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PHARMACY/MEDICAL POLICY – 5.01.595

Injectable Clostridial Collagenase for Fibroproliferative Disorders

BCBSA Ref. Policy:	5.01.19	
Effective Date:	Apr. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Mar. 24, 2025	None
Replaces:	5.01.19	

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Dupuytren's contracture is a hand condition where knots of tissue form beneath the skin of the palm. Over time these knots create a cord, which pulls on one or more fingers. The cord is inflexible, causing the fingers to curl into a bent position. The ring finger and pinky fingers are usually affected, with the middle finger affected less often. It's rare that the index finger and thumb are affected. The condition advances slowly and usually starts with a thickening of skin on the palm. A knot then forms, followed by another and another. Men older than 50 and of northern European descent have the highest incidence of Dupuytren's contracture. There are a few treatment options, one of which calls for injecting a specific enzyme (clostridial collagenase) into the cord. The enzyme makes the cord softer, allowing it to stretch and break as a doctor straightens the fingers. The enzyme also has been used to try to treat other conditions. This policy describes the conditions for which injections of this enzyme may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Indication	Medical Necessity
Dupuytren's contracture	**Injectable clostridial collagenase (Xiaflex) may be considered medically necessary for the treatment of Dupuytren's contracture in adult individuals with a palpable cord, for up to 3 injections at intervals of at least 30 days.** • Physicians should treat no more than 2 joints in the same hand per treatment visit for Dupuytren's contracture, consistent with FDA labeling.
Peyronie's disease	**Injectable clostridial collagenase (Xiaflex) may be considered medically necessary in adult individuals for the treatment of Peyronie's disease for a maximum of 4 treatment cycles (each cycle consists of 2 injection procedures) (see Table 2) when the following criteria are met:** • The individual has a palpable plaque **AND** • Has a curvature deformity of at least 30 degrees at the start of therapy, consistent with FDA labeling **Note:** The treatment of sexual dysfunction is excluded under many benefit plans, regardless of the underlying condition. Therefore, use of Xiaflex for Peyronie's disease may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).

Indication	Investigational
Adhesive capsulitis **Other indications**	**Injectable clostridial collagenase (Xiaflex) is considered investigational for all other indications including, but not limited to, adhesive capsulitis.**

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for Xiaflex may be approved up to 12 months.** **All other reviews for Xiaflex may be approved up to 3 months for the treatment of Dupuytren's contracture.** **All other reviews for Xiaflex may be approved up to 6 months for the treatment of Peyronie's disease.**
Re-authorization criteria	**Re-authorization of Xiaflex for the treatment of Dupuytren's contracture for the same palpable cord is considered investigational.** **Re-authorization of Xiaflex for the treatment of Dupuytren's contracture for a different palpable cord will be reviewed as a new request.** **Re-authorization of Xiaflex for the treatment of Peyronie's disease is considered investigational.**

Documentation Requirements
The individual's medical records submitted for review should document that medical necessity criteria are met. The record should include clinical documentation of: • Diagnosis/condition • History and physical examination documenting the severity of the condition

Coding

Code	Description
CPT	
20527	Injection, enzyme (e.g., collagenase), palmar fascial cord (ie, Dupuytren's contracture)

Code	Description
26341	Manipulation, palmar fascial cord (ie, 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
54235	Injection of corpora cavernosa with pharmacologic agent(s) (e.g., papaverine, phentolamine)
HCPCS	
J0775	Injection, collagenase clostridium histolyticum, 0.01 mg

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Individual Subgroups

For individuals with Peyronie's Disease, the 2015 American Urological Association clinical practice guidelines noted that clinicians should bear in mind that based on the inclusion and exclusion criteria for the IMPRESS trials, the use of collagenase treatment in certain individual subgroups or clinical situations has not been sufficiently evaluated. These subgroups are individuals with hourglass deformity, ventral curvature, calcified plaque, or plaque located proximal to the base of the penis.

Benefit Application

This is an office-based procedure, and general anesthesia is not required**.**

Some plans may require prior authorization before injection of collagenase clostridium histolyticum. For questions about benefit information, providers should contact customer service using the telephone number on the back of the member's identification card.

