Clinical Policy Title: Platelet rich plasma

Clinical Policy Number: 05.02.10

Effective Date: February 1, 2017
Initial Review Date: November 16, 2016
Most Recent Review Date: November 16, 2016
Next Review Date: November 2017

Related policies:

CP# 14.02.08 Prolotherapy
CP# 16.02.02 Growth factor treatment for wound healing/musculoskeletal uses
CP# 00.02.08 Intra-articular hyaluronic acid injection for osteoarthritis

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Prestige Health Choice when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Prestige Health Choice’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers the use of platelet rich plasma (PRP) to be investigational and, therefore, not medically necessary.

Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website can be accessed at http://ahca.myflorida.com/Medicaid/.

Prestige Health Choice considers all other uses of PRP to be investigational and, therefore, not medically necessary.
This includes, but is not limited to, use in all of the following indications:

- Primary use (injection) for other conditions, such as:
  - Epicondylitis (i.e., tennis elbow).
  - Plantar fasciitis.
  - Chronic achilles tendinopathy.
  - Anterior cruciate ligament (ACL) reconstruction.
  - Rotator cuff repair.
  - Spinal fusion.
  - Tonsillectomy.
  - Osteochondral lesions.
  - Osteoarthritis.
  - Dupuytren’s contracture.

- Adjunctive use in surgical procedures.

The platelet-derived growth factor (PDGF) products listed below are considered investigational and, therefore, not medically necessary:

- Autologous PRP injections (e.g., Procuren®, Magellan®).
- Autologous platelet gel or concentrate (e.g., AutoloGel®).
- Autologous platelet-derived growth factors (e.g., SafeBlood®).

Alternative covered services:

- Primary care and specialty physician (including surgical) evaluation and management including:
  - Simple analgesics.
  - Anti-inflammatory medications.
  - Corticosteroid injections.
  - Physical or occupational therapy.
  - Immobilization.
  - Using heat or cold.
  - Reducing workload and increasing rest.
  - Relaxation and biofeedback techniques.
  - Strengthening and conditioning exercises.
  - Stretching exercises and therapeutic massage.

Background

The use of PRP for expedited amelioration and repair of musculoskeletal derangements has been popularized in the media with wide-spread reports of its use by injured Olympic and professional athletes. In recent years, PRP and autologous adult stem cell sources, typically taken from bone marrow or adipose tissue, have achieved the most prominence in this regard.
The exact mechanism of action of proliferative healing has not been clearly established but it is hypothesized that proliferant agents in the platelets stimulate growth factors in the native inflammatory healing cascade and promote organic musculoskeletal repair.

**Searches**

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on October 10, 2016. Searched terms were: "recombinant human platelet-derived growth factor (MeSH)," "autologous platelet-derived growth factors (MeSH)" and "platelet rich plasma."

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Martinez-Zapata (2016) wrote for the Cochrane group that “PRP may improve the healing of foot ulcers associated with diabetes, but this conclusion is based on low quality evidence from two small RCTs. It is unclear whether PRP influences the healing of other chronic wounds. The overall quality of evidence of autologous PRP for treating chronic wounds is low. There are very few randomized controlled trials (RCTs) evaluating PRP, they are underpowered to detect treatment effects, if they exist, and are generally at high or unclear risk of bias. Well designed and adequately powered clinical trials are needed.”

The authors identified a total of ten RCTs inclusive of 442 participants with a range of chronic wounds (e.g., venous leg ulcers, foot ulcers in people with diabetes). The median length of treatment was 12 weeks (range 8 to 40 weeks). They found no clear evidence that autologous PRP improves the healing of chronic wounds generally compared with standard treatment (with or without placebo) (risk ratio [RR] 1.19, 95 percent confidence interval [CI] 0.95 to 1.50). Autologous PRP may increase the healing of foot
ulcers in people with diabetes compared with standard care (with or without placebo) (RR 1.22, 95 percent CI 1.01 to 1.49). It was unclear if autologous PRP affects the healing of venous leg ulcers (RR 1.02, 95 percent CI 0.81 to 1.27). It was unclear if there was a difference in the risk of adverse events in people treated with PRP or standard care (RR 1.05, 95 percent CI 0.29 to 3.88).

Holtby (2016) examined the effectiveness of PRP application in improving perioperative pain and function and promoting healing at 6 months after arthroscopic repair of small- or medium-sized rotator cuff tears.

