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| MEDICAL POLICY | Platelet-Rich Plasma (PRP) for Orthopedic Indications, Wound Care and Other Miscellaneous Conditions (All Lines of Business Except Medicare) | |
| Effective Date: 10/01/2020  <div style="text-align: right;">10/1/2020</div> | Section: MED | Policy No: 307 |
| | Technology Assessment Committee Approved Date: 3/07; 8/09; 1/2010; 4/10; 4/11 Medical Policy Committee Approved Date: 6/13; 6/14; 9/15; 6/16; 8/17; 10/18; 11/19; 09/2020 | |
| Medical Officer | Date | |

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Medicaid 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.

POLICY CRITERIA

Note: This does not address platelet-derived growth factors, including recombinant growth factors (e.g., Regranex® [becaplermin gel]) and growth factors that are autologous in origin.

- I. The use of platelet-rich plasma (PRP) as an adjunct to surgery or a stand-alone treatment is **considered investigational and not covered** for any indication, including, but not limited to:
 - A. Orthopedic Indications, including but not limited to:
 1. Achilles tendon rupture and/or tendinopathy
 2. Anterior cruciate ligament (ACL) tendinopathy

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| <ul style="list-style-type: none"> 3. Lateral epicondylitis 4. Osteoarthritis of the ankle 5. Osteoarthritis of the hip 6. Osteoarthritis of the knee 7. Patellar tendinopathy 8. Plantar fasciitis 9. Rotator cuff tears (full and partial) and tendinopathy B. Wound care, including but not limited to: <ul style="list-style-type: none"> 1. Acute wounds 2. Chronic leg and/or foot wounds (diabetic and non-diabetic) 3. Pilonidal disease wounds C. Other miscellaneous conditions, including but not limited to: <ul style="list-style-type: none"> 1. Aesthetic indications, including but not limited to: <ul style="list-style-type: none"> a. Ageing skin and other dermatological conditions b. Alopecia 2. Erectile dysfunction <p>Link to Policy Summary</p> |
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CPT/HCPCS CODES

| All Lines of Business Except Medicare | |
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| Not Covered | |
| 0232T | Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed |
| G0460 | Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment |
| P9020 | Platelet rich plasma, each unit |

DESCRIPTION

Platelet-Rich Plasma (PRP)

Platelet-rich plasma (PRP) is an autologous blood preparation with a high platelet concentration, and therefore is also known as autologous platelet concentrate (APC). PRP is derived from the patient’s own

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blood and is with concentrated with platelet-derived growth factors, which may be the primary contributors to the purported benefits of PRP therapy.¹ The concentration of the PRP and its growth factors occurs through specialized centrifugation systems.

Exposure of PRP to a solution of thrombin and calcium chloride results in the polymerization of fibrin from fibrinogen, creating an autologous platelet gel (APG). The platelet gel can then be applied to wounds or surgical sites with the hope of promoting hemostasis and accelerating healing for a variety of indications. An example commercially available APC, created with the patient’s own blood, is Aurix® (Nuo Therapeutics, Inc.) (formerly known as Autologel).

However, it must be noted that PRP preparations are not standardized and exhibit wide variability in platelet and white blood cell concentrations and the use of thrombin activators. How these variations in PRP composition may affect clinical outcomes is unclear.

Once the PRP is prepared, it can be administered directly to the site during surgical repair of an orthopedic injury, or injected into the lesion, with or without ultrasound guidance, in the case of nonsurgical intervention.

Although the mechanism by which PRP works is not known, it is been hypothesized that the growth factors and cytokines concentrated in the PRP may stimulate regeneration and promote tissue repair by triggering stem cell recruitment, angiogenesis and fibroblast stimulation at the site of injury.

Clinical Alternatives

Orthopedic Applications

Depending on the indication and its severity, examples of nonsurgical treatment alternatives include rest, ice, physical therapy, orthotics, anti-inflammatory medications, pain medications, hyaluronic acid injections, and corticosteroid injections. Surgery may be indicated for more severe indications.¹⁻³

Chronic Wounds

Medical management of chronic wounds should involve treatment of the primary cause, such glycemic control for people with diabetes, vascular surgery for people with chronic venous disease, or ischemic vascular disease. “Removal of necrotic or infected tissue, off-loading, compression therapy, maintenance of a moist wound environment, management of wound infection, wound cleansing, and diet,” are also thought to be important.⁴

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REVIEW OF EVIDENCE

Due to the large body of evidence published on the use of platelet-rich plasma (PRP) for a large number of indications, the evidence review below is focused on recent, high-quality systematic reviews with meta-analyses. A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of PRP as a treatment for wound healing and musculoskeletal/orthopedic conditions. Below is a summary of the available evidence identified through August of 2020.

