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

Policy Statement

Use of platelet-rich plasma (PRP) (i.e., autologous blood-derived preparations) is considered investigational for the treatment of acute or chronic wounds, including surgical wounds, nonhealing ulcers, and certain other non-orthopedic conditions.

Note: Please refer to the Rationale section of this policy for the non-orthopedic conditions and to Blue Shield of California’s Medication Policy: REGRANEX (becaplermin) for coverage criteria.

Policy Guidelines

Platelet-Rich Plasma (IE, Autologous Blood-Derived Preparations)

Coding

There is a CPT category III code for injections of platelet-rich plasma (PRP):
- **0232T**: Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed

The instructions issued with the code state that it is not to be reported with codes 20550, 20551, 20600-20610, 20926, 76942, 77002, 77012, 77021, or 86965. Code 0232T includes the harvesting and preparation of the PRP.

For situations other than injection (when 0232T would be reported), no specific CPT codes describe the preparation of autologous blood-derived products, but the following CPT code can be used:
- **86999**: Unlisted transfusion medicine procedure

It is questionable whether platelet-rich plasma is appropriately considered a tissue graft, but it has been reported that providers have used the following CPT code to describe the overall procedure:
- **20926**: Tissue grafts, other (e.g., paratenon, fat, demis) (effective January 1, 2020, code 20926 has been deleted)

The American Medical Association’s Department of Coding instructs that placement of PRP into an operative site is an inclusive component of the operative procedure performed and not separately reported.

There is also a HCPCS code for this treatment:
- **G0450**: Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment

The following HCPCS code represents other human platelet-derived growth factor preparations used to promote wound healing:
- **59055**: Procuren or other growth factor preparation to promote wound healing

Description

The use of blood-derived growth factors, including recombinant platelet-derived growth factors (PDGFs) and platelet-rich plasma (PRP), has been suggested as a treatment for wounds or other
miscellaneous non-orthopedic conditions, including but not limited to, diabetic ulcers, pressure ulcers, venous stasis ulcers, and surgical and traumatic wounds.

**Related Policies**

- Bio-Engineered Skin and Soft Tissue Substitutes
- Electrostimulation and Electromagnetic Therapy for Treating Wounds
- Negative Pressure Wound Therapy in the Outpatient Setting
- Noncontact Ultrasound Treatment for Wounds
- Orthopedic Applications of Platelet-Rich Plasma

**Benefit Application**

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**Regulatory Status**

**Platelet-Rich Plasma**

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 1270 and 1271. Blood products such as 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, the FDA has not attempted to regulate activated PRP.²

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 at the point of care during bone grafting procedures. 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.

In 2018, the “Boxed Warning” and “Warnings and Precautions” were changed to remove “increased rate of cancer mortality” and “cancer mortality,” respectively.

**Rationale**

**Background**

**Wound Healing Treatment**

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factor (PDGF), 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, and osteoblasts), and vascular endothelial growth factors.
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 various growth factors, and results in the polymerization of fibrin from fibrinogen, creating a platelet gel. The platelet gel can then be applied to wounds or may be used as an adjunct to surgery to promote hemostasis and accelerate 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 transforming growth factor, 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.

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 International) and Hemaseel® (Haemacure Corp.) are examples of commercially available fibrin sealants. Autologous fibrin sealants can also be created from platelet-poor plasma. This evidence review does not address the use of fibrin sealants.

Wound Closure Outcomes

This review addresses the use of PRP for nonorthopedic indications, which include a number of wound closure-related indications.

For this review, the primary endpoints of interest for the study of wound closure are as follows, consistent with guidance from the U.S. Food and Drug Administration (FDA) for the industry in developing products for the treatment of chronic cutaneous ulcer and burn wounds:

1. Incidence of complete wound closure
2. Time to complete wound closure (reflecting accelerated wound closure)
3. Incidence of complete wound closure following surgical wound closure
4. Pain control

Literature Review

The platelet-rich plasma (PRP) portion of this evidence review on the platelet-derived wound healing formulae was originally based on a 1992 Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment that primarily focused on the Procuren process. This preparation method is no longer commercially available. Currently, a large number of devices are available for the preparation of PRP or PRP gel. The amount and mixture of growth factors produced by different cell-separating systems vary, and it is unknown whether platelet activation before an injection is necessary.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is
preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Platelet-Rich Plasma for Chronic Wounds**

**Clinical Context and Therapy Purpose**
The purpose of PRP is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with chronic wounds.