Patients (n=28) were randomized to either repair and PRP application (study group) or repair only (control group) groups. The mean age of participants was 59 ± 8 years. Both the PRP and control groups showed a significant improvement in their pain level based on the visual analog scale within the first 30 days (P < .0001), with the PRP group reporting less pain than the control group (P = .012), which was clinically significantly different from days 8 through 11. The PRP group reported taking less painkillers (P = .026) than the control group within the first 30 days. All outcome measure scores and range of motion (ROM) improved significantly after surgery (P < .0001), with no between-group differences. No differences were observed between groups in inflammatory or coagulation marker test results (P > .05), retear (14% vs 18% full retear; P = .44), or fatty infiltration rate (P = .08).

Hou (2016) in a systematic review of 12 RCTs evaluated the efficacy of PRP by comparing clinical attachment level (CAL) and pocket depth (PD) for patients who received PRP as an adjunct to periodontal intrabony defect therapy with those for patients who did not. The authors also analyzed the influence of guided tissue regeneration (GTR) and different study designs (parallel and split-mouth studies) on the clinical outcomes of intrabony defects. Clinically and significantly greater CAL gains and PD reductions were observed in subjects who received PRP as an adjunct to periodontal intrabony defect therapy than in subjects who did not (CAL: wound mean depth [WMD] 0.76 mm, 95 percent CI = 0.34 to 1.18 mm, P = 0.0004; PD: WMD 0.53 mm, 95 percent CI = 0.21 to 0.85 mm, P = 0.001). Subgroup meta-analyses of patients who underwent GTR demonstrated that this approach did not significantly affect treatment outcomes (CAL: WMD 0.08 mm, 95 percent CI = −0.30 to 0.46 mm, P = 0.67), as indicated by a comparison with patients who did not undergo GTR (CAL: WMD 1.22 mm, 95 percent CI = 0.88 to 1.57 mm, P < 0.00001). Univariate meta-regression analyses revealed that the use of GTR explained the heterogeneity among the included studies (P < 0.05).

The National Institute for Health and Clinical Excellence (NICE) promulgated clinical guidelines in 2015 for treatment of diabetic foot ulcers and made the following recommendations:

“Do not offer the following to treat diabetic foot ulcers, unless as part of a clinical trial:

- Electrical stimulation therapy, autologous platelet-rich plasma gel, regenerative wound matrices and dalteparin.
- Growth factors (granulocyte colony-stimulating factor [G-CSF], platelet-derived growth factor [PDGF], epidermal growth factor [EGF] and transforming growth factor beta [TGF-β]).
- Hyperbaric oxygen therapy.”
Sanderson (2015) conducted a systematic review inclusive of three RCTs and five case series in which the medical evidence suggests prolotherapy injections are safe and effective in reducing pain and improving function for Achilles tendinopathy, plantar fasciopathy and Osgood-Schlatter disease. The authors concluded that prolotherapy provides equal or superior short-, intermediate- and long-term results to alternative treatment modalities, including eccentric loading exercises for Achilles tendinopathy, platelet-rich plasma for plantar fasciopathy and usual care or lidocaine injections for Osgood-Schlatter disease. However, the authors called for more study with large, methodologically sound RCTs to substantiate these findings.

Hayes (2015) reviewed the uses of PRP for orthopedic indications and found no additional medical evidence to change its previously established assessment (Hayes 2012) of efficacy for the technology:

- **C (potential but unproven benefit)** – For PRP for the treatment of lateral epicondylitis. This rating reflects limited evidence of comparable or greater improvement in patient outcomes relative to standard treatments in controlled trials.
- **D1 (no proven benefit)** – For PRP injection as an adjunct to surgical repair of ACL injuries. This rating reflects the evidence suggesting no improvement in patient outcomes, particularly functional outcomes, for this indication.
- **D1 (no proven benefit)** – For PRP as an adjunct to arthroscopic rotator cuff repair. This rating reflects the evidence suggesting no improvement in patient outcomes, particularly functional outcomes, for this indication in the available controlled trials.
- **D1 (no proven benefit)** – For treatment of Achilles tendinopathy or Achilles rupture with PRP. This rating reflects the evidence suggesting no improvement in patient outcomes for this indication.
- **D2 (no proven benefit/insufficient evidence)** – For treatment of tendinosis or partial tear of the rotator cuff with PRP. This rating reflects the very limited evidence regarding patient outcomes for this indication.
- **D2 (no proven benefit/insufficient evidence)** – For PRP as an adjunct to open subacromial decompression surgery in type II shoulder impingement. This Rating reflects the very limited evidence regarding this indication.

