This Protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following Protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

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<th>Populations</th>
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<td>• Other treatment (e.g., corticosteroid injection)</td>
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<td>• Conservative therapy (e.g., rest, physical therapy)</td>
<td>• Symptoms</td>
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<td>Individuals:</td>
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<td>• Conservative therapy (e.g., rest, physical therapy)</td>
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**Description**

This Protocol addresses the use of platelet-rich plasma (PRP) as a treatment of a variety of musculoskeletal conditions and as an adjunctive procedure in orthopedic surgical procedures. The potential benefit of PRP has received considerable interest due to the appeal of a simple, safe, low-cost, and minimally invasive method of applying growth factors.

**Summary of Evidence**

The evidence for platelet-rich plasma (PRP) injections in individuals who have tendinopathy includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. In pooled analyses of RCTs on PRP for tendinopathy, findings were mixed and generally found that PRP did not have a statistically and/or clinically significant impact on symptoms (i.e., pain) or functional outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PRP injections in individuals who have non–tendon soft tissue injury or inflammation (e.g., plantar fasciitis) includes RCTs and at least one systematic review. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The systematic review, which identified three RCTs on PRP for plantar fasciitis, did not pool study findings. The largest RCT enrolled 40 patients and had mixed findings on the relative efficacy of PRP and corticosteroid injection. Confirmation of these results in larger double-blind RCTs is needed to allow greater certainty regarding the efficacy of PRP in plantar fasciitis. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PRP injections in individuals who have osteochondral lesions includes an unblinded 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 significantly greater impact on outcomes in the PRP group than in the group that received hyaluronic acid. 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 the effects of the technology on health outcomes.

The evidence for PRP injections in individuals who have knee osteoarthritis includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Although there are a number of RCTs, only one was placebo-controlled and those data are insufficient for drawing conclusions on whether PRP has a clinically meaningful effect on subjective outcomes beyond a placebo effect. Other RCTs and systematic reviews have compared PRP with hyaluronic acid, another novel intervention. Studies comparing these two interventions should also include a placebo group since it is not known whether either of them have an effect beyond placebo. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PRP injections in individuals who have scheduled orthopedic surgery includes RCTs and systematic reviews. Relevant outcomes are morbid events, resource utilization, and treatment-related morbidity. Systematic reviews with pooled analyses (e.g., Cochrane reviews) on PRP as an adjunct to anterior cruciate ligament reconstruction and to rotator cuff repair, did not find that outcomes were significantly better when using PRP compared with no PRP. Only a single small RCT was available for some types of surgery (e.g., PRP as an adjunct to patellar tendon harvest and subacromial decompression surgery). The evidence is insufficient to determine the effects of the technology on health outcomes.
Policy
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:**
  - Anterior cruciate ligament reconstruction
  - Hip fracture
  - Long-bone nonunion
  - Patellar tendon repair
  - Rotator cuff repair
  - Spinal fusion
  - Subacromial decompression surgery
  - Total knee arthroplasty

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

Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma (PRP), 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, PRP has been investigated as an adjunct to a variety of periodontal, reconstructive, and orthopedic procedures. For example, bone morphogenetic proteins are a type of transforming growth factors, and thus PRP has been used in conjunction with bone-replacement grafting (using either autologous grafts or bovine-derived xenograft) in periodontal and maxillofacial surgeries. Alternatively, PRP may be injected directly into various tissues. PRP injections have been proposed as a primary treatment of miscellaneous conditions, such as epicondylitis, plantar fasciitis, and Dupuytren contracture. Injection of PRP for tendon and ligament pain is theoretically related to prolotherapy (discussed in the Prolotherapy Protocol). However, prolotherapy differs in that it involves injection of chemical irritants that are intended to stimulate inflammatory responses and induce release of endogenous growth factors.
PRP is distinguished from fibrin glues or sealants, which have been used for many years 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 Hemaseel® (Haemacure Corp) are examples of commercially available fibrin sealants. Autologous fibrin sealants can be created from platelet-poor plasma. This Protocol does not address the use of fibrin sealants.

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 (CFR) title 21, parts 1270 and 1271. Blood products such as platelet-rich plasma (PRP) are included in these regulations. Under these regulations, certain products including blood products such as PRP are exempt and therefore do not follow the traditional FDA regulatory pathway. To date, FDA has not attempted to regulate activated PRP.

A number of PRP preparation systems on the market today, many of which were cleared for marketing by FDA through the 510(k) process for producing platelet-rich preparations intended to be used to mix with bone graft materials to enhance bone grafting properties in orthopedic practices. The Aurix System™ (previously called AutoloGel™; Cytomedix) and SafeBlood® (SafeBlood Technologies) are two related but distinct autologous blood-derived preparations that can be prepared at the bedside for immediate application. Both AutoloGel and SafeBlood have been specifically marketed for wound healing. Other devices may be used in the operating room setting (e.g., Medtronic Electromedics, Elmd-500 Autotransfusion system, the Plasma Saver device, the Smart PreP device). The Magellan Autologous Platelet Separator System (Medtronic) includes a disposables kit designed for use with the Magellan Autologous Platelet Separator portable tabletop centrifuge. BioMet Biologics was cleared for marketing by FDA through the 510(k) process for a gravitational platelet separation system (GPS®II), which uses a disposable separation tube for centrifugation and a dual cannula tip to mix the platelets and thrombin at the surgical site. 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 active platelets and associated proteins, increasing variability between studies of clinical efficacy.

Related Protocols

Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions

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

Prolotherapy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.
References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


37. National Government Services, Inc. Local Coverage Determination (LCD): Category III CPT® Codes (L33392), Revision Effective Date for services performed on or after 02/08/2016.