MEDICAL POLICY

Excellus
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Medical Policy Title	**Prolotherapy**
Policy Number	**8.01.10**
Current Effective Date	October 15, 2025
Next Review Date	June 2026

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

POLICY STATEMENT(S)

Prolotherapy is considered **investigational** as a treatment of musculoskeletal pain or instability (e.g., laxity, weakness).

RELATED POLICIES

Corporate Medical Policy

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

Not Applicable

DESCRIPTION

Prolotherapy is a regenerative injection technique that uses irritant solutions, typically dextrose, to stimulate the body's natural healing processes. Prolotherapy is sometimes referred to as proliferation therapy; joint sclerotherapy; regenerative injection therapy; growth factor stimulation injection or nonsurgical tendon, ligament and joint reconstruction. Prolotherapy is a procedure for healing and strengthening lax ligaments by injecting proliferating agents/sclerosing solutions directly into torn or stretched ligaments. Proliferative therapy acts to promote tissue repair or growth by prompting release of growth factors, such as cytokines, or increasing the effectiveness of existing circulating growth factors. Prolotherapy may involve a single injection or a series of injections, often diluted with a local anesthetic. Agents used with prolotherapy include zinc sulfate; psyllium seed oil; dextrose, and combinations of dextrose, glycerin phenol, and sarapin. Advances in regenerative medicine have made the use of more advanced formulas possible, such as platelet rich plasma (PRP) which contains growth factors, and autologous adult stem cell sources. Polidocanol and sodium morrhuate, which are vascular scleroscants, have also been utilized to work by sclerosing or hardening areas of high blood flow in the affected tissue, potentially promoting tissue healing. Prolotherapy has been investigated as a treatment of various etiologies of pain, including arthritis, degenerative disc disease, fibromyalgia, tendonitis, and plantar fasciitis.

SUPPORTIVE LITERATURE

Scientific data demonstrating the effectiveness of prolotherapy for the treatment of chronic back pain and joint and ligament instability are limited, and interpretation is complicated by variations in treatment protocols, the use of concomitant treatments, and the lack of a non-injection control group. As with any therapy for pain, a placebo effect is anticipated; therefore, randomized, placebo-controlled trials are necessary to investigate the extent of the placebo effect and to determine whether any improvement with prolotherapy exceeds that associated with a placebo.

Kim et al (2010) compared intra-articular prolotherapy with intra-articular corticosteroid injection for sacroiliac pain. The randomized double-blind study included 48 patients with sacroiliac joint pain lasting more than three months, confirmed by a greater than 50% improvement in response to local anesthetic block. The injections were performed on a biweekly schedule (maximum of three injections) under fluoroscopic guidance with confirmation of the intra-articular location with an arthrogram. Pain and disability scores were assessed at baseline, two weeks, and monthly after completion of treatment. At 15 months after treatment, 58.7% of patients in the prolotherapy group reported relief greater than 50% in comparison with 10.2% of the steroid group. Key differences between this and other studies on prolotherapy were the selection of patients using a diagnostic sacroiliac joint block and the use of an arthrogram to confirm the location of the injection. Additional trials are needed to confirm the safety and efficacy of this procedure.

Akcay and colleagues (2020) compared the effect of dextrose prolotherapy (DPT) with saline in the treatment of chronic lateral epicondylopathy (LE) in a triple-blinded randomized control trial (RCT). A total of 60 participants with chronic LE were included in the study. The participants were randomly divided into two groups with either saline or hypertonic dextrose (15 %) injected into the participants' elbow joint at the study baseline, and then at the end of the 4th and 8th week. Participant evaluations were carried out at baseline, and at the end of the 4th, 8th, and 12th week. Primary outcome measures were Visual Analog Scale (VAS) for pain, Patient Rated Tennis Elbow Evaluation (PRTEE-Total [PRTEE-T], PRTEE-Pain, PRTEE-Function); secondary outcome measures were disabilities of the arm, shoulder, and hand score (DASH) and pain-free handgrip strength. Intra-group analysis demonstrated that both groups significantly improved in VAS, PRTEE, DASH scores, and handgrip strength during the study period ($p < 0.001$,for all outcome measurements in both groups). Inter-group analysis showed that PRTEE-T score changes between baseline -4th and -12th week; VAS rest change between baseline and 4th week in the DPT group were significantly higher than the saline group ($p = 0.041$, $p = 0.038$, $p = 0.013$ respectively). There was no significant difference between groups in VAS, DASH scores, and handgrip strength between any time points, in terms of improvement ($p > 0.05$). The authors concluded that the study findings showed that DPT outperformed saline in PRTEE-T score. The authors also stated that although saline appeared to be a comparable clinical effect with DPT, further clinical studies comparing the effects of DPT and saline injection are needed in chronic LE.