The question addressed in this evidence review is: does the use of PRP improve health outcomes compared with standard care for diabetic ulcers, pressure ulcers, venous stasis ulcers, chronic wounds, and surgical and traumatic wounds?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest are individuals with chronic wounds.

**Interventions**
The therapy being considered is PRP.

Patients with chronic wounds are actively managed by primary care providers in an outpatient clinical setting.

**Comparators**
Comparators of interest include standard wound care.

Patients with chronic wounds are actively managed by primary care providers in an outpatient clinical setting.

**Outcomes**
The general outcomes of interest are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity.

Though not completely standardized, follow-up for chronic wounds symptoms would typically occur in the months after starting treatment.

**Study Selection Criteria**
Methodologically credible studies were selected using the principles described in the first indication.

**Systematic Reviews**
A number of systematic reviews of the evidence on PRP have been published. A 2012 Cochrane review included 9 RCTs (total n=325 participants) of PRP for treating chronic wounds. This review was restricted to trials comparing PRP with no additional treatment or placebo. Four RCTs included patients with mixed chronic wounds, three included patients with venous leg ulcers, and two included patients with DFUs. Only 1 trial was considered to be at low-risk of bias. After a median treatment duration of 12 weeks, there was no significant difference between the PRP and control groups in complete healing of DFUs, venous leg ulcers, or mixed chronic wounds. There was no significant difference in the area epithelialized in 3 RCTs of mixed chronic wounds. In 2 RCTs of mixed chronic wounds, there was a significant difference favoring PRP in the wound area that was healed. Reviewers concluded there was no current evidence to suggest that autologous PRP would be of value for treating chronic wounds, given the small number of RCTs included, most of which were either at high or unclear risk of bias.
This Cochrane review was updated in 2016; it added a new RCT, for a total of 10 RCTs (total n=442 patients). Conclusions about the quality of the overall body of evidence were similar to the 2012 review. For the outcome of overall wound healing, autologous PRP did not significantly increase healing compared with standard treatment (RR=1.19; 95% CI, 0.95 to 1.50; P=27%, low-quality evidence). For wound healing in foot ulcers in people with diabetes, the evidence suggested that autologous PRP might increase healing compared with standard care (RR=1.22; 95% CI, 1.01 to 1.49; P=0%, low-quality evidence). It was unclear whether autologous PRP increased wound healing compared with standard care for venous leg ulcers (RR=1.05; 95% CI, 0.29 to 3.88; P=0% low-quality evidence).

Other systematic reviews reached similar conclusions. For example, one from 2009 identified 42 controlled trials on PRP; of these, 20 were RCTs and were included in the systematic review, which found results to be inconclusive. The 20 RCTs comprised 11 trials on oral and maxillofacial surgery, 7 on chronic skin ulcers, and 2 on surgical wounds. An industry-funded systematic review from 2011 included 21 studies of PRP gel for cutaneous wound healing, 12 of which were RCTs (Table 2; 3). There were 3 main types of wounds, including open chronic wounds, acute surgical wounds with primary closure, and acute surgical wound with secondary closure. Study quality varied considerably, with three studies rated as high-quality and six rated as poor-quality. Two additional studies could not be rated because they were published only as an abstract and letter. Meta-analysis of the effect of PRP on complete wound healing of chronic wounds was limited by the inclusion of poor-quality studies. No high-quality RCTs showed improvement in complete healing with PRP. A 2015 systematic review of PRP for DFUs identified 6 small RCTs published between 1992 and 2011. Although 5 of the studies reported positive results with PRP, the studies were small, and the possibility of selective publication bias was not assessed.

Since the publication of the 2016 update to the Cochrane review on PRP for wounds, Escamilla Cardenosa et al (2017) reported on an unblinded RCT comparing PRP and saline for venous ulcer treatment. The trial included 61 patients (102 ulcers) who were randomized to the weekly application of a PRP dressing (31 patients, 55 ulcers) or weekly wet-to-dry dressing changes with saline (30 patients, 47 ulcers) over a 24-week period. The average percentage healed area in the PRP group was 67.7% and 11.2% in the control group (p<0.001). PRP group members had greater reductions in pain with the intervention.

