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MEDICAL POLICY – 2.01.26

Prolotherapy

BCBSA Ref. Policy: 2.01.26

Effective Date:	Feb. 1, 2025
Last Revised:	Jan. 13, 2025
Replaces:	N/A

RELATED MEDICAL POLICIES:

2.01.98	Orthopedic Applications of Platelet-Rich Plasma
2.01.543	Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions
6.01.527	Diagnosis and Treatment of Sacroiliac Joint Pain

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Prolotherapy therapy (proliferative therapy) is a method to try to heal joints and connective tissue. A solution is injected in the area. The solution irritates the tissue, causing inflammation. This inflammation is supposed to stimulate the body's natural healing response. These injections are repeated over time. The hope is to gradually build up new tissue in the injured area and restore strength. Prolotherapy is investigational (unproven). The studies that have been done are small and don't show substantial improvement. There's not enough medical evidence to show if this technique works.

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

Service	Investigational
Prolotherapy	**Prolotherapy is considered investigational as a treatment of musculoskeletal pain.**

Coding

Code	Description
HCPCS	
M0076	Prolotherapy

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

N/A

Evidence Review

Description

Prolotherapy describes a procedure intended for healing and strengthening ligaments and tendons by injecting an agent that induces inflammation and stimulates endogenous repair mechanisms. Prolotherapy may also be referred to as proliferant injection, prolo, joint sclerotherapy, regenerative injection therapy, growth factor stimulation injection, or nonsurgical tendon, ligament, and joint reconstruction.

Background

The goal of prolotherapy is to promote tissue repair or growth by prompting the release of growth factors, such as cytokines, or by increasing the effectiveness of existing circulating growth factors. The mechanism of action is not well-understood but may involve local irritation and/or cell lysis. Agents used with prolotherapy have included zinc sulfate, psyllium seed oil, combinations of dextrose, glycerin, and phenol, or dextrose alone, often combined with a local anesthetic. Polidocanol, sodium morrhuate, and vascular sclerosants have also been used to sclerose areas of high intratendinous blood flow associated with tendinopathies. Prolotherapy typically involves multiple injections per session conducted over a series of treatment sessions.

A similar approach involves the injection of autologous platelet-rich plasma, which contains a high concentration of platelet-derived growth factors. Treatment of musculoskeletal pain conditions (e.g., tendinopathies) with platelet-rich plasma is discussed in a separate policy (see **Related Policies**).

Summary of Evidence

For individuals with musculoskeletal pain (e.g., chronic neck, back pain), osteoarthritic pain, or tendinopathies of the upper or lower limbs who receive prolotherapy, the evidence includes small, randomized trials with inconsistent results. The relevant outcomes are symptoms, functional outcomes, and quality of life. The strongest evidence evaluates the use of prolotherapy for the treatment of osteoarthritis, but the clinical significance of the therapeutic results is uncertain. 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			
NCT03411811	Dextrose Prolotherapy in Chronic Ulnar Wrist Pain Resistant to Usual Care: Comparison to a Naive-to-Treatment Cohort Who Receive Usual Care	60	Jan 2023 (unknown status)
NCT05160532	Intraarticular Dextrose Prolotherapy for Symptomatic Knee Osteoarthritis	160	May 2025
NCT05548738	The Efficacy of Ultrasound and Fluoroscopy Guided Caudal Epidural Prolotherapy Versus Steroids for Chronic Pain Management in Failed Back Surgery Syndrome	80	Jun 2024
NCT05918146	Effects of Hypertonic Dextrose Prolotherapy on Conventional Physical Therapy in Patients With Subdeltoid Bursitis: a Double-blind, Randomized, Placebo-controlled Study	46	Jun 2024
Unpublished			
NCT05966948	Hypertonic Dextrose Prolotherapy Versus Normal Saline Intra-articular Injection Among Knee Osteoarthritis With Obese Patient	40	Oct 2023
NCT01934868	A Comparison of the Long-Term Outcomes of Prolotherapy Versus Interlaminar Epidural Steroid Injections (ESI) for Lumbar Pain Radiating to the Leg	110	Apr 2023
NCT05984121	Which is Outstanding, Local Ozone Injection or Dextrose Prolotherapy Injection in Chronic Plantar Fasciitis?: A Randomised Controlled Study"	60	Mar 2024
NCT04805242	Effects of Dextrose Prolotherapy in Rotator Cuff Disease: A Randomized Controlled Study	60	Nov 2021

NCT: national clinical trial

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.

American College of Foot and Ankle Surgeons

A 2017 guideline from the American College of Foot and Ankle Surgeons on acquired infracalcaneal heel pain states that evidence regarding the efficacy and safety of prolotherapy for treatment of plantar fasciitis is uncertain, which makes its use neither appropriate nor inappropriate.[37] The same statement is made for platelet-rich plasma, amniotic tissue, botulinum toxin, and needling.

