing for the treatment of Peyronie's disease **AND**
- f. The prescribed medication Xiaflex® is requested for a maximum of 4 treatment cycles at 6 weeks intervals (each cycle of two 0.58 mg injections into the target plaque separated by 1 to 3 days).

IF ALL CRITERIA MET, APPROVE FOR 5 MONTHS

RENEWAL CRITERIA

- 1. Patient continues to meet the diagnostic criteria after initial treatment of Xiaflex® for Dupuytren's contracture with palpable cord (and contracted cord persists) or Peyronie's Disease with palpable plaque and curvature of ≥ 15 degrees **AND**
- 2. Patient does not have history of unacceptable toxicity which precludes safe administration of the drug. (Examples of unacceptable toxicity include the following: corporal or tendon rupture, severe penial hematoma, hypersensitivity reactions, etc.) **AND**
- 3. Patient will continue to receive comprehensive treatment based on standards of care for Dupuytren's contracture or Peyronie's Disease (examples include the following: finger extension or penile modeling procedures after injection) **AND**
- 4. Patient demonstrates clinical benefit based on the prescriber's assessment.

IF ALL CRITERIA MET, APPROVE FOR 1 MONTH

NOTE: Maximum of 3 treatment cycles for Dupuytren's contracture per cord (unless contracted cord persists) and maximum of 4 treatment cycles for each plaque for Peyronie's Disease.

DOSAGE AND ADMINISTRATION

See package labeling.

RISK FACTORS/SIDE EFFECTS

See package labeling.

MONITORING

Efficacy

- Physical Findings
 - Dupuytren’s contracture
 - Improvement in range of motion in affected hand(s)
 - Peyronie’s disease
 - Improvement in curvature deformity
 - Decreased pain during erection.

CONTRAINDICATIONS

Xiaflex® is contraindicated in:

- Treatment of Peyronie’s plaque involving the penile urethra due to potential risk to this structure.
- History of hypersensitivity to Xiaflex® or to collagenase used in other therapeutic applications.

BLACK BOX WARNING

CORPORAL RUPTURE (PENILE FRACTURE) OR OTHER SERIOUS PENILE INJURY IN THE TREATMENT OF PEYRONIE’S DISEASE:

Corporal rupture (penile fracture) was reported as an adverse reaction in 5 of 1044 (0.5%) XIAFLEX[™] treated patients in clinical studies. In other XIAFLEX[™]-treated patients (9 of 1044; 0.9%), a combination of penile ecchymoses or hematoma, sudden penile detumescence, and/or a penile “popping” sound or sensation was reported, and in these cases, a diagnosis of corporal rupture cannot be excluded.

Severe penile hematoma was also reported as an adverse reaction in 39 of 1044 (3.7%) XIAFLEX[™]-treated patients. Signs or symptoms that may reflect serious penile injury should be promptly evaluated to assess for corporal rupture or severe penile hematoma which may require surgical intervention.

Because of the risks of corporal rupture or other serious penile injury, Xiaflex® is available for the treatment of Peyronie’s disease only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XIAFLEX[™]REMS Program.

CLINICAL EVIDENCE

DUPUYTREN’S CONTRACTURE

The efficacy of 0.58 mg of XIAFLEX® was evaluated in two randomized, double-blind, placebo controlled, multi-centered trials in 374 adult patients with Dupuytren’s contracture (Studies 1 and 2).

At study entry, patients had: (1) 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 (2) a positive “tabletop test” defined as the inability to simultaneously place the affected finger(s) and palm flat against a tabletop.

Patients who had surgical treatment (e.g., fasciectomy, fasciotomy) on the selected primary joint within 90 days before the first injection of study medication and patients on anticoagulation medication (except for up to 150 mg of aspirin per day) within 7 days before the first injection of study medication were excluded.

The cord affecting the selected primary joint received up to 3 injections of 0.58 mg of Xiaflex® or placebo on Days 0, 30, and 60. About 24 hours after each injection of study medication, if needed, the investigator manipulated (extended) the treated finger in an attempt to facilitate rupture of the cord (finger extension procedure).

Following manipulation, patients were fitted with a splint, instructed to wear the splint at bedtime for up to 4 months, and instructed to perform a series of finger flexion and extension exercises each day.

RESULTS: In Studies 1 and 2, the primary endpoint was to evaluate the proportion of patients who achieved a reduction in contracture of the selected primary joint (MP or PIP) to within 0° to 5° of normal, 30 days after the last injection of that joint on Days 30, 60, or 90 (after up to 3 injections). The results demonstrate a greater proportion of XIAFLEX™-treated patients compared to placebo treated patients achieved the primary endpoint. The proportion of patients who achieved a contracture reduction of the primary joint to 0° to 5° after the first injection was 39% and 1% in Study 1 and 27% and 5% in Study 2 in the Xiaflex® and placebo groups respectively. XIAFLEX™-treated patients, compared to placebo-treated patients, showed a greater increase from baseline in the range of motion of MP and PIP joints.