Many benefit plans exclude the diagnosis and treatment of sexual dysfunctions, regardless of origin or cause; surgical, medical, or psychological, including drugs, medications, or implants;

and any direct or indirect complications and aftereffects thereof. Please refer to the applicable benefit plan to determine benefit availability and the terms, conditions, and limitations of coverage.

Evidence Review

Description

Clostridial collagenase is a bacterial collagenase, derived from Clostridium histolyticum, which has been evaluated for the treatment of fibroproliferative disorders such as Dupuytren's contracture, Peyronie's disease, and adhesive capsulitis.

Background

Fibroproliferative Disorders

Fibrotic tissue disorders, characterized by excessive collagen deposits, can affect the musculoskeletal system, causing pain and limiting movement and reducing joint range of motion. Examples of fibroproliferative disorders include Dupuytren's disease, Peyronie's disease, and adhesive capsulitis. The mechanisms that contribute to the pathology of fibroproliferative disorders are poorly understood, though likely the etiology is multifactorial and includes genetic, environmental, and immunologic components.

Dupuytren's Disease

Dupuytren's disease is a progressive disorder of the palmar and digital fascia of the hand, leading to flexion deformity in up to 40% of those affected. Prevalence increases with age, from about 12% at age 55 years to 29% at 75 years.[1] Disease that has progressed to the point of limited hand function or digital flexion of 30 degrees or more is generally treated with surgery.

Treatment

The standard of care for Dupuytren's disease is surgery, most commonly open fasciectomy. Other surgical procedures are percutaneous fasciotomy and needle fasciotomy. Surgery is recommended in individuals with functional impairment and metacarpophalangeal joint contractures of 30° or more. There is no effective pharmacotherapy.

Peyronie's Disease

Peyronie's disease is characterized by deformities, including curvature, shortening, indentation and narrowing, in an erect penis.[2] Men with Peyronie's disease may also have erectile dysfunction and penile pain, along with anxiety and depression. Peyronie's disease occurs most commonly in middle-aged men (45-60 years), although up to 10% of cases involve men younger than 40 years; prevalence is estimated to be 9%, though underreporting is likely. Comorbidities associated with Peyronie's disease include diabetes and cardiovascular disease. Individuals with early-stage disease may be managed medically, though the effectiveness of many non-surgical treatments is unclear. Later disease can be treated surgically.

Treatment

The goal of treatment is to reduce pain and maintain sexual function. Treatments in early stages (before calcification) include vitamin E or para-aminobenzoate tablets (e.g., Potaba), although studies of oral therapies have demonstrated inconsistent benefit. Intralesional injection therapy consisting of injection of interferon-α-2b or calcium channel-blockers (e.g., verapamil) is the current standard of therapy.[28] Surgical procedures involve the excision of hardened tissue and skin graft, the removal or pinching (plication) of tissue opposite the plaque to reduce curvature (the Nesbit procedure), penile implant, or a combination of these.

Adhesive Capsulitis

The prevalence of adhesive capsulitis (commonly referred to as frozen shoulder) is estimated at 2% to 3% in the general population and increases with advancing age. Additionally, adhesive capsulitis is more common in people with diabetes or thyroid disease and among women.[3] Adhesive capsulitis is treated with physical therapy and mobilization in combination with analgesics or nonsteroidal anti-inflammatory drugs. Corticosteroid injection is used with caution.

Clostridial Collagenase

Injection with clostridial collagenase is intended to provide a nonoperative treatment option for fibroproliferative disorders. Clostridial collagenase histolyticum is an enzyme produced by the bacterium Clostridium histolyticum, which has the physiologic effect of breaking down collagen. It has been developed and marketed pharmacologically as a treatment for disorders associated with collagen overdevelopment.