The use of PRP has been evaluated and reported by systematic reviews for the following indications:

- Orthopedic/musculoskeletal indications:
 - Achilles tendon rupture and/or tendinopathy^{3,5-7}
 - Anterior cruciate ligament (ACL) tendinopathy^{8,9}
 - Carpal tunnel syndrome¹⁰
 - Lateral epicondylitis^{9,11-17}
 - Myofascial pain¹⁸
 - Osteoarthritis of the ankle¹⁹
 - Osteoarthritis of the hip²⁰⁻²⁴
 - Osteoarthritis of the knee^{2,20,22,25-39}
 - Osteoarthrosis of the temporomandibular joint^{40,41}
 - Patellar tendinopathy^{5,8,42,43}
 - Plantar fasciitis^{3,5,44,45}
 - Rotator cuff tears (full and partial) and tendinopathy^{1,9,13,16,46-48}
 - Wound care, including:
 - Acute wounds⁴⁹
 - Chronic leg and/or foot wounds (diabetic and non-diabetic)^{4,50}
 - Other chronic wounds⁵¹
 - Pilonidal disease wounds⁵²
- Other miscellaneous conditions:
 - Aesthetic indications including:
 - Ageing skin and other dermatological conditions⁵³⁻⁵⁶
 - Alopecia^{53,54,57-59}
 - Erectile dysfunction⁶⁰
 - Preventive dental treatments in people with cancer receiving radiotherapy to the head and neck⁶¹

Overall, the body of evidence for any given indication suffers from one or more of the following limitations:

- low-quality of randomized controlled trials (RCTs) due to methodological limitations including:

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- small sample size
- underpowered to detect treatment effects
- heterogeneity of comparator treatment
- variability in PRP preparation/concentration, administration and dosing protocols
- inconsistent data reporting
- high risk of bias, including insufficient blinding of physicians and/or patients
- incomplete details regarding randomization methods
- limited number of RCTs reporting outcomes for any given indication
- systematic reviews deemed of low quality, due to methodological limitations, including:
 - inclusion of nonrandomized studies
 - lack of transparency on literature search/study inclusion methodology
 - high risk of bias
- conflicting or no evidence of short-term improvements in pain and/or function (first few months following treatment) when compared to placebo or non-PRP treatments
- conflicting or no evidence of long-term benefit on function or pain outcomes

CLINICAL PRACTICE GUIDELINES

Osteoarthritis

American Academy of Orthopaedic Surgeons (AAOS)

In 2017, the AAOS published guidelines on the management of osteoarthritis of the hip.⁶² The association conducted an evidence review of PRP versus other comparators, but did not identify enough high-quality evidence on PRP to formally address the treatment in their recommendations.

In 2013, the AAOS published guidelines on the management of osteoarthritis of the knee, stating the following.⁶³

- “We are unable to recommend for or against growth factor injections and/or platelet rich plasma for patients with symptomatic osteoarthritis of the knee. (Strength of Recommendation: Inconclusive)
- There was a paucity of articles on the use of platelet concentrates in the treatment of osteoarthritis.
- The studies showed decreased levels of pain in the post injection period but they were not constructed to allow for a comparative analysis of clinical effectiveness. The lack of controlled, prospective, blinded, randomized clinical trials with a placebo control, prevent the work group from making any recommendation on the use of platelets or platelet derived growth factor concentrates in the treatment of osteoarthritis of the knee.”

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American Society of Interventional Pain Physicians (ASIPP)

In 2019, the ASIPP published guidelines on responsible, safe, and effective use of biologics in the management of low back pain.⁶⁴ Methods for evidence collection and grading were employed following recommendations described by the Agency for Healthcare Research and Quality (AHRQ). Regarding PRP, the authors identified on one high-quality RCT, multiple moderate-quality observational studies, a single-arm meta-analysis and evidence from a systematic review. For intradiscal injections of PRP, they assessed the evidence to be Level III (on a scale of Level I through V) using a qualitative modified approach to the grading based on best-evidence synthesis. This was the same for mesenchymal stem cells. The evidence was reported as being Level IV for lumbar facet joint, lumbar epidural, and sacroiliac joint injections of PRP. According to the qualitative modified approach to grading of evidence, Level III is considered fair, and Level IV is limited.

