

Prolotherapy

MEDICAL POLICY NUMBER: 200

Effective Date: 7/1/2026	COVERAGE CRITERIA	2
Last Review Date: 6/2026	POLICY CROSS REFERENCES	2
Next Annual Review: 6/2027	POLICY GUIDELINES	3
	REGULATORY STATUS.....	3
	CLINICAL EVIDENCE AND LITERATURE REVIEW.....	3
	BILLING GUIDELINES AND CODING	6
	REFERENCES	6
	POLICY REVISION HISTORY	9

INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ Commercial

☐ Medicaid/OHP*

☐ Medicare**

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

PHP follows Guideline Notes 172 and 173 of the OHP Prioritized List of Health Services for guidance on New and Emerging Technology. In the absence of OHP guidance, PHP will follow this policy.

**Medicare Members

This Company policy may be applied to Medicare Plan members only when directed by a separate Medicare policy. Note that investigational services are considered “**not medically necessary**” for Medicare members.

COVERAGE CRITERIA

Note: This policy does not address stem cell therapy for orthopedic applications. Please see Policy Cross References section below.

- I. Prolotherapy is considered **not medically necessary** for the treatment of any indication, including, but not limited to the following (A-D):
 - A. Osteoarthritis
 - B. Spinal and pelvic pain
 - C. Joint and muscle pain
 - D. Tendinopathies

Link to [Evidence Summary](#)

POLICY CROSS REFERENCES

- [Stem Cell Therapy for Orthopedic Applications](#), MP36

The full Company portfolio of current Medical Policies is available online and can be [accessed here](#).

POLICY GUIDELINES

BACKGROUND

According to the American Academy of Orthopaedic Medicine (AAOM):¹

Prolotherapy (also known as regenerative injection therapy, sclerotherapy, proliferative therapy, ligament reconstruction therapy, and fibro-osseous injection therapy) is the injection of a substance that promotes growth of normal cells, tissues, or organs. The injections contain anesthetic agents and/or additional substances that are thought act as mild irritants that may stimulate the healing response. The primary agent is dextrose, but providers may tailor the selection of substances according to the patients' needs. Other substances used may include:

1. Growth Factors: Injection of a growth factor that specifically initiates growth of a certain cell line (e.g., erythropoietin). This type of prolotherapy is in early stages of study for arthritis (growing cartilage cells) and sprain and strain (growing fibroblasts).
2. Non-Inflammatory Agents: Injection of a non-inflammatory substance that may cause the body to produce growth factors (e.g., 5-10% dextrose solution).
3. Inflammatory Agents: Injection of a substance that causes activation of the inflammatory cascade to produce growth factors. These solutions often include 12.5%-25% dextrose, phenol-containing-solutions, and/or sodium-morrhuate-containing sclerosing agents.

Proposed Mechanism of Action: Prolotherapy is thought to create a mild, controlled injury that stimulates the body's natural healing processes to strengthen joints weakened by traumatic or over-use injury. The mild inflammatory response that is created by the injection may encourage growth of new ligament or tendon fibers on the weakened structure.

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

Due to the volume of literature on prolotherapy as a treatment for a wide variety of conditions, the evidence review below is focused on recent systematic reviews. A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of prolotherapy as a treatment for all indications, including but not limited to musculoskeletal pain. Below is a summary of the available evidence identified through April 2026.

The use of prolotherapy has been evaluated and reported by systematic reviews and/or meta-analyses for several orthopedic/musculoskeletal indications, including the following:

- Osteoarthritis:²
 - Osteoarthritis of the first carpometacarpal joint³⁻⁵
 - Osteoarthritis of the knee³⁻¹⁰
 - Osteoarthritis of the thumb and finger^{3-5,11}
- Myofascial Pain Syndrome¹¹
- Spinal and Pelvic Pain:¹²
 - Discogenic leg pain
 - Coccygodynia¹³
 - Sacroiliac joint pain³
 - Iliac crest pain syndrome
 - Cervical, thoracic or lumbar pain
 - Neck pain
 - Low back and pelvic pain^{2,3,14-17}
- Tendinopathies:^{2,18-22}
 - Achilles tendinopathy or tendinosis^{3,11,15,23-27}
 - Groin pain (e.g., osteitis pubis, abdominal or adductor tendinopathy)¹¹
 - Lateral epicondylitis^{3,11,15,23,28-30}
 - Osgood–Schlatter disease^{11,26}
 - Patellar tendinopathy^{3,11,15,31,32}
 - Plantar fasciitis^{3,11,15,23,26,33,34}
 - Shoulder pain (e.g., rotator cuff disease or tendinopathy, supraspinatus tendinosis/tear)^{3,11,15,23,35-37}
 - Temporomandibular joint hypermobility (TMJ)^{3,11,23,38,39}