American College of Rheumatology/Arthritis Foundation

The 2019 American College of Rheumatology/Arthritis Foundation guideline for osteoarthritis of the hand, hip, and knee conditionally recommends against the use of prolotherapy in patients with knee and/or hip osteoarthritis, given limited number of trials involving small sample sizes showing limited effect.[38] The guideline does not make any recommendation regarding hand osteoarthritis, given lack of trials.

North American Spine Society

A 2020 guideline on low back pain from the North American Spine Society does not provide a recommendation on prolotherapy but states that sacroiliac ligament prolotherapy deserves further study.[39]

Medicare National Coverage

The Centers for Medicare & Medicaid currently do not cover prolotherapy, joint sclerotherapy, and ligamentous injections with sclerosing agents.[40]

Regulatory Status

Sclerosing agents have been approved by the US Food and Drug Administration for use in treating spider veins, varicose veins, or esophageal varices. These sclerosing agents include Asclera (polidocanol), Varithena (an injectable polidocanol foam), Sotradecol (sodium tetradecyl sulfate), and Ethamolin (ethanolamine oleate). These agents are not currently approved as joint and ligamentous sclerosing agents.

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History

Date	Comments
02/01/00	Add to Medicine Section - New Policy
12/21/00	Replace Policy - Deleted statement in policy guidelines regarding CPT 20550.
12/11/01	Replace Policy - Policy reviewed; policy statement unchanged. New references included.
08/12/03	Replace Policy - Policy updates; policy statement unchanged. Medicare and 2002 updates added.
01/01/04	Replace Policy - CPT code updates only.
06/08/04	Replace Policy - Policy reviewed with literature search; policy statement unchanged.
07/12/05	Replace Policy - Policy updated with literature review; policy statement unchanged.
07/11/06	Replace Policy - Policy updated with literature review; references added; policy statement unchanged.
10/09/07	Replace Policy - Policy updated with literature review; references added; policy statement unchanged.

Date	Comments
08/12/08	Replace Policy - Policy updated with literature search; no change to the policy statement. References and codes added.
10/13/09	Replace Policy - Policy updated with literature search; no change to the policy statement. Rationale revised and references added.
07/27/10	Codes Updated - CPT 0232T added to the policy; no other updates.
10/12/10	Replace Policy - Policy updated with literature review through June 2010; the policy statement remains unchanged. Code 0232T has been removed.
12/27/10	Codes Updated - CPT code 0232T added to policy; no other changes.
10/11/11	Replace Policy – Policy updated with literature review through May 2011; reference 17 added; policy statement unchanged.
08/24/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
10/26/12	Replace policy. Policy updated with literature review through June 2012; reference added; policy statement unchanged.
08/15/13	Update Related Policies. Add 6.01.23.
10/14/13	Replace policy. Policy updated with literature review through July 1, 2013. Reference 11 added; others renumbered/removed. Policy statement unchanged.
01/21/14	Update Related Policies. Add 7.01.551.
11/20/14	Annual Review. Policy updated with literature review through July 17, 2014; policy statement unchanged.
09/01/15	Update Related Policies. Add 2.01.98.
10/13/15	Annual Review. Policy updated with literature review through June 30, 2015; references 12 and 15 added; policy statement unchanged. ICD-9 and ICD-10 diagnosis and procedure codes removed; these are for informational purposes only. CPT codes 20550-20553, 27096, 64490-64495 removed due to lack of specificity or application.
12/01/16	Annual Review, approved November 8, 2016. Policy updated with literature review through September 2016; references added. Policy statement unchanged.
01/01/18	Annual Review, approved December 6, 2017. Policy updated with literature review through September 14, 2017; reference 22 added. Policy statement unchanged. Removed CPT code 0232T.
12/01/18	Annual Review, approved November 21, 2018. Policy updated with literature review; no references added. Policy statement unchanged.
02/01/19	Annual Review, approved January 4, 2019. Policy updated with literature review through September 2018; no references added. Policy statement unchanged. Removed CPT code 20999.
02/01/20	Annual Review, approved January 9, 2020. Policy updated with literature review through September 2019; no references added. Policy statement unchanged.

Date	Comments
02/01/21	Annual review, approved January 6, 2021. Policy updated with literature review through October 7, 2020; references added. Policy statement unchanged.
02/01/22	Annual review, approved January 10, 2022. Policy updated with literature review through September 11, 2021; references added. Policy statement unchanged.
02/01/23	Annual Review, approved January 9, 2023. Policy updated with literature review through September 9, 2022; references added. Policy statement unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
09/22/23	Minor correction to Introduction.
02/01/24	Annual Review, approved January 8, 2024. Policy updated with literature review through September 20, 2023; references added. Policy statement unchanged.
02/01/25	Annual Review, approved January 13, 2025. Policy updated with literature review through September 17, 2024; references added. Policy statement unchanged. Replaced Reference policy 2.01.16 to 2.01.543 Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions.

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.