PEYRONIE’S DISEASE

The efficacy of Xiaflex® was evaluated in two randomized, double-blind, placebo-controlled, multi-centered trials in 832 adult males with Peyronie’s disease (Studies 1 and 2). At study entry, patients had penile curvature deformity of at least 30 degrees in the stable phase of Peyronie’s disease. Patients 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 (98%) patients. In these trials, patients were given up to 4 treatment cycles of Xiaflex® or placebo (weeks 0, 6, 12, 18) and were followed in a non-treatment follow-up period (weeks 24 -52). In each treatment cycle, two injections of Xiaflex® or two injections of placebo were administered 1 to 3 days apart. A penile modeling procedure was performed on patients at the study site 1 to 3 days after the second injection of the cycle. The treatment cycle was repeated at approximately six-week intervals for up to three additional times, for a maximum of 8 total injection procedures and 4 total modeling procedures. In addition, patients were instructed to perform penile modeling at home for six weeks after each treatment cycle.

Before the first dose of study drug was administered, eligible subjects were stratified by the degree of curvature deformity (30 to 60 degrees, and 61 to 90 degrees) and then randomized into two treatment groups to receive either Xiaflex® or placebo in a 2:1 ratio. The efficacy population (modified intent-to-treat (mITT) population) comprised a total of 612 intent-to-treat subjects who had both a curvature deformity measurement and a PDQ assessment at baseline, and at one or more subsequent time points in Studies 1 and 2 and had engaged in vaginal intercourse within 3 months prior to each PDQ assessment.

In Studies 1 and 2, the co-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 of the PDQ.

The Bother domain score is a composite of the following: concern about erection pain, erection appearance, and the impact of Peyronie's disease on intercourse and on frequency of intercourse.

RESULTS: Xiaflex® treatment significantly improved penile curvature deformity in patients with Peyronie's disease compared with placebo. The improvement in curvature deformity was numerically similar among subjects with baseline curvature deformity from 30 to 60 degrees and those with curvature deformity from 61 to 90 degrees. Xiaflex® significantly reduced patient-reported bother associated with Peyronie's disease compared with placebo. The reduction in the bother domain score was numerically similar between patient groups stratified by degree of baseline curvature deformity (30 to 60 degrees, and 61 to 90 degrees). There were no clinically meaningful differences in the mean percent improvement in curvature deformity or mean reduction in the bother domain score following treatment with XIAFLEX® based on the severity of baseline erectile dysfunction or concomitant phosphodiesterase type 5 (PDE5) inhibitor use.

BACKGROUND

DUPUYTREN'S CONTRACTURE

Dupuytren disease is predominantly a benign, slowly progressive myofibroblastic disease that affects the palmar and digital fascia of the hand that can lead to contracture deformities. The most commonly affected fingers are the fourth (ring) and fifth (small or pinky) digits.

Pathologically, Dupuytren's contracture is characterized by fibroblastic proliferation and disorderly collagen deposition with fascial thickening. Formation of a nodule or nodules occurs in the early proliferative stage of the disease and is the pathognomonic lesion of Dupuytren's contracture. The transformation of normal fascial bands is what causes the contracture of the hand. Central cords originate from the pre-tendinous bands and can cause pitting edema in the hand and MCP joint contracture. Natatory cords are responsible for webspace contractures. Spiral cords are most important as the disease process and can cause PIP contracture. Joint stiffness and loss of full extension develops typically over decades but can vary depending on patient demographics and risk factors.

The cause of Dupuytren's contracture is unknown; Important factors include genetics, ethnicity, sex, and age and may include certain environmental factors and other diseases. Dupuytren contracture is most commonly found in patients

with Northern European/Scandinavian descent. It is uncommon in patients who are South European and South American populations and rarely seen in patients who are African and Asian. In Asian populations, the palm is more likely to be involved than the digits and often goes unnoticed. Males are at risk of being diagnosed with Dupuytren's contracture than women (2:1 ratio) and are more likely to be at risk for severe disease.

Dupuytren's contracture has been observed in association with the following conditions and habits cigarette smoking and alcohol consumption; diabetes mellitus; palmar fasciitis; repetitive handling tasks of vibration. There are also genetic factors involved in Dupuytren disease. In a study involving patients from the Netherlands, Germany, and the United Kingdom, six of nine genetic loci found associated with genetic susceptibility to Dupuytren's disease contained genes encoding proteins in the Wnt-signaling pathway.

In about 50-70% of patients disease may stabilize or regress.

