

Prolotherapy

MEDICAL POLICY NUMBER: 200

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COVERAGE CRITERIA 2
POLICY CROSS REFERENCES 2
POLICY GUIDELINES 3
REGULATORY STATUS..... 3
CLINICAL EVIDENCE AND LITERATURE REVIEW..... 3
BILLING GUIDELINES AND CODING 5
REFERENCES 6
POLICY REVISION HISTORY 8

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.

**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 **investigational and is not covered** 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 2023.

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:
 - Discogenic leg pain
 - Coccygodynia¹²
 - Sacroiliac joint pain³
 - Iliac crest pain syndrome
 - Cervical, thoracic or lumbar pain
 - Neck pain
 - Low back and pelvic pain^{2,3,13-16}
- Tendinopathies:^{2,17-21}
 - Achilles tendinopathy or tendinosis^{3,11,14,22-26}
 - Groin pain (e.g., osteitis pubis, abdominal or adductor tendinopathy)¹¹
 - Lateral epicondylitis^{3,11,14,22,27-29}
 - Osgood–Schlatter disease^{11,25}
 - Patellar tendinopathy^{3,11,14,30,31}
 - Plantar fasciitis^{3,11,14,22,25,32,33}
 - Shoulder pain (e.g., rotator cuff disease or tendinopathy, supraspinatus tendinosis/tear)^{3,11,14,22,34-36}
 - Temporomandibular joint hypermobility (TMJ)^{3,11,22,37,38}

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 injects 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 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).^{39,40} 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 investigational as a treatment for any indication.

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.

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POLICY REVISION HISTORY

| DATE | REVISION SUMMARY |
|--------|--|
| 2/2023 | Converted to new policy template. |
| 7/2023 | Annual Review. Inclusion of Regulatory Guideline language. No changes. |