



Louisiana

Injectable Clostridial Collagenase for Fibroproliferative Disorders

Policy # 00256

Original Effective Date: 06/16/2010

Current Effective Date: 02/08/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Dupuytren's Contracture

Based on review of available data, the Company considers the use of injectable clostridial collagenase (Xiaflex[®])[†] for Dupuytren's contracture with palpable cord, to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of injectable clostridial collagenase (Xiaflex) will be considered when ALL of the following criteria are met:

- Patient has a diagnosis of Dupuytren's contracture with palpable cord; AND
- Patient is 18 years of age or older.

Peyronie's Disease

Based on review of available data, the Company considers the use of injectable clostridial collagenase (Xiaflex) for Peyronie's disease to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of one course of injectable clostridial collagenase (Xiaflex) per palpable plaque will be considered when ALL of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of Peyronie's disease with a palpable plaque; AND

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- Patient has a curvature deformity of at least 30 degrees at the start of therapy; AND
- Xiaflex will be used in combination with a penile modeling procedure

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of injectable clostridial collagenase (Xiaflex) when patient selection criteria are not met OR for other uses including, but not limited to adhesive capsulitis to be **investigational**.*

Background/Overview

Collagenases are enzymes that digest native collagen and are being evaluated for treatment of fibroproliferative disorders such as Dupuytren's contracture and Peyronie's disease. Clostridial collagenase is a bacterial collagenase derived from *Clostridium histolyticum*. Treatment of Dupuytren's contracture consists of injection of collagenase into the cord followed by manipulation of the finger if contracture persists. Injection may be done up to 3 times at 4-week intervals. Treatment with Xiaflex for Peyronie's disease is indicated in patients with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy. A treatment cycle consists of two Xiaflex injection procedures and a penile modeling procedure. The penile modeling procedure involves manipulations of the flaccid penis to stretch and elongate the treated plaque. Both hands should be used to apply firm, steady pressure to elongate and stretch the plaque. The goal is to gradually create bending opposite to the patient's penile curvature, with stretching to the point of moderate resistance. Pressure should be held for 30 seconds and then released. Allow a 30 second rest period, and repeat the modeling procedure for a total of 3 modeling attempts at 30 seconds each. Patients should also perform penile modeling at home at least 3 times daily for 30 seconds. For each plaque causing the curvature deformity, up to four treatment cycles may be administered. Each cycle can be repeated at 6 week intervals therefore making each course approximately 24 weeks.

Injection with clostridial collagenase is intended to provide a nonoperative treatment option for fibroproliferative disorders. Fibrotic tissue disorders, characterized by excessive collagen deposits, can affect the musculoskeletal system, causing pain and limitation of movement and reduction of

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joint range of motion. Dupuytren's disease and adhesive capsulitis are such musculoskeletal disorders; Peyronie's disease is another example.

The mechanisms that contribute to the pathology are poorly understood. In Dupuytren's disease, collagen deposition in nodules and cords in the palm and fingers results in pitting of the overlying cutis and flexion contractures. 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 patients with functional impairment and metacarpophalangeal (MCP)-joint contractures of 30 degrees or more. There is no effective pharmacotherapy. Adhesive capsulitis or "frozen shoulder" is treated with physiotherapy and mobilization in combination with analgesics or nonsteroidal anti-inflammatory drugs. Corticosteroid injection is used with caution. The prevalence of Dupuytren's disease and adhesive capsulitis is estimated at 3–6% and 2–3%, respectively, in the general population and increases with advancing age. Both conditions are more common in patients with diabetes or thyroid disease. Dupuytren's disease is more common in men, and adhesive capsulitis more common in women.