Systematic reviews were heterogeneous in the methods used to examine primary studies evaluating prolotherapy. Many reviews included or focused entirely on nonrandomized studies, and many included more than one indication. Comparative treatment modalities, when present, were varied. Saline injections, exercise/conservative measures, steroid injections, and injections of platelet rich plasma were all discussed. In general, the reviews reported heterogeneity in prolotherapy protocols and severity of the condition being evaluated among included studies. Reviews published on the same indication often had partial or complete overlap of the studies that were included. All reviews mentioned the need for larger, better-quality studies with standardized protocols and longer-term follow-up. The majority of recent reviews did indicate that prolotherapy was safe with no major adverse effects but were unable to draw definitive conclusions regarding the efficacy of prolotherapy as a treatment for any indication.

Overall, the body of evidence for any given indication suffers from one or more of the following limitations:

- limited number of randomized controlled trials (RCTs) reporting outcomes for any given indication
- for indications where RCTs have been published, these trials are of low-quality of due to methodological limitations including:
 - small sample size (frequently under 100 patients)
 - primary outcomes reported consisted entirely of subjective, patient-reported outcomes
 - use of co-interventions in the prolotherapy groups

- heterogeneity of:
 - comparator treatment
 - primary outcomes reported
 - use of different scales for self-reporting of subjective pain, stiffness and function
 - treatment protocol, including variability in agent(s) used, concentrations used and number of injections administered
- inconsistent data reporting
- risk of publication and/or selection bias
- study results indicate, minimal, inconsistent or no evidence of short-term improvements in pain and/or function (first few months following treatment) when compared to placebo, exercise or non-prolotherapy injection treatments
- conflicting or no evidence of long-term benefit on function or pain outcomes

CLINICAL PRACTICE GUIDELINES

American Academy of Orthopaedic Surgeons (AAOS)

The AAOS published evidence-based clinical practice guidelines on the management of osteoarthritis of the hip (2017) and the knee (2021).^{40,41} The association conducted evidence reviews of prolotherapy versus other comparators for these indications, but did not identify enough high-quality evidence to formally address the treatment in their recommendations.

EVIDENCE SUMMARY

There is insufficient evidence that the use of prolotherapy is effective and consistently improves health outcomes for any indication, including but not limited to osteoarthritis, spinal and pelvic pain, or tendinopathies. Due to heterogeneity in prolotherapy treatment protocol, including variability in agent(s) used, concentrations used and number of injections administered; interpreting results and drawing conclusions about treatment efficacy is difficult. This limitation is consistently reported for the use of prolotherapy for all indications. Other major limitations of prolotherapy observed across all indications include a lack of large, well-designed randomized controlled trials, and inconsistency in terms of whether or not prolotherapy has a beneficial effect. In addition, no clinical practice guidelines were identified that support the use of prolotherapy as a treatment for any indication. Therefore, prolotherapy is considered not medically necessary as a treatment for any indication.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly

reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online [here](#).

BILLING GUIDELINES AND CODING

- Prolotherapy may only be billed using M0076 or an unlisted code, including but not limited to 20999 or 22899.
- Note: The following codes may not be used to report prolotherapy services, as they are considered inappropriate:
 - 20550-20553
 - 20600-20611
 - 62281
 - 62292
 - 62310-62311
 - 0231T-0218T

CODES*		
CPT	20999	Unlisted procedure, musculoskeletal system, general
	22899	Unlisted procedure, spine
HCPCS	M0076	Prolotherapy

*Coding Notes:

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- See the non-covered and prior authorization lists on the Company [Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website](#) for additional information.
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. American Academy of Orthopaedic Medicine. Prolotherapy. <http://www.aaomed.org/prolotherapy>. Published 2020. Accessed 5/11/2026.

