



**POLICY:** Xiaflex® (collagenase clostridium histolyticum for intralesional injection – Endo Pharmaceuticals)

**APPROVAL DATE:** 01/30/2019

### OVERVIEW

Xiaflex is a combination of bacterial collagenases indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord, and for the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.<sup>1</sup>

Dupuytren's contracture is a disorder of the palmar and digital fascia of the hand.<sup>2</sup> Abnormal deposition of collagen initially causes nodules in the palm of the hand, which may thicken and lead to formation of cords. As the disease progresses, the cords gradually contract, leading to flexion deformities of the fingers. Joint contractures are typically painless but are associated with significant functional impairment. The exact etiology of Dupuytren's contracture is unknown, although a number of risk factors have been reportedly associated with the condition, including alcohol, smoking, diabetes, epilepsy, thyroid disorders, and trauma. Prevalence varies widely by age and geographical location but is most common among Caucasian males greater than 50 years of age. Surgical intervention, either by open partial fasciectomy or percutaneous needle fasciotomy, is the mainstay of therapy for severe cases. However, surgery may be associated with complications including neurovascular injury or hematoma, and recurrence after surgery is common. In clinical studies of Dupuytren's contracture, patients were eligible to participate if they had a finger contraction of 20 degrees to 100 degrees in a metacarpophalangeal (MP) joint or 20 degrees to 80 degrees in a proximal interphalangeal (PIP) joint.<sup>1</sup>

Peyronie's disease is an acquired penile abnormality caused by fibrosis of the tunica albuginea, which may lead to pain, deformity, erectile dysfunction, and/or distress.<sup>3</sup> It is thought that 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. Peyronie's disease has a variable course; for most patients, pain will resolve over time without intervention, but curvature deformities are less likely to resolve without treatment. Intralesional therapy with Xiaflex may be used to treat curvature associated with Peyronie's disease and is supported by American Urological Association guidelines (2015).

### POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Xiaflex. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration specified below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Xiaflex, approval requires it to be administered by a healthcare provider with expertise in the condition being treated.

Medical benefit coverage is not recommended for Xiaflex for cosmetic uses.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

### FDA-Approved Indications

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**1. Dupuytren's Contracture.** Approve Xiaflex for 3 months in patients meeting all of the following criteria (A, B, C, and D):

- A) The patient is  $\geq 18$  years of age; AND
- B) At baseline (prior to initial injection of Xiaflex), the patient had contracture of a metacarpophalangeal (MP) or proximal interphalangeal (PIP) joint of at least 20 degrees; AND
- C) The patient will not be treated with more than a total of three injections (maximum) per affected cord; AND
- D) Xiaflex is administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of Dupuytren's contracture.

**Dosing.**<sup>1</sup> Approve if the dose meets all of the following:

- A) The dose is 0.58 mg per injection into an affected cord; AND
- B) A maximum of two cords (up to 1.16 mg) are injected per treatment visit. Note: If there are other affected cords in the same hand, treatment may be administered to those on a different day; AND
- C) For each affected cord, subsequent doses are administered no sooner than 4 weeks following the previous Xiaflex injection.

For treatment of Dupuytren's contracture, up to three cycles of Xiaflex may be administered per affected cord, at approximately 4-week intervals.<sup>1</sup> Therefore, an approval duration of 3 months allows adequate duration for the maximum number of recommended cycles. Two injections may be given per treatment session. If there are other affected cords, treatment may be administered to those on a different day.

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**2. Peyronie's Disease.** Approve Xiaflex for 6 months if the patients meets ALL of the following (A, B, C, and D):

- A) The patient is  $\geq 18$  years of age; AND
- B) The patient meets ONE of the following (i or ii):
  - i. At baseline (prior to use of Xiaflex), the patient has a penile curvature deformity of at least 30 degrees; OR
  - ii. In a patient who has received prior treatment with Xiaflex, the patient has a penile curvature deformity of at least 15 degrees; AND
- C) The patient has not previously been treated with a complete course (8 injections) of Xiaflex for Peyronie's disease; AND
- D) The medication is being administered by a healthcare provider experienced in the treatment of male urological diseases.

**Dosing.**<sup>1</sup> Approve the following dosing:

- A) Up to a total of eight 0.58 mg injections (Note: this is enough Xiaflex to treat with four dosing cycles, each consisting of two 0.58 mg injections given 1 to 3 days apart).  
Note: For a patient who has already received one or more injections of Xiaflex, approve the duration requested up to the amount needed to complete one course therapy (e.g., a patient who has received 3 injections may be approved for 5 additional injections to complete one course of therapy); AND
- B) Cycles are separated by at least 6 weeks from the previous Xiaflex cycle.

In the pivotal studies, patients were required to have a penile deformity of at least 30 degrees.<sup>1</sup> For treatment of Peyronie's disease, up to four cycles of Xiaflex may be administered, given at approximately 6-week intervals. The safety of more than one treatment course (8 injections) is unknown.

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### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Xiaflex has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Cosmetic Uses (e.g., cellulite of buttocks).** Cosmetic use is not recommended for coverage as this indication is excluded from coverage in a typical medical benefit.
- 2. Retreatment (i.e., treatment beyond three injections per affected cord for those with Dupuytren's Contracture or beyond eight injections for Peyronie's Disease).** For Dupuytren's contracture, injections and finger extension procedures may be administered up to three times per cord.<sup>1</sup> However, this does not limit treatment of additional cords. For Peyronie's disease, the safety of more than one treatment course (8 injections) is unknown.
- 3.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

- Xiaflex® [prescribing information]. Malvern, PA: Endo Pharmaceuticals, Inc; June 2018.
- Brazzelli M, Cruickshank M, Tassie E, et al. Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation. Southampton (UK): NIHR Journals Library; 2015 Oct. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK326596/>. Accessed on January 2, 2019.
- Nehra A, Alterowitz R, Culkin D, et al. Peyronie's disease: AUA guideline. *J Urol*. 2015;194(3):745-753.

### HISTORY

Type of Revision	Summary of Changes*	Approval Date
New policy	--	01/30/2019