A meta-analysis by del Pino-Sedeno et al (2018) assessed 8 RCTs and 2 longitudinal-observational studies (total participants N=525) to determine the safety and efficacy of PRP to treat diabetic foot ulcers. Results indicated PRP significantly increased chronic wound healing compared with standard treatment (RR=1.41; 95% CI: 1.08 to 1.84; p=0.01; 12=51%). Subgroup analysis showed that PRP source affected the proportion of completely healed diabetic foot ulcers (autologous RR=1.21; 95% CI: 1.04 to 1.42; p=0.02; allogenic RR=3.20; 95% CI: 1.14 to 9.03; p=0.3). PRP preparation method also influenced healing (homemade RR=1.22; 95% CI: 1.04 to 1.44; p=0.02; commercial protocol RR=1.13; 95% CI: 0.58 to 2.20; p=0.71; blood bank RR=3.20; 95% CI: 1.14 to 9.03; p=0.3). The 2 trials that reported mean time for complete wound healing showed that PRP resulted in quicker healing (mean difference=-11.18 days; 95% CI: -20.69 to -1.68; p=0.02; 12=53%). Overall, the studies reported no significant differences in rates of wound complications or dermatitis, and rates of recurrences were similar between PRP and standard treatment. The authors noted, however, that results of their analysis should be interpreted cautiously because no statistical differences were found in the epithelialized area before and after wound treatment (mean difference=0.70 cm2; 95% CI: -0.96 to 2.35; p=0.41; 12=70%). This study was limited by the low number and quality of studies available on PRP for diabetic foot ulcers.

In their meta-analysis, Li et al (2019) assessed the efficacy and safety of autologous platelet-rich gel for topical treatment of diabetic chronic cutaneous ulcers. Their analysis included 15 RCTs with 829 patients. Results indicated that autologous platelet-rich gel had a significant positive effect on healing rate, shorter healing time, and lower risk of infection than conventional treatment (Table 2; 3). Autologous platelet-rich gel also had a significantly lower incidence of infection when compared with conventional treatment (odds ratio=0.34; 95% CI: 0.15 to 0.77;
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p = .009). This meta-analysis was limited by a high or unclear risk of bias among the trials, which may indicate the trials were underpowered. Also, some studies had small sample sizes and limited outcome information. Finally, most of the trials were 8-12 weeks long and others only 2-5 weeks, making it difficult to analyze the relationship of time of observation to ulcer healing.

Tables 1 and 2 summarize the 2 systematic reviews described above with the least study overlap and most recent data.

### Table 1. Characteristics of Key Systematic Reviews with Meta-Analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li (2019)</td>
<td>2004-2017</td>
<td>15</td>
<td>Patients with diabetic chronic cutaneous wounds/ulcers that do not show signs of healing in 4 weeks</td>
<td>N=829 (14-117)</td>
<td>RCTs</td>
<td>NR</td>
</tr>
<tr>
<td>Carter (2011)</td>
<td>2001-2011</td>
<td>21</td>
<td>Patients with a cutaneous ulcer or wound</td>
<td>N=31,310 (8-26,599)</td>
<td>RCTs, cohort studies, comparative, retrospective</td>
<td>3 wk-1 y</td>
</tr>
</tbody>
</table>

NR: not reported; wk: week(s); y: year(s).

### Table 2. Results of Key Systematic Reviews with Meta-Analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Healing Rate</th>
<th>Healing Time</th>
<th>Complete Wound Healing</th>
<th>Risk of Infection</th>
<th>Pain Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li (2019)</td>
<td>RR 1.39</td>
<td>-9.18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR 0.34</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>1.29 to 1.50</td>
<td>-11.32 to -7.05</td>
<td>0.15 to 0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carter (2011)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk difference</td>
<td>0.22</td>
<td>-0.02</td>
<td>-0.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.05 to 0.38</td>
<td>-0.06 to 0.01</td>
<td>-2.38 to 0.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Z</td>
<td>2.54</td>
<td>1.42</td>
<td>0.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>.01</td>
<td>.16</td>
<td>.37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI: confidence interval; MD: mean difference; OR: odds ratio; RR: risk ratio; Z indicates overall effect.