Summary of Evidence

For individuals with Dupuytren's contracture who receive clostridial collagenase injection(s), the evidence includes systematic reviews, randomized controlled trials (RCTs), and nonrandomized comparative studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Findings from randomized and nonrandomized studies comparing clostridial collagenase to surgery suggest similar benefits and harms. However, limited data on the most clinically meaningful outcomes preclude reaching strong conclusions based on their findings. Findings from systematic reviews of randomized, placebo-controlled trials, nonrandomized controlled studies and noncomparative studies consistently demonstrated clinically important benefits for clostridial collagenase. However, data on quality of life have not yet emerged. Rates of mild local adverse events, including local swelling, contusion and pain, are generally high, but serious adverse events have been rare. In comparative studies, the risk of contracture recurrence appears to increase over time regardless of treatment group. However, as recurrence rates vary by the definition of recurrence (contracture greater than 20 degrees, or 30 degrees, and/or when further intervention is needed), standardization of the definition is still needed. Although clostridial collagenase offers the potential benefit of less-invasive treatment for Dupuytren's contracture with clinically meaningful benefits and a low risk of major complications, important gaps in the evidence base exist related to treatment durability and impact on quality of life. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have Peyronie's disease who receive local clostridial collagenase injection(s), the evidence includes a systematic review, RCTs and numerous nonrandomized comparative studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The available double-blind, placebo-controlled randomized trials have demonstrated short-term improvement in penile curvature and reductions in self-reported distress from symptoms related to Peyronie's disease. However, evidence demonstrating

improvements in health outcomes is lacking, as are studies comparing clostridial collagenase with other therapies for Peyronie's disease. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. Despite the important uncertainties that remain in the peer-reviewed scientific literature limiting determination of the effect of the technology on net health outcomes; the 2010 FDA labeling and the 2015 American Urological Association guidelines identify a individual population for use of intralesional collagenase Clostridium histolyticum in combination with modeling in individuals with stable Peyronie's disease, penile curvature greater than 30° and less than 90°, and intact erectile function.

For individuals who have adhesive capsulitis who receive local clostridial collagenase injection(s), evidence is lacking. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. One small substudy of an RCT found no benefit of clostridial collagenase injection over placebo in functional outcomes, with increased adverse events. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03406338	Surgical Fasciectomy Versus Collagenase Injection in Treating Recurrent Dupuytren Disease: a Randomized Controlled Trial	60	Sept 2027
NCT04786106[a]	Comparison of Collagenase Clostridium Histolyticum to Surgery for the Management of Peyronie's Disease: A Randomized Trial	40	Feb 2027
NCT03192020	DupuytrEn Treatment EffeCtiveness Trial (DETECT): Prospective, Randomised, Controlled, Outcome Assessor-blinded, Three-armed Parallel 1:1:1, Multicenter Trial Comparing the Effectiveness and Cost	303	May 2031

NCT No.	Trial Name	Planned Enrollment	Completion Date
	of Collagenase Clostridium Histolyticum, Percutaneous Needle Fasciotomy and Limited Fasciectomy as Short-term and Long-term Treatment Strategies in Dupuytren's Contracture		
Unpublished			
NCT03000114	Comparison of Collagenase Injection and Percutaneous Needle Aponeurotomy for Treatment of Dupuytren's Disease	334	Jan 2021 (status: unknown)
NCT02725528	A Multi-Center, Randomized Controlled Trial Comparing The Clinical Effectiveness and Cost-Effectiveness of Collagenase Injection (Xiaflex) and Palmar Fasciectomy in the Management of Dupuytren's Disease	128	Nov 2019 (status: completed)
NCT02301078	Comparing Short-term Function and Pain After Treatment With Collagenase Clostridium Histolyticum or Percutaneous Needle Aponeurotomy for Dupuytren's Disease	60	Nov 2017 (status: unknown)
NCT02006719[a]	A Randomized, Double-blind, Placebo-controlled Study of the Safety and Efficacy of AA4500 for the Treatment of Adhesive Capsulitis of the Shoulder	322	Dec 2014 (status: completed)[b]

ISRCTN: International Standard Randomised Controlled Trials Number; NCT: national clinical trial

[a] Denotes industry-sponsored or cosponsored trial.

