

POLICY TITLE	PROLOTHERAPY
POLICY NUMBER	MP 2.061

CLINICAL BENEFIT	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	4/1/2024

[POLICY RATIONALE](#)
[DISCLAIMER](#)
[POLICY HISTORY](#)

[PRODUCT VARIATIONS](#)
[DEFINITIONS](#)
[CODING INFORMATION](#)

[DESCRIPTION/BACKGROUND](#)
[BENEFIT VARIATIONS](#)
[REFERENCES](#)

I. POLICY

Prolotherapy is considered **investigational** as a treatment of musculoskeletal pain, as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-references:

- MP 2.062** Temporomandibular Joint Disorder
- MP 4.039** Orthopedic Applications of Platelet Rich Plasma
- MP 5.048** Diagnosis and Treatment of Sacroiliac Joint Pain

II. PRODUCT VARIATIONS

[Top](#)

This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

III. DESCRIPTION/BACKGROUND

[Top](#)

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.

The goal of prolotherapy is to promote tissue repair or growth by prompting release of growth factors, such as cytokines, or increasing the effectiveness of existing circulating growth

POLICY TITLE	PROLOTHERAPY
POLICY NUMBER	MP 2.061

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, glycerine, and phenol, or dextrose alone, often combined with a local anesthetic. Polidocanol and sodium morrhuate, 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 (PRP), which contains a high concentration of platelet-derived growth factors. Treatment of musculoskeletal pain conditions (e.g., tendinopathies) with PRP is discussed in MP 4.039 Orthopedic Applications of Platelet Rich Plasma.

Regulatory status

The U.S. Food and Drug Administration has approved sclerosing agents for use in treating spider/varicose veins. These sclerosing agents include Asclera® (polidocanol), Varithena® (an injectable polidocanol foam), Sotradecol® (sodium tetradecyl sulfate), Ethamolin® (ethanolamine oleate), and Scleromate® (sodium morrhuate). These agents are not currently approved as joint and ligamentous sclerosing agents.

IV. RATIONALE

[Top](#)

SUMMARY OF EVIDENCE

For individuals who have musculoskeletal pain (eg, 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. 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 the effects of the technology on health outcomes.

V. DEFINITIONS

[Top](#)

CYTOKINES refer to one or more than one hundred (100) distinct proteins produced primarily by white blood cells. They provide signals to regulate immunological aspects of cell growth and function during both inflammation and specific immune response.

VI. BENEFIT VARIATIONS

[Top](#)

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

POLICY TITLE	PROLOTHERAPY
POLICY NUMBER	MP 2.061

VII. DISCLAIMER

[Top](#)

Capital Blue Cross’s medical policies are developed to assist in administering a member’s benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member’s benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member’s plan of benefits, please contact Capital Blue Cross’ Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

[Top](#)

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore, not covered:

Procedure Codes							
M0076							

IX. REFERENCES

[Top](#)

1. Dagenais S, Yelland MJ, Del Mar C, et al. Prolotherapy injections for chronic low-back pain. *Cochrane Database Syst Rev.* Apr 18 2007; (2): CD004059. PMID 17443537
2. Dagenais S, Mayer J, Haldeman S, et al. Evidence-informed management of chronic low back pain with prolotherapy. *Spine J.* Jan-Feb 2008; 8(1): 203-12. PMID 18164468
3. Chou R, Atlas SJ, Stanos SP, et al. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. *Spine (Phila Pa 1976).* May 01 2009; 34(10): 1078-93. PMID 19363456
4. Yelland MJ, Glasziou PP, Bogduk N, et al. Prolotherapy injections, saline injections, and exercises for chronic low-back pain: a randomized trial. *Spine (Phila Pa 1976).* Jan 01 2004; 29(1): 9-16; discussion 16. PMID 14699269
5. Klein RG, Eek BC, DeLong WB, et al. A randomized double-blind trial of dextrose-glycerine-phenol injections for chronic, low back pain. *J Spinal Disord.* Feb 1993; 6(1): 23-33. PMID 8439713
6. Ongley MJ, Klein RG, Dorman TA, et al. A new approach to the treatment of chronic low back pain. *Lancet.* Jul 18 1987; 2(8551): 143-6. PMID 2439856
7. Kim WM, Lee HG, Jeong CW, et al. A randomized controlled trial of intra-articular prolotherapy versus steroid injection for sacroiliac joint pain. *J Altern Complement Med.* Dec 2010; 16(12): 1285-90. PMID 21138388