**Section Summary: PRP for Chronic Wounds**

The evidence for autologous PRP for a variety of chronic wounds includes systematic reviews, RCTs, which have been summarized in several systematic reviews, and nonrandomized trials. For chronic wounds, including diabetic ulcers, pressure ulcers, and vascular ulcers, results on efficacy of PRP over standard of care are mixed. Overall, the studies are small and of low quality, and the results should be interpreted with caution.

**Platelet-Rich Plasma for Acute Surgical or Traumatic Wounds**

**Clinical Context and Therapy Purpose**

The purpose of PRP is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with acute surgical or traumatic wounds.

The question addressed in this evidence review is: does the use of PRP improve health outcomes compared with standard care for diabetic ulcers, pressure ulcers, venous stasis ulcers, chronic wounds, and surgical and traumatic wounds?

The following PICOTS were used to select literature to inform this review.
Patients
The relevant population of interest are individuals with acute surgical or traumatic wounds.

Interventions
The therapy being considered is PRP.

Patients with acute surgical or traumatic wounds are actively managed by primary care providers in an outpatient clinical setting.

Comparators
Comparators of interest include standard wound care.

Patients with acute surgical or traumatic wounds are actively managed by primary care providers in an outpatient clinical setting.

Outcomes
The general outcomes of interest are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity.

Though not completely standardized, follow-up for acute surgical or traumatic wounds symptoms would typically occur in the months after starting treatment.

Methodologically credible studies were selected using the principles described in the first indication.

Surgical Wounds
Aortic Arch Repair
Zhou et al (2015) reported on a double-blind RCT with 80 patients that assessed the effect of PRP on the amount of blood transfused in the perioperative period for elective ascending and transverse aortic arch repair. An anesthesiologist prepared the PRP so that the surgeon was unaware of the treatment group. The volume of PRP transfused was 726 mL and led to a reduction in transfusion rates for red blood cells, frozen plasma, cryoprecipitate, and platelets by 34% to 70% (p<0.02). Hospital length of stay was also reduced (9.4 days vs 12.7 days). There was no difference in mortality between the 2 groups (one patient in each group) and no significant differences in postoperative complications or other outcome measures. Corroboration of the effect of PRP on perioperative blood transfusion is needed.

Sternotomy Wounds
Serraino et al (2015) reported on a large series with historical controls that assessed the occurrence of deep sternal wound infections in patients who underwent cardiac surgery either with (2010-2012, 422 consecutive patients) or without (2007-2009, 671 consecutive patients) application of PRP. The 2 groups were comparable at baseline. At the end of cardiac surgery, PRP gel was applied on the sternal before the closure of subcutaneous tissue. Rates of both deep and superficial wound infection were reduced in the patients treated with PRP (deep: 0.2% vs 1.5%, superficial: 0.5% vs 2.8%). Interpretation of these results is limited by likely differences in treatments over time. RCTs are needed to evaluate this potential use of PRP.

Otolaryngology
El-Anwar et al (2016) reported on an RCT that evaluated PRP in 44 children (age range, 12-23 months) undergoing repair of a complete cleft palate. Speech and velopharyngeal valve movement on follow-up were evaluated by 3 judges who “usually assessed every patient blindly,” physical examination, video nasoendoscopy, and audio recording of audio perceptual assessment. At 6 months, PRP-treated patients had better nasality grade on audio perceptual assessment (p=0.024) and better velopharyngeal closure on endoscopy (p=0.016).
A 2008 double-blind RCT assessed the efficacy of PRP following tonsillectomy in 70 children (age range, 4-15 years). PRP was placed into the tonsil beds of half of the children, where it was directly visible. To compare pain symptoms and recovery, a daily diary was completed by the patient or a family member for 10 days after surgery. A FACES Pain Scale was used for children ages 4 to 7 years, while a numeric pain rating scale was used for children older than 7 years. Diaries from 83% of patients showed no differences in pain, medication doses, activity, and days eating solid foods between the 2 conditions.

Other Wounds
A 2011 Norwegian trial of PRP applied to saphenous vein harvest sites after wound closure found no differences in the incidence of wound infection or cosmetic result.