2. Kim SR, Stitik TP, Foye PM, Greenwald BD, Campagnolo DI. Critical review of prolotherapy for osteoarthritis, low back pain, and other musculoskeletal conditions: a physiatric perspective. *Am J Phys Med Rehabil.* 2004;83(5):379-389.
3. Bae G, Kim S, Lee S, Lee WY, Lim Y. Prolotherapy for the patients with chronic musculoskeletal pain: systematic review and meta-analysis. *Anesth Pain Med (Seoul).* 2021;16(1):81-95.
4. Hung CY, Hsiao MY, Chang KV, Han DS, Wang TG. Comparative effectiveness of dextrose prolotherapy versus control injections and exercise in the management of osteoarthritis pain: a systematic review and meta-analysis. *J Pain Res.* 2016;9:847-857.
5. Krsticevic M, Jeric M, Dosenovic S, Jelcic Kadic A, Puljak L. Proliferative injection therapy for osteoarthritis: a systematic review. *Int Orthop.* 2017;41(4):671-679.
6. Wang J, Liang J, Yao J, et al. Meta-analysis of clinical trials focusing on hypertonic dextrose prolotherapy (HDP) for knee osteoarthritis. *Aging Clin Exp Res.* 2021.
7. Wee TC, Neo EJR, Tan YL. Dextrose prolotherapy in knee osteoarthritis: A systematic review and meta-analysis. *J Clin Orthop Trauma.* 2021;19:108-117.
8. Arias-Vázquez PI, Tovilla-Zárate CA, Castillo-Avila RG, et al. Hypertonic Dextrose Prolotherapy, an alternative to intra-articular injections with Hyaluronic Acid in the treatment of knee osteoarthritis: systematic review and meta-analysis. *Am J Phys Med Rehabil.* 2021.
9. Hassan F, Trebinjac S, Murrell WD, Maffulli N. The effectiveness of prolotherapy in treating knee osteoarthritis in adults: a systematic review. *Br Med Bull.* 2017;122(1):91-108.
10. Sit RW, Chung V, Reeves KD, et al. Hypertonic dextrose injections (prolotherapy) in the treatment of symptomatic knee osteoarthritis: A systematic review and meta-analysis. *Sci Rep.* 2016;6:25247.
11. Hauser RA, Lackner JB, Steilen-Matias D, Harris DK. A Systematic Review of Dextrose Prolotherapy for Chronic Musculoskeletal Pain. *Clin Med Insights Arthritis Musculoskelet Disord.* 2016;9:139-159.
12. Hayes I. *Prolotherapy for Treatment of Joint and Ligamentous Conditions.* Lansdale, PA: Hayes, a symplr Company; August 8, 2008 2008.
13. White WD, Avery M, Jonely H, Mansfield JT, Sayal PK, Desai MJ. The interdisciplinary management of coccydynia: A narrative review. *Pm r.* 2021.
14. Giordano L, Murrell WD, Maffulli N. Prolotherapy for chronic low back pain: a review of literature. *Br Med Bull.* 2021;138(1):96-111.
15. Goh S-L JZ, Gan Y-N, Choong A, Kaur J, Kundakci B, et al. Efficacy of prolotherapy in comparison to other therapies for chronic soft tissue injuries: A systematic review and network meta-analysis. *PLoS ONE* 16(5): e0252204. <https://doi.org/10.1371/journal.pone.0252204>. Published 2021. Accessed 5/11/2026.
16. Hauser RA, Matias D, Woznica D, Rawlings B, Woldin BA. Lumbar instability as an etiology of low back pain and its treatment by prolotherapy: A review. *J Back Musculoskelet Rehabil.* 2021.
17. Fullerton BD. Prolotherapy for the Thoracolumbar Myofascial System. *Phys Med Rehabil Clin N Am.* 2018;29(1):125-138.
18. Chung M-W, Hsu C-Y, Chung W-K, Lin Y-N. Effects of dextrose prolotherapy on tendinopathy, fasciopathy, and ligament injuries, fact or myth?: A systematic review and meta-analysis. *Medicine (Baltimore).* 2020;99(46):e23201-e23201.
19. Bae G, Kim S, Lee S, Lee WY, Lim Y. Prolotherapy for the patients with chronic musculoskeletal pain: systematic review and meta-analysis. *Anesth Pain Med (Seoul).* 2021;16(1):81-95.
20. Zhu M, Rabago D, Chung VC, Reeves KD, Wong SY, Sit RW. Effects of Hypertonic Dextrose Injection (Prolotherapy) in Lateral Elbow Tendinosis: A Systematic Review and Meta-analysis. *Arch Phys Med Rehabil.* 2022.