[b] Results from one center (of 46) reported in Fitzpatrick et al (2020)

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2011 Input

In response to requests, input was received from two physician specialty societies (two reviews) and five academic medical centers (six reviews) while this policy was under review in 2011. Two

reviewers indicated injectable clostridium collagenase is investigational for the treatment of Dupuytren's contracture, noting lack of long-term data and head-to-head trials comparing collagenase with surgical options. However, despite considering this treatment investigational due to insufficient long-term evidence of effectiveness, another reviewer noted that injectable clostridial collagenase for Dupuytren's contracture is approved by the US Food and Drug Administration (FDA), and there is evidence of short-to-medium-term effectiveness. Five reviewers indicated injectable clostridial collagenase for Dupuytren's contracture might be considered medically necessary; they noted it is a treatment alternative to surgery. This recommendation was considered to be near-uniform support for the medical necessity of injectable clostridial collagenase for the treatment of Dupuytren's contracture.

Four reviewers agreed that injectable clostridium collagenase is investigational for the treatment of Peyronie's disease. One of these reviewers also commented that, while this treatment is considered investigational, it may be indicated for Peyronie's disease when it is bothersome, noting that surgery is intrusive. Four reviewers also agreed injectable clostridium collagenase is investigational for the treatment of adhesive capsulitis. Finally, six reviewers agreed injectable clostridium collagenase is investigational for all other indications.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or the National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Peyronie's Disease

American Urological Association

In 2015, the American Urological Association (AUA) issued guidelines based on a systematic review on the diagnosis and treatment of Peyronie's disease.[5] For individuals with stable Peyronie's disease, penile curvature greater than 30° and less than 90°, and intact erectile function (with or without the use of medications), the Association recommended intralesional

collagenase Clostridium histolyticum in combination with modeling (moderate recommendation; evidence strength grade B). The AUA panel discussion indicated that their recommendation was based primarily on the IMPRESS I and II RCTs discussed above. They acknowledge that some uncertainty remains about the long-term durability of curvature improvements, replication by another group of investigators, and generalizability to other individual subgroups such as those with hourglass deformity, ventral curvature, calcified plaque, or plaque located proximal to the base of the penis. Ultimately, their moderate recommendation for clostridial collagenase was because of the modest curvature reductions obtained and the low risk of serious adverse events in IMPRESS I and II.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Table 2 lists indications for clostridial collagenase (Xiaflex; Auxilium Pharmaceuticals [Norristown, PA]) that have been approved by the FDA.

Table 2. FDA-Approved Indications for Clostridial Collagenase (Xiaflex)

Indication	Approved	Indications	Additional Information
Dupuytren's contracture	2010	• Adults with Dupuytren;s contracture with a palpable cord • Up to 3 injections at 4-week intervals into a palpable Dupuytren's cord with a contracture of a metacarpophalangeal or a proximal interphalangeal joint	• Approval accompanied by REMS. The manufacturer must: ○ Evaluate and mitigate risks and serious adverse events ○ Instruct health care providers on procedure to inject Xiaflex and perform finger extension procedures ○ Inform individuals of potential risks of treatment
	2014		Indication expanded: up to 2 joints in same hand may be treated during a treatment visit
Peyronie's disease	2013	• Men with a palpable[a] penile plaque and penile curvature greater than 30 degrees • A maximum of 4 cycles, each of which consists of 2 Xiaflex injection procedures	• Approval accompanied by a boxed warning of corporal rupture and penile hematoma • Only available through a restricted program (Xiaflex REMS), due to risk of corporal rupture. REMS requirements:

Indication	Approved	Indications	Additional Information
			○ Prescribers must enroll and complete training in the administration of Xiaflex for the treatment of Peyronie's disease ○ Health care sites must be certified with the program and ensure that only certified prescribers administer Xiaflex

[a] Adapted from Food and Drug Administration (2023)[4]
FDA: Food and Drug Administration
REMS: Risk Evaluation and Mitigation Strategy

The discussion section of the 2015 American Urological Association guideline for use of clostridial collagenase in Peyronie's disease indicates that the exclusion criteria for the pivotal trials "included severe pain with penile palpation by the clinician, ED that was unresponsive to PDE5 inhibitors, and lack of full erectile response to prostaglandin E1 during curvature measurement".[5]

