



## FEP Medical Policy Manual

### FEP 2.01.98 Orthopedic Applications of Platelet-Rich Plasma

**Annual Effective Policy Date: July 1, 2024**

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**Related Policies:**

2.01.26 - Prolotherapy

8.01.52 - Orthopedic Applications of Stem Cell Therapy (Including Allografts and Bone Substitutes Used With Autologous Bone Marrow)

## Orthopedic Applications of Platelet-Rich Plasma

### Description

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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.

#### OBJECTIVE

The objective of this evidence review is to determine whether the use of platelet-rich plasma improves the net health outcome in individuals with musculoskeletal conditions and those undergoing orthopedic surgical procedures.

## POLICY STATEMENT

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;
  - Plantar fasciitis;
  - Osteochondral lesions;
  - Osteoarthritis.
- Adjunctive use in the following surgical procedures:
  - Anterior cruciate ligament reconstruction;
  - Hip fracture;
  - Long-bone nonunion;
  - Patellar tendon repair;
  - Rotator cuff repair;
  - Spinal fusion;
  - Subacromial decompression surgery;
  - Total knee arthroplasty.

## POLICY GUIDELINES

None

## BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Treatment of osteoarthritis with platelet-rich plasma is a specialized procedure being performed at few centers. Therefore, there may be a request for out-of-network referral.

## FDA REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, title 21, parts 1,270 and 1,271. Blood products such as platelet-rich plasma are included in these regulations. Under these regulations, certain products including blood products such as platelet-rich plasma are exempt and therefore do not follow the traditional FDA regulatory pathway. To date, the FDA has not attempted to regulate activated platelet-rich plasma.

A number of platelet-rich plasma preparation systems are available, many of which were cleared for marketing by the FDA through the 510(k) process for producing platelet-rich preparations intended to be mixed with bone graft materials to enhance the bone grafting properties in orthopedic practices. The use of platelet-rich plasma outside of this setting (eg, an office injection) would be considered off-label. The Aurix System (previously called AutoloGel™; Nuo Therapeutics) and SafeBlood (SafeBlood Technologies) are 2 related but distinct autologous blood-derived preparations that can be used at the bedside for immediate application. Both AutoloGel™ and SafeBlood have been specifically marketed for wound healing. Other devices may be used during surgery (eg, autoLog Autotransfusion system [Medtronic], the SmartPREP [Harvest Technologies] device). The Magellan Autologous Platelet Separator System (Isto Biologics ) includes a disposable kit for use with the Magellan Autologous Platelet Separator portable tabletop

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centrifuge. GPS II (BioMet Biologics), a gravitational platelet separation system, was cleared for marketing by the FDA through the 510(k) process for use as disposable separation tube for centrifugation and a dual cannula tip to mix the platelets and thrombin at the surgical site (GPS III [Zimmer Biomet] is now available). Filtration or plasmapheresis may also be used to produce platelet-rich concentrates. The use of different devices and procedures can lead to variable concentrations of activated platelets and associated proteins, increasing variability between studies of clinical efficacy.

## RATIONALE

### Summary of Evidence

#### 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 visual analog scale (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.

## SUPPLEMENTAL INFORMATION

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

#### American Academy of Orthopaedic Surgeons

In 2021, the American Academy of Orthopaedic Surgeons (AAOS) guidelines for the management of osteoarthritis of the knee made the following recommendation:<sup>56</sup>

- "Platelet-rich plasma (PRP) may reduce pain and improve function in patients with symptomatic osteoarthritis of the knee. (Strength of Recommendation: Limited)" The variability of study findings was noted to have contributed to the low strength of recommendation rating.

In 2023, the AAOS updated evidence-based guidelines on the management of osteoarthritis of the hip.<sup>57</sup> In the section on intra-articular injectables, the guidelines gave a moderate recommendation based on high-quality evidence supporting the use of intra-articular corticosteroids as an option to improve function and reduce pain in the short term for patients with osteoarthritis of the hip. There was also a strong recommendation based on high-quality evidence against the use of intra-articular hyaluronic acid, as it does not perform better than placebo in improving function, stiffness, and pain in patients with hip osteoarthritis. The guidelines did not mention any evidence or make recommendations related to the use of platelet-rich plasma for the treatment of osteoarthritis of the hip.

In 2019, the AAOS issued evidence-based guidelines on the management of rotator cuff injuries.<sup>58</sup> The guideline noted the following recommendations related to the use of platelet-rich plasma in this setting:

- "There is limited evidence supporting the routine use of platelet-rich plasma for the treatment of cuff tendinopathy or partial tears (Strength of Recommendation: Limited)." The variability of study findings was noted to have contributed to the low strength of recommendation rating.
- "Strong evidence does not support biological augmentation of rotator cuff repair with platelet-derived products on improving patient reported outcomes; however, limited evidence supports the use of liquid platelet-rich plasma in the context of decreasing re-tear rates (Strength of Recommendation: Strong)."
- "In the absence of reliable evidence, it is the consensus of the work group that we do not recommend the routine use of platelet-rich plasma in the non-operative management of full-thickness rotator cuff tears (Strength of Recommendation: Consensus)."

#### National Institute for Health and Care Excellence

In 2013, the NICE issued guidance on the use of autologous blood injection for tendinopathy.<sup>59</sup> The NICE concluded that the current evidence on the safety and efficacy of autologous blood injection for tendinopathy was "inadequate" in quantity and quality.

In 2013, the NICE also issued guidance on the use of autologous blood injection (with or without techniques for producing platelet-rich plasma) for plantar fasciitis.<sup>60</sup> The NICE concluded that the evidence on autologous blood injection for plantar fasciitis raised no major safety concerns but that the evidence on efficacy was "inadequate in quantity and quality."

In 2019, the NICE issued guidance on the use of platelet-rich plasma for osteoarthritis of the knee.<sup>61</sup> The NICE concluded that current evidence on platelet-rich plasma injections for osteoarthritis of the knee raised "no major safety concerns"; however, the "evidence on efficacy is limited in quality." Therefore, NICE recommended that "this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."

### U.S. Preventive Services Task Force Recommendations

Not applicable.

## Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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## POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2015	New policy	Policy created on the orthopedic applications of platelet-rich plasma that were previously described in Policy No. 2.01.16
June 2018	Archive policy	Policy updated with literature review through February 5, 2018; references 7, 21, 26, 33, 37, 40, and 46 added. Policy statement unchanged.
June 2020	Reactive policy	Policy updated with literature review through February 25, 2020; references added. Policy statements unchanged.
June 2021	Replace policy	Policy updated with literature review through March 5, 2021; references added. Policy statements unchanged.
June 2022	Replace policy	Policy updated with literature review through February 25, 2022; references added. Policy statements unchanged.
June 2023	Replace policy	Policy updated with literature review through March 1, 2023; references added. Policy statements unchanged.
June 2024	Replace policy	Policy updated with literature review through February 13, 2024; no references added. Policy statements unchanged.

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.