POLICY TITLE	PROLOTHERAPY
POLICY NUMBER	MP 2.061

8. Reeves KD, Hassanein KM. Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity. *Altern Ther Health Med.* May-Jun 2003; 9(3): 58-62. PMID 12776476
9. Wee TC, Neo EJR, Tan YL. Dextrose prolotherapy in knee osteoarthritis: A systematic review and meta-analysis. *J Clin Orthop Trauma.* Aug 2021; 19: 108-117. PMID 34046305
10. Sert AT, Sen EI, Esmaeilzadeh S, et al. The Effects of Dextrose Prolotherapy in Symptomatic Knee Osteoarthritis: A Randomized Controlled Study. *J Altern Complement Med.* May 2020; 26(5): 409-417. PMID 32223554
11. Rabago D, Patterson JJ, Mundt M, et al. Dextrose prolotherapy for knee osteoarthritis: a randomized controlled trial. *Ann Fam Med.* May-Jun 2013; 11(3): 229-37. PMID 23690322
12. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med.* Mar 2000; 6(2): 68-74, 77-80. PMID 10710805
13. Jahangiri A, Moghaddam FR, Najafi S. Hypertonic dextrose versus corticosteroid local injection for the treatment of osteoarthritis in the first carpometacarpal joint: a double-blind randomized clinical trial. *J Orthop Sci.* Sep 2014; 19(5): 737-43. PMID 25158896
14. Rabago D, Mundt M, Zgierska A, et al. Hypertonic dextrose injection (prolotherapy) for knee osteoarthritis: Long term outcomes. *Complement Ther Med.* Jun 2015; 23(3): 388-95. PMID 26051574
15. Reeves KD, Hassanein K. Randomized, prospective, placebo-controlled double-blind study of dextrose prolotherapy for osteoarthritic thumb and finger (DIP, PIP, and trapeziometacarpal) joints: evidence of clinical efficacy. *J Altern Complement Med.* Aug 2000; 6(4): 311-20. PMID 10976977
16. Goh SL, Jaafar Z, Gan YN, et al. Efficacy of prolotherapy in comparison to other therapies for chronic soft tissue injuries: A systematic review and network meta-analysis. *PLoS One.* 2021; 16(5): e0252204. PMID 34038486
17. Chung MW, Hsu CY, Chung WK, et al. Effects of dextrose prolotherapy on tendinopathy, fasciopathy, and ligament injuries, fact or myth?: A systematic review and meta-analysis. *Medicine (Baltimore).* Nov 13 2020; 99(46): e23201. PMID 33181700
18. Rabago D, Best TM, Zgierska AE, et al. A systematic review of four injection therapies for lateral epicondylitis: prolotherapy, polidocanol, whole blood and platelet-rich plasma. *Br J Sports Med.* Jul 2009; 43(7): 471-81. PMID 19028733
19. Scarpone M, Rabago DP, Zgierska A, et al. The efficacy of prolotherapy for lateral epicondylitis: a pilot study. *Clin J Sport Med.* May 2008; 18(3): 248-54. PMID 18469566
20. Akcay S, Gurel Kandemir N, Kaya T, et al. Dextrose Prolotherapy Versus Normal Saline Injection for the Treatment of Lateral Epicondylopathy: A Randomized Controlled Trial. *J Altern Complement Med.* Dec 2020; 26(12): 1159-1168. PMID 32990454
21. Apaydin H, Bazancir Z, Altay Z. Injection Therapy in Patients with Lateral Epicondylalgia: Hyaluronic Acid or Dextrose Prolotherapy? A Single-Blind, Randomized Clinical Trial. *J Altern Complement Med.* Dec 2020; 26(12): 1169-1175. PMID 32931308

POLICY TITLE	PROLOTHERAPY
POLICY NUMBER	MP 2.061

22. Bayat M, Raeissadat SA, Mortazavian Babaki M, et al. Is Dextrose Prolotherapy Superior To Corticosteroid Injection In Patients With Chronic Lateral Epicondylitis?: A Randomized Clinical Trial. *Orthop Res Rev.* 2019; 11: 167-175. PMID 31819675
23. Carayannopoulos A, Borg-Stein J, Sokolof J, et al. Prolotherapy versus corticosteroid injections for the treatment of lateral epicondylitis: a randomized controlled trial. *PM R.* Aug 2011; 3(8): 706-15. PMID 21871414
24. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. *Br J Sports Med.* Apr 2011; 45(5): 421-8. PMID 19549615
25. Kazempour Mofrad M, Rezasoltani Z, Dadarkhah A, et al. Periarticular Neurofascial Dextrose Prolotherapy Versus Physiotherapy for the Treatment of Chronic Rotator Cuff Tendinopathy: Randomized Clinical Trial. *J Clin Rheumatol.* Jun 01 2021; 27(4): 136-142. PMID 32975923
26. Bertrand H, Reeves KD, Bennett CJ, et al. Dextrose Prolotherapy Versus Control Injections in Painful Rotator Cuff Tendinopathy. *Arch Phys Med Rehabil.* Jan 2016; 97(1): 17-25. PMID 26301385
27. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Rheumatol.* Feb 2020; 72(2): 220-233. PMID 31908163
28. Centers for Medicare and Medicaid Services. *National Coverage Determination (NCD) for PROLOTHERAPY, Joint Sclerotherapy, and Ligamentous Injections with Sclerosing Agents (150.7).* 1999.
29. *Blue Cross Blue Shield Association Medical Policy Reference Manual.* 2.01.26, Prolotherapy. December 2023

X. POLICY HISTORY

[Top](#)

MP 2.061	8/3/20 Consensus Review. No change to policy statements. References reviewed.
	6/3/2021 Consensus Review. No change to policy statement. References and coding reviewed.
	11/15/2022 Consensus review. Updated cross-references, FEP, coding table, and references.
	12/15/2023 Consensus review. Updated references. No changes to coding.

[Top](#)

Health care benefit programs issued or administered by Capital Blue Cross and/or its subsidiaries, Capital Advantage Insurance Company®, Capital Advantage Assurance Company® and Keystone Health Plan® Central. Independent licensees of the BlueCross BlueShield Association. Communications issued by Capital Blue Cross in its capacity as administrator of programs and provider relations for all companies.