Peyronie's disease is the development of abnormal scar tissue, or plaques, in the tunica albuginea layer of the penis causing distortion, curvature, and pain, usually during erection. It occurs in 3–9% of men, most commonly between the ages of 45 and 60 years. In some cases, plaque does not cause severe pain or curvature, and the condition resolves on its own. In severe cases, erectile dysfunction can occur. 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 demonstrate inconsistent benefit. Intralesional injection therapy consisting of injection of interferon-alpha-2b or calcium channel-blockers (e.g., verapamil) is the current standard of therapy. Surgical procedures involve the excision (removal) of hardened tissue and skin graft, the removal or pinching (plication) of tissue opposite the plaque to reduce curvature (called the Nesbit procedure), a penile implant, or a combination of these.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In February 2010, the FDA approved Auxilium Pharmaceutical Inc.'s biologics license application for clostridial collagenase histolyticum (Xiaflex) for treatment of adult patients with Dupuytren's contracture with a palpable cord. The FDA labeling for Xiaflex states that up to 3 injections at 4-

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week intervals may be given into a palpable Dupuytren's cord with a contracture of a MCP joint or a proximal interphalangeal (PIP) joint.

In December 2013, the FDA approved Xiaflex 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. A treatment cycle consists of two Xiaflex injection procedures and a penile modeling procedure. For each plaque causing the curvature deformity, up to four treatment cycles may be administered. Each cycle can be repeated at 6 week intervals.

Centers for Medicare and Medicaid Services (CMS)

There is no national coverage determination.

Rationale/Source

A number of nonsurgical interventions for fibroproliferative disease have been studied. Investigations of a potential role for injectable clostridial collagenase have been ongoing over a period of 20 years. The FDA approval was granted in 2010 for treatment of Dupuytren's contracture with a palpable cord. FDA approval for Peyronie's disease was granted in 2013.

Dupuytren's Disease (Dupuytren's Contracture)

Chen and colleagues published a systematic review in 2011 of various treatments for Dupuytren's contracture. Studies published through December 2010 were examined and included 4 prospective studies (including 2 randomized studies) on collagenase injections, 6 studies on open partial fasciotomy (including 2 randomized studies) and 3 studies on needle aponeurotomy. Sample sizes for all of the studies included in the review ranged from 13–261 patients. The authors found recurrence rates for collagenase injections (mean follow-up times of 120 days to 4 years) ranged from 10–31%. Needle aponeurotomy had the highest recurrence rates of 50-58% (mean follow-up of 3-5 years), which were significantly higher than the open partial fasciectomy recurrence rates of 12–39% (mean follow-up time of 1.5–7.3 years). Additionally, open partial fasciectomy recurrence rates were significantly higher than collagenase injection. Complications occurred most often with open partial fasciectomy, although 2 cord ruptures were reported with collagenase injection. The authors concluded further studies are needed to understand the long-term outcomes of these interventions and how to address contracture recurrence. It was also noted that it is unclear whether collagenase injection can be used for Dupuytren's revision.

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In 2009, Hurst and colleagues published results from CORD I, a randomized, double-blind placebo-controlled, multicenter trial (16 sites) of collagenase clostridium histolyticum for Dupuytren's contracture with 308 subjects with joint contractures of 20 degrees or more. This study was included in the Chen review described above. Joints were stratified according to type (MCP or PIP joints) and severity of contracture and randomly assigned in a 2:1 ratio to receive up to 3 injections of either collagenase or placebo in the contracted collagen cord at 30-day intervals. Secondary and tertiary joints were identified for possible subsequent injections. Joints were manipulated one day after injection if necessary. The primary endpoint was reduction in contracture to 0–5 degrees of full extension 30 days after last injection. Twenty-six secondary endpoints were also evaluated. Recurrence of contracture was defined as an increase in joint contracture equal to or greater than 20 degrees and was considered an adverse event. Efficacy results were based on 306 primary joints: 203 injected with collagenase and 103 injected with placebo. In the collagenase-treated group, 130 of 203 (64%) cords met the primary endpoint versus 7 of 103 (6.8%) placebo-injected cords ($p < 0.001$). More than half of the collagenase-injected joints that did not meet the primary endpoint did not receive the maximum allowable number of injections, most commonly because a cord could not be palpated or the patient was satisfied with the result. Median time to reach the primary endpoint for collagenase-treated joints was 56 days. At the 90-day visit, there was no recurrence of contracture in collagenase-treated primary joints that had reached the primary endpoint.

