Reference number(s)
2309-A

STANDARD MEDICARE PART B MANAGEMENT

XIAFLEX
(collagenase clostridium histolyticum)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

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

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:

A. Dupuytren's contracture: Chart notes or medical record indicating the affected joint, contracture, and a positive table top test (for new starts and continuation) and the number of injections the member has received (for continuation only).
B. Peyronie's disease: Chart notes or medical record indicating palpable plaque, curvature, intact erectile function (for new starts and continuation) and the number of injections the member has received (for
C. continuation only).

III. PRESCRIBER SPECIALTIES

A. Dupuytren's contracture: The medication must be administered by a healthcare provider experienced in injection procedures of the hand and in the treatment of Dupuytren's contracture.
B. Peyronie's disease: The medication must be administered by a healthcare provider experienced in the treatment of urological disease and who has completed the Xiaflex REMS program requirements.

IV. EXCLUSIONS

Coverage will not be provided for cosmetic use (e.g., cellulite reduction treatment).

V. CRITERIA FOR INITIAL APPROVAL

A. Dupuytren's contracture

Authorization of 6 months may be granted for the treatment of Dupuytren's contracture when the following criteria are met:

1. The member has a finger flexion contracture with a palpable cord in a metacarpophalangeal joint or a proximal interphalangeal joint.
2. The contracture is at least 20 degrees.
3. The member had a positive tabletop test, defined as the inability to simultaneously place the affected finger(s) and palm flat against a table.
4. The member will receive a maximum of 3 injections per cord (4 weeks apart).

B. Peyronie's disease

Authorization of 12 months may be granted for the treatment of Peyronie's disease when the following criteria are met:

1. Xiaflex is prescribed for a member 18 years of age or older with stable Peyronie's disease.
2. The member has a palpable plaque and curvature deformity of at least 30 degrees and less than 90 degrees with intact erectile function (with or without medication) at the start of therapy.
3. The member will receive a maximum of one treatment course or a maximum of 8 injections total, including any injections the member has received for any previous treatment.

VI. CONTINUATION OF THERAPY

Authorization for 6 months (Dupuytren's contracture) or 12 months (Peyronie's disease) to complete a treatment course may be granted for all members (including new members) who are continuing with Xiaflex therapy when the following criteria are met:

A. Xiaflex is requested for treating a diagnosis or condition enumerated in Section V.
B. For Dupuytren's contracture, the member is continuing with a treatment course for the same cord and has received less than 3 injections total. Requests for treatment of a new cord or recurrence in a previously treated cord must meet initial criteria for approval.
C. For Peyronie's disease, the member has not yet completed treatment with the maximum of 8 injections, including any injections the member has received for any previous treatment and curvature deformity is 15 degrees or more.

VII. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Xiaflex.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. Peyronie's Disease: AUA Guideline
4. Injectable collagenase clostridium histolyticum for Dupuytren's contracture

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Xiaflex are covered.

VIII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for Dupuytren's contracture can be found in a study published in 2009 by the CORD I study group (Hurst et al). The study enrolled 308 patients with joint contractures of 20 degrees or more in this prospective, randomized, double-blind, placebo-controlled, multicenter trial. The primary metacarpophalangeal or proximal interphalangeal joints of these patients were randomly assigned to receive up to three injections of collagenase clostridium histolyticum (at a dose of 0.58 mg per injection) or placebo in the contracted collagen cord at 30-day intervals. One day after injection, the joints were manipulated. The primary end point was a reduction in contracture to 0 to 5 degrees of full extension 30 days after the last injection. Twenty-six secondary end points were evaluated, and data on adverse events were collected. Collagenase treatment significantly improved outcomes. More cords that were injected with collagenase than cords injected with placebo met the primary end point (64.0% vs. 6.8%, $P<0.001$), as well as all secondary end points ($P\leq0.002$). Overall, the range of motion in the joints was significantly improved after injection with collagenase as compared with placebo (from 43.9 to 80.7 degrees vs. from 45.3 to 49.5 degrees, $P<0.001$). The most commonly reported adverse events were localized swelling, pain, bruising, pruritus, and transient regional lymph-node enlargement and tenderness. Three treatment-related serious adverse events were reported: two tendon ruptures and one case of complex regional pain syndrome. No significant changes in flexion or grip strength, no systemic allergic reactions, and no nerve injuries were observed.
According to the prescribing information, four weeks after the initial Xiaflex injection and finger extension procedure, if a contracture remains, the cord may be re-injected with a single dose of 0.58 mg of Xiaflex and the finger extension procedure may be repeated. Injections and finger extension procedures may be administered up to 3 times per cord at approximately 4-week intervals.

Support for using Xiaflex for Peyronie's disease can be found in a guideline published by the American Urological Association. The AUA states clinicians may administer intralesional collagenase clostridium histolyticum in combination with modeling by the clinician and by the patient for the reduction of penile curvature in patients with stable Peyronie's disease, penile curvature >30° and <90°, and intact erectile function (with or without the use of medications).
According to the prescribing information, a treatment course consists of a maximum of 4 treatment cycles. Each treatment cycle consists of two XIAFLEX injection procedures and one penile modeling procedure [see Dosage and Administration (2.2)]. The second XIAFLEX injection procedure is performed 1 to 3 days after the first. The penile modeling procedure is performed 1 to 3 days after the second injection of the treatment cycle. The interval between treatment cycles is approximately 6 weeks. The treatment course therefore, consists of a maximum of 8 injection procedures and 4 modeling procedures.

IX. REFERENCES

1. Xiaflex [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; August 2021.
2. Hurst LC, Badalamente MA, Hentz VR, et al. Injectable collagenase clostridium histolyticum for Dupuytren's contracture. N Engl J Med. 2009;361(10):968-979.
3. Nehra A, Alterowitz R, Culkin DJ, et al. Peyronie's Disease: AUA Guideline. *J Urol.* 2015;194(3):745-753.