PEYRONIE'S DISEASE

Peyronie's disease is a penile abnormality characterized by the fibrosis of tunica albuginea that may cause pain, deformity, erectile dysfunction, and/or distress. It is an acquired inflammatory disorder that causes microvascular trauma to the penile shaft; this can cause penis to buckle in the erect or semi-erect state. The repetitive minor trauma to the penis initiates a cascade involving significant extravascular protein deposition, fibrin trapping, macrophage recruitment, cytokine overexpression, and release of elastase that leads to the changes of the tunical collagen from type 1 to predominantly type 3 collagen. The trauma is also associated with changes in the tunica's elastin leading to scarring and inelasticity. The natural degradation of fibrin may be altered secondarily to proteins, such as transforming growth factor 1 and plasminogen activator inhibitor type 1, leading to irregular tunical healing. Excess fibrin deposition in response to microvascular injury and upregulation of transforming growth factor (TGF)-1 results in one or more areas of plaque formation.

American Urology Association maintains the diagnosis and treatment guidelines for Peyronie's disease. Peyronie's Disease is known to have two types of disease states, which are active and stable; it is useful to identify if the patient has active or stable disease because it can help determine the type of treatment the patient receives benefit based on if the symptoms are dynamic or stable.

Active Disease: It is characterized by dynamic and changing symptoms. The defining symptoms of the active stage can be penile and/or glandular pain and discomfort with or without erection. Distress may be present in response to pain and to progressive deformity. Erectile function may be intact or may be compromised by pain and/or developing deformity.

Stable Disease: In stable disease, symptoms have been clinically quiescent or unchanged for at least three months based on patient reports or clinical documentation. Pain with or without erection may be present but less common. In stable disease, the deformity is no longer progressing. Plaque can be palpated or documented on ultrasound. The typical patient presents with a dorsal, dorso-lateral, or ventral penile deformity. Erectile function may be compromised by pain and/or deformity or may be reduced because of symptoms of ED not related to deformity or pain. It is reported that ED may be present in up to 33% of PD patients with greater than 50% of patients reporting that ED predated the onset of PD symptoms.

Peyronie's disease symptoms are variable. In some patients they can resolve without treatment. Data suggests that for many or most patients pain will resolve over time without intervention. Curvature and other types of deformities are much less likely to improve and may require treatment if it compromises sexual function and/or is the source of patient or partner distress.

CODING

Note: *The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that may be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.*

CPT® is a registered trademark of the American Medical Association.

CPT Code	Description
20527	Injection, enzyme (e.g., collagenase), palmar fascial cord (i.e., Dupuytren's contracture)
20550	Injection(s); single tendon sheath, or ligament, aponeurosis (e.g., plantar "fascia")
26341	Manipulation, palmar fascial cord (i.e., Dupuytren's cord), post enzyme injection (e.g., collagenase), single cord

54200	Injection procedure for Peyronie disease;
54205	Injection procedure for Peyronie disease; with surgical exposure of plaque

HCPSC Code	Description
J0775	Injection, collagenase, clostridium histolyticum, 0.01 mg

ICD-10 Codes	Description
N48.6	Induration penis plastica
M72.0	Palmar fascial fibromatosis [Dupuytren]

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change.

For Jefferson Health Plans EverWell and Jefferson Health Plans CHIP products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2026 Annual review. Revisions to Dosage & Administration, Monitoring, Contraindications and Background Sections. References updated.	D	09/18/2025
2025 Annual Review. Additions to Dosage and Administration, Contraindications and Risk Factor and Side Effects sections. References updated.	D	09/18/2025
2024 Annual Review. References updated.	C	09/01/2023
2023 Annual Review. References Updated; Initial Criteria Reformatted.	C	09/01/2023
2022 Annual Review. The following sections of the policy were updated: Prior Authorization Criteria, Dosing and Administration, Risk Factors. A new section was added for Clinical Trials. Policy version changed from "A" to "B".	B	10/01/2022
New policy.	A	08/01/2021

REFERENCES

1. Walthall, J., Anand, P., Rehman, UH. Dupuytren's Contracture. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK526074/#article-20763.s16/>. Published Nov 2, 2020. Updated Feb 26, 2023. Accessed July 10, 2024.
2. Aggarwal, R., Blazar, PE. Dupuytren's Contracture. In: Post TW, ed. *UpToDate*. Waltham, MA: UpToDate, Inc; 12/14/2022. https://www.uptodate.com/contents/dupuytren-s-contracture?search=dupuytren&source=search_result&selectedTitle=1-27&usage_type=default&display_rank=1. Last update 4/8/2025 , Current through June 2025.
3. Brant WO., Bella AJ., Lue TF. Peyronie's Disease: Diagnosis and medical management. In: Post TW, ed. *UpToDate*. Waltham, MA: UpToDate, Inc; September 27,2023, Current through June 2026.

4. Xiaflex®. *Endo Pharma*. <https://www.xiaflex.com/>. Published Aug 2019. Accessed July 15, 2026.
5. Xiaflex® Prescribing Information.
[FDA.gov. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125338s109lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125338s109lbl.pdf). Published 2010. Updated March 2026. Accessed July 2026.