### Summary of clinical evidence:

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<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
<th>Key points:</th>
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- Four RCTs recruited people with a range of chronic wounds; three RCTs recruited people with venous leg ulcers, and three RCTs considered foot ulcers in people with diabetes.  
- The median length of treatment was 12 weeks (range 8 to 40 weeks).  
- It was unclear whether autologous PRP improved the healing of chronic wounds. |
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| Holtby (2016) | compared to standard treatment with or without placebo (RR 1.19, 95% CI 0.95 to 1.50; I² = 27%).
• Healing of diabetic foot ulcers was influenced favorably compared with standard care with or without placebo (RR 1.22, 95% CI 1.01 to 1.49; I² = 0%).
• It was unclear if autologous PRP affected the healing of venous leg ulcers (RR 1.02, 95% CI 0.81 to 1.27; I² = 0%).
• All of these events were adjudged to be of low quality in weight of medical evidence. | **Key points:**
• RCT (n=82) examined the effectiveness of PRP application in improving perioperative pain and function and promoting healing at 6 months after arthroscopic repair of small- or medium-sized rotator cuff tears.
• Patients were randomized to either repair and PRP application (study group) or repair only (control group) groups.
• Mean age of participants was 59 ± 8 years.
• Both the PRP and control groups showed a significant improvement in their pain level based on the visual analog scale within the first 30 days (P < .0001), with the PRP group reporting less pain than the control group (P = .012), which was clinically significantly different from days 8 through 11.
• The PRP group reported taking less painkillers (P = .026) than the control group within the first 30 days.
• All outcome measure scores and ROM improved significantly after surgery (P < .0001), with no between-group differences.
• No differences were observed between groups in inflammatory or coagulation marker test results (P > .05), retear (14% vs 18% full retear; P = .44), or fatty infiltration rate (P = .08). |
| Hou (2016) | The effect of platelet-rich plasma on clinical outcomes of the surgical treatment of periodontal intrabony defects: A systematic review and meta-analysis. | **Key points:**
• Systematic review of 12 RCTs evaluated the efficacy of PRP by comparing CAL and PD for patients who received PRP as an adjunct to periodontal intrabony defect therapy with those for patients who did not.
• Also analyzed the influence of GTR and different study designs (parallel and split-mouth studies) on the clinical outcomes of intrabony defects.
• Clinically and significantly greater CAL gains and PD reductions were observed in subjects who received PRP as an adjunct to periodontal intrabony defect therapy than in subjects who did not (CAL: WMD 0.76 mm, 95% CI = 0.34 to 1.18 mm, P = 0.0004; PD: WMD 0.53 mm, 95% CI = 0.21 to 0.85 mm, P = 0.001).
• Subgroup meta-analyses of patients who underwent GTR demonstrated that this approach did not significantly affect treatment outcomes (CAL: WMD 0.08 mm, 95% CI = −0.30 to 0.46 mm, P = 0.67), as indicated by a comparison with patients who did not undergo GTR (CAL: WMD 1.22 mm, 95% CI = 0.88 to 1.57 mm, P < 0.00001).
• Univariate meta-regression analyses revealed that the use of GTR explained the heterogeneity among the included studies (P < 0.05). |
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| NICE (2015) | Clinical guidelines promulgated in 2016 for treatment of diabetic foot ulcers and made the following recommendations:  
  - “Do not offer the following to treat diabetic foot ulcers, unless as part of a clinical trial:  
    - Electrical stimulation therapy, autologous PRP gel, regenerative wound matrices and dalteparin.  
    - Growth factors (G-CSF, PDGF, TGF-β).  
    - Hyperbaric oxygen therapy.” |
  - Limited evidence suggests prolotherapy injections are safe and effective in reducing pain and improving function for Achilles tendinopathy, plantar fasciopathy and Osgood-Schlatter disease.  
  - Prolotherapy provides equal or superior short-, intermediate- and long-term results to alternative treatment modalities, including eccentric loading exercises for Achilles tendinopathy, platelet-rich plasma for plantar fasciopathy and usual care or lidocaine injections for Osgood-Schlatter disease. |
  D1 (no proven benefit) – For PRP injection as an adjunct to surgical repair of ACL injuries.  
  D1 (no proven benefit) – For PRP as an adjunct to arthroscopic rotator cuff repair.  
  D1 (no proven benefit) – For treatment of Achilles tendinopathy or Achilles rupture with PRP.  
  D2 (no proven benefit/insufficient evidence) – For treatment of tendinosis or partial tear of the rotator cuff with PRP.  
  D2 (no proven benefit/insufficient evidence) – For PRP as an adjunct to open subacromial decompression surgery in type II shoulder impingement. |

**Glossary**

**Platelet-rich plasma (PRP)** — Platelets are separated from other blood cells and their concentration is increased during centrifugation, then an increased concentration of platelets is combined with plasma to create a “platelet-rich” solution.

**References**

**Professional society guidelines/other:**

Hayes Inc., Hayes Medical Technology Report. Bone Marrow Aspirate Concentrate and Platelet-Rich


Peer-reviewed references:


**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.
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