National Institute for Health and Care Excellence (NICE)

In 2014, NICE published guidance that stated the following:⁶⁵

- “Current evidence on platelet-rich plasma injections for osteoarthritis of the knee raises no major safety concerns; however, the evidence on efficacy is inadequate in quality.
- Clinicians wishing to undertake platelet-rich plasma injections for osteoarthritis of the knee should ensure that patients understand the uncertainty about the procedure’s efficacy.”

Plantar Fasciitis

National Institute for Health and Care Excellence (NICE)

In 2013, NICE published guidance that stated the following:

- “The evidence on the efficacy of autologous blood injection for plantar fasciitis is inadequate in quantity and quality.
- The evidence on autologous blood injection for plantar fasciitis raises no major safety concerns.
- Clinicians wishing to undertake autologous blood injection for plantar fasciitis should ensure that patients understand the uncertainty about the procedure’s efficacy and make them aware of alternative treatments.
- Further research into comparing autologous blood injection (with and without techniques to produce PRP) with established nonsurgical treatments is encouraged.”

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Tendinopathies

National Institute for Health and Care Excellence (NICE)

In 2013, NICE published guidance for tendinopathy (including but not limited to elbow, heel and knee) that stated the following:

- “The evidence on efficacy of autologous blood injection for tendinopathy remains inadequate, with few studies available that use appropriate comparators.
- The evidence on autologous blood injection for tendinopathy raises no major safety concerns.
- Clinicians wishing to undertake autologous blood injection for tendinopathy should ensure that patients understand the uncertainty about the procedure’s efficacy and make them aware of alternative treatments.”
- Further research into comparing autologous blood injection (with and without techniques to produce PRP) with established nonsurgical treatments is encouraged.

Wound Treatment

Association for the Advancement of Wound Care (AAWC)

In 2015, the AAWC published an updated international consolidated venous ulcer (VU) guideline which stated the following:⁶⁶

- “Platelet-rich plasma has not yet been shown to significantly improve VU healing.”
- This was based on evidence considered to be of moderate strength (one RCT, one nonrandomized controlled study and a Cochrane systematic review).

In 2018, the AAWC published an updated international consolidated wound infection guideline which stated:⁶⁷

- “Do not use platelet rich plasma to prevent infection.”
- This was based on evidence considered to be of moderate strength (one Cochrane systematic review).

National Institute for Health and Care Excellence (NICE)

In 2015 NICE published guidelines (updated in 2016) on the management of diabetic foot problems which stated:

- “Do not offer autologous platelet-rich plasma gel to treat diabetic foot ulcers, unless as part of a clinical trial.”

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POLICY SUMMARY

There is insufficient evidence that the use of platelet-rich plasma (PRP), whether as an adjunct to surgery, or as a stand-alone treatment, is effective and consistently improves health outcomes for any indication, including but not limited to orthopedic indications, wound care, and aesthetic indications. Due to heterogeneity in PRP processing and administration protocols, interpreting results and drawing conclusions about treatment efficacy is difficult. This limitation is consistently reported for the use of PRP for all indications. PRP treatment protocols must be optimized before it can be implemented into standard clinical practice. Other major limitations of PRP observed across all indications include a lack of large, well-designed randomized controlled trials, and inconsistency in terms of whether or not PRP has a beneficial effect. In addition, no clinical practice guidelines were identified that support the use of PRP as a treatment for any indication.

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 Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

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.

REGULATORY STATUS

U.S. Food & Drug Administration (FDA)

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research. Blood products such as PRP are included in these regulations. Under these regulations, blood products such as PRP are exempt and therefore, do not follow the traditional FDA regulatory pathway.⁶⁸

Numerous PRP preparation systems have been cleared for marketing by the FDA through the 510(k) process. These devices are intended to concentrate patient plasma either at the point of care during procedures or off-site at certified laboratories. However, the use of different devices and procedures

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can lead to variable concentrations of active platelets and associated proteins and growth factors, increasing variability between studies.

Mental Health Parity Statement

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.

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