When analyzed by joint type, more collagenase-treated joints achieved the primary endpoint than placebo (MCP 76.7% vs. 7.2% and proximal PIP joint 40.9% vs. 5.9%, both respectively) ($p < 0.001$ for both comparisons). The mean change in contracture from baseline to 30 days after last injection was 48.0 to 7.2 degrees in the collagen-injected MCP joints and 45.4 to 43.1 degrees in the placebo-injected MCP joints. Thirty days after last injection, 84.7% of collagenase-injected joints versus 11.7% of placebo-injected joints showed clinical improvement. Results were better in MCP joints than in PIP joints: 94.0% versus 67.1%, respectively, in the collagenase group and 11.6% versus 11.8%, respectively, in the placebo group. Overall, 96.6% of patients who received collagenase reported at least 1 treatment-related adverse event. They had significantly more injection- and manipulation-related events, such as contusion, hemorrhage, injection-site pain, upper extremity pain, and lymphadenopathy ($p \leq 0.02$), than patients who received placebo injection. Most were mild or moderate in intensity; however, 20 patients in the collagenase group and 2 in the placebo group reported events that were severe in intensity. Three severe adverse events were considered to be treatment related: a case of complex regional pain syndrome and 2 tendon ruptures, both requiring surgical procedures. The CORD I authors note that the timeframe of this study was insufficient to

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assess recurrence, and they could not make any claims about this outcome. In 2011, Witthaut and colleagues reported on range of motion (ROM) outcomes from the CORD I study. On day 30, mean ROM increased from 43.9 degrees to 80.7 degrees in joints treated with collagenase. In the joints treated with placebo, mean ROM increased 45.3 degrees to 49.5 degrees on day 30. Using regression models to create a ROM severity classification, the authors reported joints treated with collagenase had a significant mean increase in ROM of 36.7 degrees ($p < 0.001$) whereas, joints treated with placebo had a non-significant mean increase of 4.0 degrees.

In a letter to the editor in response to publication of the study, Holzer and Holzer comment that successful treatment of Dupuytren's disease correlates with the percentage of excised Dupuytren's tissue and the extent of the intervention. They caution that the value of collagenase injection must be confirmed in a long-term follow-up study that focuses on the recurrence rate.

In 2010, Gilpin and colleagues published results of the CORD II study. In this study, 66 patients were randomized to receive collagenase injection (45 cords) or placebo (21 cords) in the 90-day, double-blind phase followed by an open label phase of 9 months. The authors reported, within 30 days, collagenase injections resulted in significantly more cord contracture improvement from baseline to within 0-5 degrees of normal than placebo (44.4% vs. 4.8%, respectively). Results after the open-label treatment were reported to be similar to the double-blind phase. Recurrence of contracture (defined as increase of contracture to 20 degrees or more) did not occur during the 12-month follow-up. All study participants experienced mild adverse events (e.g., swelling and pain at injection site). Three serious adverse effects related to the treatment were reported. A flexion pulley rupture of the left small finger occurred in one patient while rapid thickening of the treated cord and sensory abnormalities occurred in another patient.

Watt and colleagues, in 2010, reported on a Phase II clinical trial of 23 patients 8 of whom completed 8-year follow-up. In the isolated MCP group ($n = 6$), average contracture was 57 degrees before treatment, 9 degrees at 1 week, 11 degrees at 1 year, and 23 degrees at 8-year follow-up. Four of 6 patients experienced recurrence by the 8-year follow-up. In the isolated PIP joint group ($n = 2$), both patients had recurrence by 8-year follow-up. Outcomes at specific intervals between 1 year and 8 years were not reported. Potential bias in patient selection and the small number of patients precludes drawing conclusions from this report.