21. 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.
22. Bisciotti GN, Chamari K, Cena E, et al. The conservative treatment of longstanding adductor-related groin pain syndrome: a critical and systematic review. *Biol Sport*. 2021;38(1):45-63.
23. Chung MW, Hsu CY, Chung WK, Lin YN. Effects of dextrose prolotherapy on tendinopathy, fasciopathy, and ligament injuries, fact or myth?: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(46):e23201.
24. Morath O, Kubosch EJ, Taeymans J, et al. The effect of sclerotherapy and prolotherapy on chronic painful Achilles tendinopathy-a systematic review including meta-analysis. *Scand J Med Sci Sports*. 2018;28(1):4-15.
25. Kearney RS, Parsons N, Metcalfe D, Costa ML. Injection therapies for Achilles tendinopathy. *Cochrane Database Syst Rev*. 2015(5):Cd010960.
26. Sanderson LM, Bryant A. Effectiveness and safety of prolotherapy injections for management of lower limb tendinopathy and fasciopathy: a systematic review. *J Foot Ankle Res*. 2015;8:57.
27. Gross CE, Hsu AR, Chahal J, Holmes GB, Jr. Injectable treatments for noninsertional achilles tendinosis: a systematic review. *Foot Ankle Int*. 2013;34(5):619-628.
28. Dong W, Goost H, Lin XB, et al. Injection therapies for lateral epicondylalgia: a systematic review and Bayesian network meta-analysis. *Br J Sports Med*. 2016;50(15):900-908.
29. Sims SE, Miller K, Elfar JC, Hammert WC. Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials. *Hand (N Y)*. 2014;9(4):419-446.
30. Krogh TP, Bartels EM, Ellingsen T, et al. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. *Am J Sports Med*. 2013;41(6):1435-1446.
31. Morath O, Beck M, Taeymans J, Hirschmüller A. Sclerotherapy and prolotherapy for chronic patellar tendinopathies - a promising therapy with limited available evidence, a systematic review. *J Exp Orthop*. 2020;7(1):89.
32. Cairns G, Owen T, Kluzek S, et al. Therapeutic interventions in children and adolescents with patellar tendon related pain: a systematic review. *BMJ Open Sport Exerc Med*. 2018;4(1):e000383.
33. Chutumstid T, Susantitapong P, Koonalinthip N. Effectiveness of Dextrose prolotherapy for the treatment of chronic Plantar Fasciitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Pm r*. 2022.
34. Lai WF, Yoon CH, Chiang MT, et al. The effectiveness of dextrose prolotherapy in plantar fasciitis: A systemic review and meta-analysis. *Medicine (Baltimore)*. 2021;100(51):e28216.
35. Catapano M, Zhang K, Mittal N, Sangha H, Onishi K, de Sa D. Effectiveness of Dextrose Prolotherapy for Rotator Cuff Tendinopathy: A Systematic Review. *Pm r*. 2020;12(3):288-300.
36. Lin MT, Chiang CF, Wu CH, Huang YT, Tu YK, Wang TG. Comparative Effectiveness of Injection Therapies in Rotator Cuff Tendinopathy: A Systematic Review, Pairwise and Network Meta-analysis of Randomized Controlled Trials. *Arch Phys Med Rehabil*. 2018.
37. Lin MT, Chiang CF, Wu CH, Huang YT, Tu YK, Wang TG. Comparative Effectiveness of Injection Therapies in Rotator Cuff Tendinopathy: A Systematic Review, Pairwise and Network Meta-analysis of Randomized Controlled Trials. *Arch Phys Med Rehabil*. 2019;100(2):336-349.e315.
38. Sit RW, Reeves KD, Zhong CC, et al. Efficacy of hypertonic dextrose injection (prolotherapy) in temporomandibular joint dysfunction: a systematic review and meta-analysis. *Sci Rep*. 2021;11(1):14638.

39. Nagori SA, Jose A, Gopalakrishnan V, Roy ID, Chattopadhyay PK, Roychoudhury A. The efficacy of dextrose prolotherapy over placebo for temporomandibular joint hypermobility: A systematic review and meta-analysis. *J Oral Rehabil.* 2018.
40. American Academy of Orthopaedic Surgeons. Management Of Osteoarthritis Of The Hip: Evidence-Based Clinical Practice Guideline. https://aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-hip/oa-hip-cpg_6-11-19.pdf. Published 2017. Accessed 5/11/2026.
41. American Academy of Orthopaedic Surgeons. Treatment of Osteoarthritis of the Knee (3rd edition)(Non-Arthroplasty): Evidence-Based Guideline. <https://www.aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-knee/osteoarthritis-of-the-knee-2nd-edition-clinical-practice-guideline.pdf>. Published 2021. Accessed 5/11/2026.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
7/2023	Annual Review. Inclusion of Regulatory Guideline language. No changes.
9/2024	Annual review. Changed denial from investigational to not medically necessary.
7/2025	Annual review. No changes.
7/2026	Annual review. No changes.