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# **Medical Policy**

# **Orthopedic Applications of Platelet-Rich Plasma**

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**Policy Number: 737** 

BCBSA Reference Number: 2.01.98 (For Plan internal use only)

#### **Related Policies**

- Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions, #111
- Bone Morphogenetic Protein #097
- Orthopedic Applications of Stem Cell Therapy #254
- Prolotherapy, #183

#### **Policy**

# Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Use of platelet-rich plasma is considered **INVESTIGATIONAL** for all orthopedic indications. This includes, but is not limited to, use in the following situations:

- Primary use (injection) for the following conditions:
  - Achilles tendinopathy
  - Lateral epicondylitis
  - Osteochondral lesions
  - Osteoarthritis
  - Plantar fasciitis.
- Adjunctive use in the following surgical procedures:
  - o ACL reconstruction
  - o Hip fracture
  - Long-bone nonunion
  - o Patellar tendon repair
  - o Rotator cuff repair
  - Spinal fusion
  - Subacromial decompression surgery
  - Total knee arthroplasty.

# **Prior Authorization Information**

## Inpatient

• For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

#### Outpatient

• For services described in this policy, see below for products where prior authorization <u>might be</u> <u>required</u> if the procedure is performed <u>outpatient</u>.

	Outpatient
Commercial Managed Care (HMO and POS)	This is <b>not</b> a covered service.
Commercial PPO and Indemnity	This is <b>not</b> a covered service.

#### **CPT Codes / HCPCS Codes / ICD Codes**

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT code is considered investigational for <u>Commercial Members: Managed Care</u> (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

#### **CPT Codes**

CPT codes:	Code Description
0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed

### **Description**

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factors, epidermal growth factor, fibroblast growth factors, transforming growth factors, and insulinlike growth factors. Autologous platelets are a rich source of platelet-derived growth factor, transforming growth factors that function as a mitogen for fibroblasts, smooth muscle cells, osteoblasts, and vascular endothelial growth factors. Recombinant platelet-derived growth factor has also been extensively investigated for clinical use in wound healing.

Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma, can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets, releasing the various growth factors. The polymerization of fibrin from fibrinogen creates a platelet gel, which can then be used as an adjunct to surgery with the intent of promoting hemostasis and accelerating healing. In the operating room setting, platelet-rich plasma has been investigated as an adjunct to various periodontal, reconstructive, and orthopedic procedures. For example, bone morphogenetic proteins are a type of transforming growth factor, and thus platelet-rich plasma has been used in conjunction with bone-replacement grafting (using either autologous grafts or bovine-derived xenograft) in periodontal and maxillofacial surgeries. Alternatively, platelet-rich plasma may be injected directly into various tissues. Platelet -rich plasma injections have been proposed as a primary treatment of miscellaneous conditions, such as epicondylitis, plantar fasciitis, and Dupuytren contracture.

Injection of platelet-rich plasma for tendon and ligament pain is theoretically related to prolotherapy (see policy #183). However, prolotherapy differs in that it involves the injection of chemical irritants intended to stimulate inflammatory responses and induce the release of endogenous growth factors.

Platelet-rich plasma is distinguished from fibrin glues or sealants, which have been used as a surgical adjunct to promote local hemostasis at incision sites. Fibrin glue is created from platelet-poor plasma and consists primarily of fibrinogen. Commercial fibrin glues are created from pooled homologous human donors; Tisseel® (Baxter) and VITASEAL™ (Johnson & Johnson Surgical Technologies) are examples of commercially available fibrin sealants. Autologous fibrin sealants can be created from platelet-poor plasma. This evidence review does not address the use of fibrin sealants.

## **Summary**

The use of platelet-rich plasma has been proposed as a treatment for various musculoskeletal conditions and as an adjunctive procedure in orthopedic surgeries. The potential benefit of platelet-rich plasma has received considerable interest due to the appeal of a simple, safe, low-cost, and minimally invasive method of applying growth factors.

# **Primary Treatment for Tendinopathies**

For individuals with tendinopathy who receive platelet-rich plasma injections, the evidence includes multiple randomized controlled trials (RCTs) and systematic reviews with meta-analyses. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Findings from meta-analyses of RCTs have been mixed and have generally found that platelet-rich plasma did not have a statistically and/or clinically significant impact on symptoms (ie, pain) or functional outcomes. Findings from a subsequently published RCT failed to find improvement compared with placebo. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## Primary Treatment for Non-Tendon Soft Tissue Injury or Inflammation

For individuals with non-tendon soft tissue injury or inflammation (eg, plantar fasciitis) who receive platelet-rich plasma injections, the evidence includes several small RCTs, multiple prospective observational studies, and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The 2014 systematic review, which identified 3 RCTs on platelet-rich plasma for plantar fasciitis, did not pool study findings. Results among the remaining RCTs were inconsistent. The largest RCT showed that treatment using platelet-rich plasma compared with corticosteroid injection resulted in statistically significant improvement in pain and disability, but not quality of life. A 2023 systematic review found improved VAS scores with platelet-rich plasma compared to corticosteroid injections out to 6 months duration, but numerical differences between groups were small. Larger RCTs completed over a sufficient duration of time (i.e., 2 years) are still needed to address important uncertainties in efficacy and safety. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

#### **Primary Treatment for Osteochondral Lesions**

For individuals with osteochondral lesions who receive platelet-rich plasma injections, the evidence includes an open-labeled quasi-randomized study. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The quasi-randomized study found a statistically significant greater impact on outcomes in the platelet-rich plasma group than in the hyaluronic acid group. Limitations of the evidence base include lack of adequately randomized studies, lack of blinding, lack of sham controls, and comparison only to an intervention of uncertain efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