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In a 2010 review, Desai and Hentz make several observations regarding the role of collagenase in the treatment of Dupuytren's contracture. They recommend caution when treating the small finger; all 3 tendon ruptures seen across all studies reported to the FDA and adverse events of boutonniere deformity and pulley injury occurred in the small finger. An active immune response was seen in patients after injection of collagen in the clinical trials, which suggests the possibility that effectiveness of subsequent injections might be impacted. The authors also note that long-term effects of repeat injections and contracture recurrence have yet to be studied, and direct comparisons with the current gold standard, palmar fasciectomy, have not been made.

In 2007, Badalamente and Hurst reported on patients who participated in a double-blind Phase III randomized controlled trial (RCT) comparing collagenase and placebo injections. During the double-blind and open-label phases, 62 joints (31 MCP and 31 PIP) were treated in 35 patients. Fifty-four (87%) were clinical successes. Twenty-seven joints were followed up for 24 months. Over the 24 months following the last injection, 5 joints had recurrences (1 MCP and 4 PIP), 1 before 12 months, 2 at 12 months, and 2 at 24 months after treatment. Three of these patients subsequently underwent fasciectomy. The most common adverse events were local reactions to injections. The limited patient follow-up makes it difficult to reach conclusions from this study.

In 2013, Raven and colleagues published a subgroup analysis of data pooled from the above 3 RCTs (CORD I, CORD II, and Badalamente and Hurst) of collagenase treatment of Dupuytren-related contractures. This analysis included 271 patients with MCP (n=167) or PIP (n=104) joint contractures greater than or equal to 20 degrees treated with collagenase injections (0.58 mg collagenase per injection). Subgroups included age, sex, and diabetes status. Endpoints included rate of clinical success (reduction in contracture to 0-5 degrees of normal) and percentage of adverse events. There was no significant difference in clinical success by age, diabetes status, or sex, with 63% of cases reaching the endpoint. In addition, there was no difference in complication rates among the subgroups, with peripheral edema, contusion, and injection-site hemorrhage being most common.

Peyronie's Disease

Authors of a 2007 systematic review of plaque injection therapy included 2 studies of collagenase in their analysis. Both papers reported positive treatment outcomes. One study was rated, according to the Oxford Centre for Evidence-Based Medicine criteria, as level 2 (RCT with low power or < 80% follow-up/retention or good-quality, randomized prospective cohort study) and the other level

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4 (case series or poor-quality cohort or case-control study). These 2 studies are noted below. Agents used in the other 19 studies reviewed were corticosteroid, verapamil, and interferon.

In a 1985 paper on a series of 31 men treated, 20 showed improvement. Pain was eliminated in 13 of 14 patients who experienced pain before treatment. One small corporeal rupture at the injection site was reported in one patient. No significant adverse events were reported in 9.8 months of follow-up. In a 1993 randomized, placebo-controlled, double-blind study with 49 subjects reported by the same author, the effects of collagenase and placebo on plaque size and penile deformity were investigated. For the group as a whole, treatment with collagenase was significantly more effective ($p < 0.007$). Patients with lesser deformity responded more favorably to treatment. In 2008, Jordan reported on a series of 25 patients with well-defined plaque treated with 3 intralesional injections of clostridial collagenase over 7–10 days with repeat treatment at 3 months. Primary endpoints were changes from baseline in deviation angle and plaque size. Significant decreases from baseline were achieved in the mean deviation angle at months 3 ($p = 0.0001$) and 6 ($p = 0.0012$), plaque width at months 3 ($p = 0.0052$), 6 ($p = 0.0239$), and 9 ($p = 0.0484$), and plaque length at months 3 ($p = 0.0018$) and 6 ($p = 0.0483$). More than 50% of patients in this series considered themselves "very much improved" or "much improved" at all timepoints in the study, and the drug was generally well-tolerated.