References

1. Layton T, Nanchahal J. Recent advances in the understanding of Dupuytren's disease. F1000Res. 2019; 8. PMID 30854193
2. Hussein AA, Alwaal A, Lue TF. All about Peyronie's disease. Asian J Urol. Apr 2015; 2(2): 70-78. PMID 29264123
3. Dias R, Cutts S, Massoud S. Frozen shoulder. BMJ. Dec 17 2005; 331(7530): 1453-6. PMID 16356983
4. Food and Drug Administration (FDA). Xiaflex: collagenase clostridium histolyticum. 2023; **https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process**. Accessed March 11, 2025.
5. Nehra A, Alterowitz R, Culkin DJ, et al. Peyronie's Disease: American Urological Association Guideline. 2015. Accessed March 11, 2025.
6. Salari N, Heydari M, Hassanabadi M, et al. The worldwide prevalence of the Dupuytren disease: a comprehensive systematic review and meta-analysis. J Orthop Surg Res. Oct 28 2020; 15(1): 495. PMID 33115483
7. Abe Y. Comparison of Treatment Outcomes after Collagenase Injection and Percutaneous Needle Fasciotomy for Dupuytren's Contracture: Objective and Subjective Comparisons with a 3-Year Follow-Up. Plast Reconstr Surg. Jun 2020; 145(6): 1464-1474. PMID 32459776
8. Strömberg J, Ibsen Sörensen A, Fridén J. Percutaneous Needle Fasciotomy Versus Collagenase Treatment for Dupuytren Contracture: A Randomized Controlled Trial with a Two-Year Follow-up. J Bone Joint Surg Am. Jul 05 2018; 100(13): 1079-1086. PMID 29975270
9. Skov ST, Bisgaard T, Søndergaard P, et al. Injectable Collagenase Versus Percutaneous Needle Fasciotomy for Dupuytren Contracture in Proximal Interphalangeal Joints: A Randomized Controlled Trial. J Hand Surg Am. May 2017; 42(5): 321-328.e3. PMID 28473158

10. Scherman P, Jenmalm P, Dahlin LB. One-year results of needle fasciotomy and collagenase injection in treatment of Dupuytren's contracture: A two-centre prospective randomized clinical trial. J Hand Surg Eur Vol. Jul 2016; 41(6): 577-82. PMID 26631343

11. Scherman P, Jenmalm P, Dahlin LB. Three-year recurrence of Dupuytren's contracture after needle fasciotomy and collagenase injection: a two-centre randomized controlled trial. J Hand Surg Eur Vol. Oct 2018; 43(8): 836-840. PMID 30012049

12. Zhou C, Hovius SER, Slijper HP, et al. Collagenase Clostridium Histolyticum versus Limited Fasciectomy for Dupuytren's Contracture: Outcomes from a Multicenter Propensity Score Matched Study. Plast Reconstr Surg. Jul 2015; 136(1): 87-97. PMID 25829153

13. Povlsen B, Povlsen SD. What is the better treatment for single digit dupuytren's contracture: surgical release or collagenase clostridium histolyticum (Xiapex) injection?. Hand Surg. 2014; 19(3): 389-92. PMID 25155703

14. Naam NH. Functional outcome of collagenase injections compared with fasciectomy in treatment of Dupuytren's contracture. Hand (N Y). Dec 2013; 8(4): 410-6. PMID 24426958

15. Smeraglia F, Del Buono A, Maffulli N. Collagenase clostridium histolyticum in Dupuytren's contracture: a systematic review. Br Med Bull. Jun 2016; 118(1): 149-58. PMID 27151958

16. Brazzelli M, Cruickshank M, Tassie E, et al. Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation. Health Technol Assess. Oct 2015; 19(90): 1-202. PMID 26524616

17. Gilpin D, Coleman S, Hall S, et al. Injectable collagenase Clostridium histolyticum: a new nonsurgical treatment for Dupuytren's disease. J Hand Surg Am. Dec 2010; 35(12): 2027-38.e1. PMID 21134613

