Clinical Policy: Collagenase Clostridium Histolyticum (Xiaflex)

Reference Number: ERX.SPA.210
Effective Date: 01.11.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Collagenase clostridium histolyticum (Xiaflex®) is a combination of bacterial collagenases.

FDA Approved Indication(s)
Xiaflex is indicated for the treatment of:
- Adult patients with Dupuytren's contracture (DC) with a palpable cord
- Adult men with Peyronie's disease (PD) with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Xiaflex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Dupuytren's Contracture (must meet all)**:**
1. Diagnosis of DC with a palpable cord;
2. Prescribed by or in consultation with a healthcare provider experienced in injection procedures of the hand and in the treatment of DC;
3. Age ≥ 18 years;
4. Member has not received surgical treatment (e.g., fasciectomy, fasciotomy) on the selected primary joint within the last 90 days;
5. If two injections (two vials) are requested, they are for one of the following (a or b):
   a. One cord affecting two joints in the same finger;
   b. Two cords affecting two joints in the same hand;
6. Dose does not exceed 0.58 mg per injection (one vial per injection).

Approval duration: 3 months (up to 2 injections)

B. Peyronie's Disease (must meet all)**:**
1. Diagnosis of PD with both of the following (a and b):
   a. Palpable plaque;
   b. Curvature deformity of ≥ 30 degrees at the start of therapy;
2. Prescribed by or in consultation with a healthcare provider experienced in the treatment of male urological diseases;
3. Age ≥ 18 years;
4. Dose does not exceed 0.58 mg per injection (one vial per injection).

Approval duration: 3 months (up to 2 injections)

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Dupuytren's Contracture (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Last treatment was ≥ 4 weeks ago;
3. Member has not received more than two total injections per affected cord;
4. Request is for one or both of the following (a or b):
   a. Metacarpophalangeal (MP) or proximal interphalangeal (PIP) contracture remains in affected cord since previous injection and the contracture is > 5 degrees;
   b. A different MP or PIP contracture will be injected;
5. If two injections (two vials) are requested, use is for one of the following (a or b):
   a. One cord affecting two joints in the same finger;
   b. Two cords affecting two joints in the same hand;
6. Member has not received surgical treatment (e.g., fasciectomy, fasciotomy) on the selected primary joint within the last 90 days;
7. If request is for a dose increase, new dose does not exceed 0.58 mg per injection (one vial per injection).

Approval duration: 3 months (up to 2 injections, total of 3 injections per affected cord)

B. Peyronie's Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Documented curvature deformity of ≥ 15 degrees remaining since last treatment cycle;
3. Last treatment cycle was ≥ 6 weeks ago;
4. Member has received < 4 treatment cycles (i.e., < 8 injections [2 injections per cycle]);
5. If request is for a dose increase, new dose does not exceed 0.58 mg per injection (one vial per injection).

Approval duration: 3 months (up to 2 injections)

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 3 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DC: Dupuytren's contracture
FDA: Food and Drug Administration
MP: metacarpophalangeal joint
PD: Peyronie's disease
PIP: proximal interphalangeal joint

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Peyronie's plaques that involve the penile urethra; hypersensitivity
- Boxed warning(s): corporal rupture (penile fracture) or other serious penile injury in the treatment of Peyronie's disease

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DC	0.58 mg per injection intralesionally into a palpable cord with a contracture of a MP joint or a PIP joint. Injections (0.58 mg) and finger extension procedures (24 hours later) may be administered up to 3 times per cord at approximately 4-week intervals. Up to 2 injections in the same hand may be performed during a treatment visit. Two palpable cords affecting 2 joints may be injected or 1 palpable cord affecting 2 joints in the same finger may be injected at 2 locations during a treatment visit. If a patient has other palpable cords with contractures of the MP or PIP joints, these cords may be injected at other treatment visits approximately 4 weeks apart.	0.58 mg/dose
PD	0.58 mg per injection intralesionally administered into a Peyronie's plaque; if more than one plaque is present, inject into the plaque causing the curvature deformity. 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. 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 six weeks. The treatment course therefore, consists of a maximum of 8 injection procedures and 4 modeling procedures. If the curvature deformity is less than 15 degrees after the first, second or third treatment cycle, or if the healthcare provider determines that further treatment is not clinically indicated, then the subsequent treatment cycles should not be administered. The safety of more than one treatment course of Xiaflex is not known.	0.58 mg/dose

VI. Product Availability

Lyophilized powder for reconstitution (single-use glass vials): 0.9 mg of collagenase clostridium histolyticum

VII. References

1. Xiaflex Prescribing Information. Malvern, PA: Endo Pharmaceuticals, Inc.; November 2019. Available at https://www.xiaflex.com/. Accessed April 12, 2021.
2. Schulze SM and Tursi JP. Postapproval clinical experience in the treatment of Dupuytren's contracture with collagenase clostridium histolyticum (CCH): the first 1,000 days. Hand. 2014; 9: 447-458.
3. Collagenase Drug Monograph. Clinical Pharmacology. Available at: http://www.clinicalpharmacology-ip.com. Accessed April 12, 2021.
4. Nehra A, Alterowitz R, Culkin DJ, et al. Peyronie's Disase: American Urological Association (AUA) Guideline, 2015. Available at: https://www.auanet.org/guidelines/guidelines/peyronies-disease-guideline. Accessed May 11, 2021.
5. Manka MG, White LA, Yafi FA, et al. Comparing and Contrasting Peyronie's Disease Guidelines: Points of Consensus and Deviation. J Sex Med 2021; 18: 363-375.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.16	01.17
4Q17 Annual Review Converted to new template. DC and PD: Added age restriction as safety and effectiveness of Xiaflex in pediatric patients < 18 years old have not been established. Added max dose. Modified approval duration to allow up to 2 injections within a 3 month period. DC: Added requirement that member has not received surgical treatment (e.g., fasciectomy, fasciotomy) on the selected primary joint within the last 90 days per clinical trials described in PI. PD: Removed prescriber requirement related to completion of training for use of Xiaflex since Xiaflex is available for the treatment of PD only through Xiaflex REMS program.	09.26.17	11.17
3Q 2018 annual review: Dupuytren's contracture – removed "table top test" and flexion contracture degree requirements (clinical trial inclusion criteria) as specialist involvement is required; references reviewed and updated.	04.30.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	04.17.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.12.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	04.12.21	08.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.