In 2013, Gelbard and colleagues published the results of 2 double-blind, placebo-controlled RCTs, IMPRESS (Investigation for Maximal Peyronie's Reduction Efficacy and Safety Studies) I and II, which examined the clinical efficacy and safety of collagenase injections in subjects with Peyronie's disease. These RCTs were sponsored by the manufacturer (Auxilium Pharmaceuticals), the findings of which were submitted to the FDA in support of their biologics license application. These 2 studies examined collagenase injections in 417 and 415 participants, respectively, through a maximum of 4 treatment cycles, each separated by 6 weeks (for up to 8 injections of 0.58 mg collagenase). Men were stratified by baseline penile curvature (30 to 60 vs. 61 to 90 degrees) and randomized to collagenase injections or placebo in a 2:1 ratio. The primary outcomes were the percent change in the penile curvature abnormality and the change in the Peyronie's Disease Questionnaire (PDQ, developed by the manufacturer) "symptoms bother" score from baseline to 52 weeks. Data from the IMPRESS I and II studies were combined. Participants treated with collagenase injections showed a mean percent improvement in penile curvature abnormality of 34%, compared to 18% improvement in penile curvature in the placebo group; this change in curvature and the percent improvement in the collagenase group were significantly greater than in the placebo group (each p

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<0.0001). The mean change in the PDQ symptom bother domain score was significantly improved in the collagenase group vs. the placebo group (-2.8 ± 3.8 vs. -1.8 ± 3.5 , $p=0.0037$). The most frequently reported complications ($\geq 45\%$) in the collagenase-treated group included penile ecchymosis, penile swelling and penile pain. Six participants experienced treatment-related serious adverse events, including corporeal rupture in 3 cases and penile hematoma in the other 3 cases. The 3 corporeal ruptures and one hematoma were successfully repaired surgically. Of the 2 remaining penile hematomas, one case was successfully resolved without intervention and the other resolved with aspiration.

Adhesive Capsulitis

No studies including patients with adhesive capsulitis were identified in the literature search.

Ongoing Clinical Trials

Several studies on injectable clostridial collagenase injections for were identified in a search of online site ClinicalTrials.gov in September 2013:

Dupuytren's contractures

- In a randomized study of 50 patients, collagenase injections will be compared to percutaneous needle fasciotomy for Dupuytren's contracture (NCT01538017); this study is currently recruiting participants with an estimated completion date of January 2015.
- In the CORDLESS observational study (Collagenase Optimal Reduction of Dupuytren's - Long-term Evaluation of Success Study), the long-term durability and safety of clostridial collagenase injections for Dupuytren's contracture will be evaluated yearly in 600 patients (NCT00954746); this is a 5-year follow-up study of which interim data after the third-year by Peimer and colleagues have been reported above.
- In a Phase IV, randomized trial, the effects of delayed manipulation of digits following collagenase injections for the treatment of Dupuytren's contracture will be examined in 60 patients (NCT01226121); the study status was last verified in September 2012 as currently recruiting participants with an estimated completion date of December 2012.
- Outcomes after collagenase injection for Dupuytren's contracture has been studied in a Phase III study of 254 patients followed for 11 months (NCT01229436); this study has been completed, but no results have been published.

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- The safety and efficacy of 2 injections of clostridial collagenase into the same hand of 60 patients with multiple Dupuytren's contractures has been evaluated in a Phase III study (NCT01407068); this study has been completed, but no results have been published.
- Retreatment with collagenase injections for recurrent Dupuytren's contracture will be evaluated in a nonrandomized study of 100 patients (NCT01498640); this study is ongoing, but not recruiting participants with an estimated completion date of September 2013.

Adhesive capsulitis

- Injectable collagenase has been evaluated in a randomized study of 50 subjects for adhesive capsulitis of the shoulder (NCT01483963); this study has been completed, but no results have been published.

Peyronie's disease

- Three Phase III studies were identified to evaluate clostridial collagenase injections for patients with Peyronie's disease (NCT01243411, NCT01221623, and NCT01221597); the latter 2 studies are the double-blind, placebo-controlled RCTs, IMPRESS I and II by Gelbard and colleagues reported above.

Clinical Input Received through 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.

2010

In response to requests, input was received from no physician specialty societies and 6 academic medical centers. The input was mixed, with half those providing input agreeing that use of this agent is investigational. While there was support for use in Dupuytren's contracture, comments were made about the limited amount of data on long-term outcomes and durability.