Zhang and colleagues (2024) conducted a meta-analysis consisting of six studies to examine the effectiveness of hypertonic glucose proliferation therapy in the treatment of rotator cuff problems. Participants with rotator cuff lesions in the intervention group were treated with hypertonic dextrose proliferation therapy (DPT), whereas the control group participants were treated with a placebo and outcome markers included the Visual Analog Scale (VAS) score and the (Shoulder Pain and Disability Index) SPADI score for pain as well as other predetermined metrics to measure mobility. The test

and control group's VAS scores improved, with the test group's score considerably out-performing the control group (SMD: 1.10;95 % Cl: 0.37 to 1.83; p < 0.01), SPADI score (SMD:8.13; 95 % Cl: 5.34to 10.91; p < 0.01), flexion (SMD:5.73; 95 % Cl: 0.99 to 10.47; p < 0.05), abduction (SMD:6.49; 95 % Cl: 0.66 to 12.31; p < 0.05), internal rotation (SMD:-1.74; 95 % Cl: -4.25 to 0.78; p = 0.176) and external rotation (SMD:2.78; 95 % Cl: -0.13 to 5.69; p = 0.062). The authors concluded that the study findings suggested that individuals with rotator cuff injuries may benefit from hypertonic dextrose proliferation treatment based on the VAS score, the SPAD score, flexion, and abduction; however, these study findings must be validated by high-caliber, follow-up investigations.

Heber et al (2024) compared the effectiveness of platelet rich plasma (PRP) injections to other conservative treatment modalities for the management of plantar fasciitis. A systematic review and a meta-analysis were conducted comparing PRP to other treatment modalities. There were 21 randomized control trials (RCT) and a total of 1356 patients included. Reported outcomes included visual analog scale (VAS) pain scores, plantar fascia thickness (PFT), American Orthopaedic Foot and Ankle Society (AOFAS) scores, and total Foot Function Index (FFI). PRP demonstrated significantly greater improvements in VAS pain scores compared to extracorporeal shock wave therapy (ESWT), corticosteroid injections (CSI), and placebo. Researchers found that PRP demonstrated significantly greater improvements in AOFAS scores over CSI and placebo but there were no significant differences among PRP, ESWT, CSI, dextrose prolotherapy (DPT), and meridian trigger points (MTP) in enhancing foot functionality. This study contained a high degree of heterogeneity among the included studies, and the method of PRP preparation varied significantly. The meta-analysis found no superiority of PRP over other treatments in measures such as VAS pain, PFT, and FFI which raises questions about the generalizability of the findings. PRP as a treatment option for a variety of musculoskeletal conditions warrants further evaluation and a more standardized approach to PRP preparation and outcome management.

PROFESSIONAL GUIDELINE(S)

Professional Society Name	Guideline/Version/Year	Summary of Content
American College of Foot and Ankle Surgeons	2017 Guideline for Acquired Heel Pain	Evidence regarding the efficacy and safety of prolotherapy for treatment of plantar fasciitis is uncertain, which makes its use neither appropriate nor inappropriate.
American College of Rheumatology/Arthritis Foundation	2019 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.
North American Spine Society	2020 Guideline for Low Back Pain	Does not provide a recommendation on prolotherapy but states that sacroiliac ligament prolotherapy deserves further study.

REGULATORY STATUS

Although individual ingredients such as dextrose and lidocaine are approved for injection by the U.S. Food and Drug Administration (FDA), they are not approved for prolotherapy. Drug solutions injected during prolotherapy are typically prepared by compound pharmacies or individual practitioners and, therefore, are not subject to regulation by the FDA.

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
Not Applicable	

HCPCS Codes

Code	Description
M0076 (E/I)	Prolotherapy

ICD10 Codes

Code	Description
Numerous	Prolotherapy is considered investigational for all diagnoses.

REFERENCES

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SEARCH TERMS

Proliferating agent, prolotherapy, sclerosing proliferation therapy, joint sclerotherapy, regenerative injection therapy, growth factor stimulation injection

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Prolotherapy (NCD 150.7) [accessed 2025 May 09]

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION

Committee Approval Dates

09/16/99, 05/01/00, 09/19/01, 07/18/02, 09/18/03, 06/17/04, 03/17/05, 03/16/06, 03/15/07, 02/21/08, 01/15/09, 10/29/09, 10/28/10, 09/15/11, 09/20/12, 09/19/13, 09/18/14, 09/17/15, 09/15/16, 09/21/17, 06/21/18, 12/20/18, 12/19/19, 12/17/20, 12/16/21, 12/22/22, 12/21/23, 12/19/24, 06/26/25

Date	Summary of Changes
06/26/25	• Annual policy review; policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
09/16/99	• Original effective date