#### **Primary Treatment for Knee or Hip Osteoarthritis**

For individuals with knee or hip osteoarthritis who receive platelet-rich plasma injections, the evidence includes multiple RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Most trials have compared platelet-rich plasma with hyaluronic acid for knee osteoarthritis. Systematic reviews have generally found that platelet-rich plasma was more effective than placebo or hyaluronic acid in reducing pain and improving function. However, systematic review authors have noted that their findings should be interpreted with caution due to important limitations including significant residual statistical heterogeneity, questionable clinical significance, and high risk of bias in study conduct. RCTs with a follow-up of at least

12 months published subsequent to the systematic reviews found statistically significantly greater 12-month reductions in pain and function outcomes, but these findings were also limited by important study conduct flaws including potential inadequate control for selection bias and limited or unclear blinding. Also, benefits were not maintained at 5 years. Using hyaluronic acid as a comparator is questionable because the evidence demonstrating the benefit of hyaluronic acid treatment for osteoarthritis is not robust. Two systematic reviews evaluating hip osteoarthritis did not report any statistically or clinically significant differences in pain or functional outcomes compared to hyaluronic acid, corticosteroids, or placebo. Additional studies comparing platelet-rich plasma with placebo and with alternatives other than hyaluronic acid are needed to determine the efficacy of platelet-rich plasma for knee and hip osteoarthritis. Studies are also needed to determine the optimal protocol for delivering platelet-rich plasma. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## **Adjunct to Surgery**

For individuals with anterior cruciate ligament reconstruction who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes several systematic reviews of multiple RCTs and prospective studies and a retrospective matched case-control study. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. In 2 systematic reviews that conducted a meta-analysis, adjunctive platelet-rich plasma treatment did not result in a significant effect on International Knee Documentation Committee (IKDC) scores, a patient-reported, knee-specific outcome measure that assesses pain and functional activity. One systematic review found improvements with platelet-rich plasma compared to controls in outcomes at 6 months, but these differences were determined to be clinically irrelevant with the exception of pain at 6 months which was improved with platelet-rich plasma. Individual trials have shown mixed results. A retrospective matched case-control study found no differences in knee function scores or time to return of activity between platelet-rich plasma and matched-control groups at 2 years; however, the platelet-rich plasma group demonstrated a higher rate of postoperative knee motion loss compared with the control group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with hip fracture who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes an open-labeled RCT. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. The single open-label RCT failed to show a statistically significant reduction in the need for surgical revision with the addition of platelet-rich plasma treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with long bone nonunion who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes 3 RCTs. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. One trial with a substantial risk of bias failed to show significant differences in patient-reported or clinician-assessed functional outcome scores between patients who received platelet-rich plasma plus allogenic bone graft versus those who received only allogenic bone graft. While the trial showed statistically significant increases in the proportion of bones that healed in patients receiving platelet-rich plasma in a modified intention-to-treat analysis, the results did not differ in the intention-to-treat analysis. An RCT that compared platelet-rich plasma with recombinant human bone morphogenetic protein-7 (rhBMP-7) also failed to show any clinical and radiologic benefits of platelet-rich plasma over rhBMP-7. The third RCT found no difference in the number of unions or time to union in patients receiving platelet-rich plasma injections or no treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with rotator cuff repair who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes multiple RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. Although systematic reviews consistently found significant reductions in pain with platelet-rich plasma at 12 months, important study conduct and relevance weaknesses limit

interpretation of these findings. While the systematic reviews and meta-analyses generally failed to show a statistically and/or clinically significant impact on other outcomes, 1 meta-analysis found a statistically significant reduction in retear rate in a subgroup analysis of 4 RCTs that were at least 24 months in duration. The findings of a subsequently published 10-year follow-up of a small RCT failed to demonstrate the superiority of platelet-rich plasma over control for clinical and radiologic outcomes. The variability in platelet-rich plasma preparation techniques and platelet-rich plasma administration limits the generalizability of the available evidence. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals undergoing spinal fusion who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes a single small RCT and a few observational studies. Relevant outcomes include symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. Studies have generally failed to show a statistically and/or clinically significant impact on symptoms (ie, pain). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with subacromial decompression surgery who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes a small RCT. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. A single small RCT failed to show a reduction in self-assessed or physician-assessed spinal instability scores with platelet-rich plasma injections. However, subjective pain, use of pain medications, and objective measures of range of motion showed clinically significant improvements with platelet-rich plasma. Larger trials are required to confirm these benefits. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with total knee arthroplasty who receive platelet-rich plasma injections plus orthopedic surgery, the evidence includes systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. The reviews showed no significant differences between the platelet-rich plasma and untreated control groups in range of motion, functional outcomes, and long-term pain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

# **Policy History**

Date	Action
6/2023	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
6/2022	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
5/2021	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for
	local coverage determination and national coverage determination reference.
	Clarified coding information.
6/2020	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
5/2019	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
5/2017	Annual policy review. New references added.
5/2016	Annual policy review. New references added.
10/2015	New medical policy describing investigational indications. Orthopedic applications of
	platelet-rich plasma transferred from policy #186. Effective 10/1/2015.

# **Information Pertaining to All Blue Cross Blue Shield Medical Policies**

Click on any of the following terms to access the relevant information: Medical Policy Terms of Use Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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