18. Hurst LC, Badalamente MA, Hentz VR, et al. Injectable collagenase clostridium histolyticum for Dupuytren's contracture. N Engl J Med. Sep 03 2009; 361(10): 968-79. PMID 19726771

19. Badalamente MA, Hurst LC. Efficacy and safety of injectable mixed collagenase subtypes in the treatment of Dupuytren's contracture. J Hand Surg Am. 2007; 32(6): 767-74. PMID 17606053

20. Nydick JA, Olliff BW, Garcia MJ, et al. A comparison of percutaneous needle fasciotomy and collagenase injection for dupuytren disease. J Hand Surg Am. Dec 2013; 38(12): 2377-80. PMID 24060510

21. Peimer CA, Blazar P, Coleman S, et al. Dupuytren contracture recurrence following treatment with collagenase clostridium histolyticum (CORDLESS study): 3-year data. J Hand Surg Am. Jan 2013; 38(1): 12-22. PMID 23200951

22. Peimer CA, Blazar P, Coleman S, et al. Dupuytren Contracture Recurrence Following Treatment With Collagenase Clostridium histolyticum (CORDLESS [Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study]): 5-Year Data. J Hand Surg Am. Aug 2015; 40(8): 1597-605. PMID 26096221

23. Alberton F, Corain M, Garofano A, et al. Efficacy and safety of collagenase Clostridium histolyticum injection for Dupuytren contracture: report of 40 cases. Musculoskelet Surg. Dec 2014; 98(3): 225-32. PMID 24254968

24. Witthaut J, Jones G, Skrepnik N, et al. Efficacy and safety of collagenase clostridium histolyticum injection for Dupuytren contracture: short-term results from 2 open-label studies. J Hand Surg Am. Jan 2013; 38(1): 2-11. PMID 23218556

25. McMahon HA, Bachoura A, Jacoby SM, et al. Examining the efficacy and maintenance of contracture correction after collagenase clostridium histolyticum treatment for Dupuytren's disease. Hand (N Y). Sep 2013; 8(3): 261-6. PMID 24426932

26. Badalamente MA, Hurst LC. Enzyme injection as nonsurgical treatment of Dupuytren's disease. J Hand Surg Am. Jul 2000; 25(4): 629-36. PMID 10913202

27. Watt AJ, Curtin CM, Hentz VR. Collagenase injection as nonsurgical treatment of Dupuytren's disease: 8-year follow-up. J Hand Surg Am. Apr 2010; 35(4): 534-9, 539.e1. PMID 20353858

28. Hellstrom WJ. Medical management of Peyronie's disease. J Androl. 2009; 30(4): 397-405. PMID 18974422

29. Cao D, Li J, Lu Y, et al. Efficacy and Safety of Collagenase Clostridium Histolyticum in the Treatment of Peyronie's Disease: An Evidence-Based Analysis. Front Med (Lausanne). 2022; 9: 780956. PMID 35252236

30. Gelbard M, Goldstein I, Hellstrom WJ, et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. J Urol. Jul 2013; 190(1): 199-207. PMID 23376148

31. Rosenberg JE, Ergun O, Hwang EC, et al. Non-surgical therapies for Peyronie's disease. Cochrane Database Syst Rev. Jul 17 2023; 7(7): CD012206. PMID 37490423

32. Lipshultz LI, Goldstein I, Seftel AD, et al. Clinical efficacy of collagenase Clostridium histolyticum in the treatment of Peyronie's disease by subgroup: results from two large, double-blind, randomized, placebo-controlled, phase III studies. BJU Int. Oct 2015; 116(4): 650-6. PMID 25711400

33. Hellstrom WJ, Feldman R, Rosen RC, et al. Bother and distress associated with Peyronie's disease: validation of the Peyronie's disease questionnaire. J Urol. Aug 2013; 190(2): 627-34. PMID 23376705

34. Coyne KS, Currie BM, Thompson CL, et al. Responsiveness of the Peyronie's Disease Questionnaire (PDQ). J Sex Med. Apr 2015; 12(4): 1072-9. PMID 25664497