2011

In response to requests, input was received from 2 physician specialty societies (2 reviews) and 5 academic medical centers (6 reviews). 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 to surgical options. However, despite considering this treatment investigational due to insufficient long-term evidence of effectiveness, one reviewer noted

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that injectable clostridial collagenase for Dupuytren's contracture is FDA-approved, and there is evidence of short-to-medium-term effectiveness available. Five reviewers indicated injectable clostridial collagenase for Dupuytren's contracture may be considered medically necessary. These reviewers noted this is a treatment alternative to surgery. This 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 surgery is intrusive. Four reviewers also agreed injectable clostridium collagenase is investigational for the treatment of adhesive capsulitis. Finally, 6 reviewers agreed injectable clostridium collagenase is investigational for all other indications.

Summary

For patients with Dupuytren's contracture, the evidence from clinical trials suggests that injectable clostridial collagenase provides short-term release of contracture. A comparison of overall outcomes compared to surgical intervention may be useful; however, studies with direct comparisons are not available. Potentially serious adverse events also warrant further investigation, and evidence on long-term recurrence rates is limited. While gaps in the evidence base remain, this may be an appropriate treatment option in adult patients with a palpable cord based on short-term evidence of effectiveness and a preponderance of agreement from clinical input. Therefore, injectable clostridial collagenase may be considered medically necessary as an alternative to surgical options. Based on trials mentioned above, the FDA approved use for Xiaflex in patients with Peyronie's disease that meet certain criteria. Therefore, injectable clostridial collagenase may be considered medically necessary in patients who meet criteria for use in Peyronie's disease.

For other disorders, there is less evidence. Therefore, based on available evidence and clinical input, injection of this agent is considered investigational for all other treatment indications.

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1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Injectable Clostridial Collagenase for Fibroproliferative Disorders", 5.01.19, 04:2020.

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Louisiana

Injectable Clostridial Collagenase for Fibroproliferative Disorders

Policy # 00256

Original Effective Date: 06/16/2010

Current Effective Date: 02/08/2021

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|------------|---|
| 06/03/2010 | Medical Policy Committee approval |
| 06/16/2010 | Medical Policy Implementation Committee approval. New policy. |
| 05/05/2011 | Medical Policy Committee review |
| 05/18/2011 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 05/03/2012 | Medical Policy Committee review |
| 05/16/2012 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 05/02/2013 | Medical Policy Committee review |
| 05/22/2013 | Medical Policy Implementation Committee approval. Added a Patient Selection Criteria section for coverage eligibility requiring that patients have a diagnosis of Dupuytren's contracture with palpable cord and are 18 years and older. Added that |

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the use of injectable clostridial collagenase (Xiaflex) if Patient Selection Criteria are not met is investigational.

01/09/2014 Medical Policy Committee review

01/15/2014 Medical Policy Implementation Committee approval. Added new indication for Peyronie’s disease and associated criteria. Updated background information and references.

01/08/2015 Medical Policy Committee review

01/21/2015 Medical Policy Implementation Committee approval. No change to coverage.

01/07/2016 Medical Policy Committee review

01/22/2016 Medical Policy Implementation Committee approval. No change to coverage.

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes

01/05/2017 Medical Policy Committee review

01/18/2017 Medical Policy Implementation Committee approval. No change to coverage.

01/04/2018 Medical Policy Committee review

01/17/2018 Medical Policy Implementation Committee approval. No change to coverage.

01/10/2019 Medical Policy Committee review

01/23/2019 Medical Policy Implementation Committee approval. No change to coverage.

01/03/2020 Medical Policy Committee review

01/08/2020 Medical Policy Implementation Committee approval. No change to coverage.

01/07/2021 Medical Policy Committee review

01/13/2021 Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 01/2022

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	20527, 20550, 26341, 54200, 54235
HCPCS	J0775
ICD-10 Diagnosis	M72.0, N48.6

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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