35. Jordan GH. The use of intralesional clostridial collagenase injection therapy for Peyronie's disease: a prospective, single-center, non-placebo-controlled study. J Sex Med. Jan 2008; 5(1): 180-7. PMID 18173766

36. Goldstein I, Lipshultz LI, McLane M, et al. Long-Term Safety and Curvature Deformity Characterization in Patients Previously Treated with Collagenase clostridium Histolyticum for Peyronie's Disease. J Urol. Jun 2020; 203(6): 1191-1197. PMID 31922462

37. Levine LA, Cuzin B, Mark S, et al. Clinical safety and effectiveness of collagenase clostridium histolyticum injection in patients with Peyronie's disease: a phase 3 open-label study. J Sex Med. Jan 2015; 12(1): 248-58. PMID 25388099

38. Fitzpatrick J, Richardson C, Klaber I, et al. Clostridium histolyticum (AA4500) for the Treatment of Adhesive Capsulitis of the Shoulder: A Randomised Double-Blind, Placebo-Controlled Study for the Safety and Efficacy of Collagenase - Single Site Report. Drug Des Devel Ther. 2020; 14: 2707-2713. PMID 32764872

History

Date	Comments
11/11/13	New Policy. Policy replaces 5.01.524. Considered medically necessary to treat Dupuytren's contracture in adult patients when criteria are met.
12/17/14	Annual Review. Policy updated with literature review through September 5, 2014. References 3, 5, 10, 13-14, 17-22, 27 added; others renumbered/removed. Rationale section reorganized. Policy statements unchanged. ICD-9 and ICD-10 diagnosis and procedure codes removed; these do not relate to policy adjudication.
12/08/15	Annual Review. Policy updated with literature review through September 10, 2015; references 16, 19-21, 28, 33, 35, and 37-38 added. Policy statements unchanged.
12/01/16	Annual Review, approved November 8, 2016. Policy updated with literature review through August 2016; references added. Policy statements unchanged.
12/01/17	Annual Review, approved November 9, 2017. Policy updated with literature review through October 2017. Reference added. Policy statements unchanged.

Date	Comments
02/01/18	Annual Review, approved January 30, 2018. Policy updated with literature review through November, 2017; reference 40 added. Policy statements unchanged.
02/01/19	Coding update, CPT codes 54200 and 54235 moved to non-covered coding section. CPT code 54205 added to policy as non-covered.
03/01/19	Annual Review, approved February 5, 2019. Policy updated with literature review through August 2018; no references added; references 3 and 41 updated. Policy statement Xiaflex for treatment of Peyronie's disease changed from investigational to not covered as a Plan exclusion.
04/01/19	Policy renumbered from 5.01.19 to 5.01.595, approved March 19, 2019. This policy replaces policy 5.01.19 which is now deleted. Injectable clostridial collagenase may be considered medically necessary when criteria are met, considered non-covered for treatment of Peyronie's disease, considered investigational for all other indications.
09/01/19	Interim Review, approved August 13, 2019. Policy statement changed: Injectable clostridial collagenase may be considered medically necessary for the treatment of Peyronie's disease (in accordance to the member contract, if the member has a treatment of sexual dysfunction benefit; otherwise it is considered a contractual exclusion if the member has no benefit for treatment of a sexual dysfunction).
06/01/20	Annual Review, approved May 5, 2020. Policy updated with literature review through January 2020; reference added. Peyronie's disease in adults may be considered medically necessary under specified criteria.
06/01/21	Annual Review, approved May 4, 2021. Policy updated with literature review through February 6, 2021; references added. Policy statements unchanged.
06/01/22	Annual Review, approved May 10, 2022. Policy updated with literature review through January 18, 2021; references added. Policy statements unchanged.
06/01/23	Annual Review, approved May 5, 2023. Policy updated with literature review through January 12, 2023; references added. Policy statements unchanged. Added previous history from policy 5.01.19. Changed the wording from "patient" to "individual" throughout the policy for standardization.
06/01/24	Annual Review, approved May 13, 2024. Policy updated with literature review through February 5, 2024; references added. Policy statements unchanged.
04/01/25	Annual Review, approved March 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.