Alamdari et al (2018) published a clinical trial evaluating the efficacy of pleurodesis with a combination of PRP and fibrin glue compared with surgical intervention. The study population consisted of 52 esophageal cancer patients with postoperative chylothorax who did not respond to conservative management. Each member of the population was consecutively and randomly allocated to either a PRP fibrin glue pleurodesis arm or a surgical thoracic duct ligation arm. Twenty-six in each arm were treated with their respective intervention. The patients were distributed into the intervention arms in a way that made each group similar in terms of tumor size and patient demographics. This distribution procedure was not described. All patients (26) in the PRP treatment arm and 20 (76.9%) in the surgery arm were successfully treated (p=0.009). Seven patients (26.92%) of the PRP required a second application of the PRP fibrin glue after a week. The mean length of hospital stay was higher in the surgery group (53.50 ± 16.662 days) than the PRP group (36.04 ± 8.224 days; p < 0.001). The study was limited due to the fact the procedure for randomization was not described and, thus, its efficacy cannot be evaluated.

Traumatic Wounds
Kazakos et al (2009) reported on a prospective RCT that evaluated treatment of acute traumatic wounds (open fractures, closed fractures with skin necrosis, friction burns) with platelet gel in 59 consecutive patients (27 PRP, 32 controls). Conventional treatment consisted of topical washing and cleaning of the wounds, removal of the necrotic tissue, and dressing in petroleum jelly gauze every 2 days. In all patients with open tibial fractures, an external fixation system was applied. PRP gel was applied to the wounds after surgical débridement and placement of the external fixation system. The time needed for preparation and application of the PRP gel was 52 minutes. After that, PRP gel was applied to the wounds once weekly in the outpatient clinic until there was adequate tissue regeneration (mean, 21 days) sufficient to undergo reconstructive plastic surgery. Control patients receiving conventional treatment required a mean of 41 days for adequate tissue regeneration. Pain scores were significantly lower in PRP-treated patients at 2 and 3 weeks (visual analog scale score, 58 PRP vs 80 controls). Although these results are encouraging, additional study with a larger number of patients is needed.

Marck et al (2016) reported on a randomized, double-blind, within-patient-controlled study in patients with deep dermal to full-thickness burns undergoing split-skin graft, comparing PRP with usual care. The study randomized 52 patients, 50 of whom received the allocated PRP intervention. There were no significant differences in short-term (5-7 days) rates in graft take in the intervention and control areas on each patient. At 3, 6, and 12 months, there were no significant differences in skin appearance or epithelialization scores.

Yeung et al (2018) performed a prospective RCT to test the efficacy of lyophilized platelet-rich plasma powder (LPRP) on the healing rate of wounds in patients with deep, second-degree bum injuries in comparison with a control group using a placebo. LPRP was dissolved in a solution and applied on deep second-degree bum wounds once per day for 4 consecutive days. Twenty-seven patients with deep second-degree burns were recruited and then those that met eligibility criteria were randomized into 2 groups. The LPRP group received the intervention (n = 15) and the control group received a placebo application (n = 12). A concentration of 1.0 x 10^7
platelets/cm² (wound area) was sprayed on the wound evenly. Function was assessed by the percentage of wound closure and bacteria picking out rate at weeks 2 and 3. The mean burn area of control for the LPRP was 75.65 ± 50.72 cm² and 99.73 ± 70.17 cm² (p=0.0013), respectively. In the control group, the original wound area was 25.49 cm² at baseline, 23.79 cm² (66.7% healed) at week 2, and 4.34 cm² (86.40% healed) at week 3. In the LPRP group, the original wound area was 84.36 cm², followed by 23.96 cm² (71.59% healed) at week 2, and 0.63 cm² (99.24% healed) at week 3. The wound closure rate at week 2 in the LPRP group reached nearly 80% and was greater than 90% by week 3, showing a significant difference (p<0.05).

Alternatively, in the control group, the wound closure rates were 60% and 80% in 2 and 3 weeks, respectively. The postoperative infection rate in the LPRP (26.67%) was lower than the control group (33.33%). Neither was significant, statistically. One limitation of this study is that the powder is made by an independent lab and dissolved in a specified amount of water. This provides an opportunity for accidental error—this may also be the case with some liquid PRP.23

Section Summary: PRP for Acute Surgical or Traumatic Wounds
The evidence for autologous PRP for a variety of acute surgical or traumatic wounds includes RCTs. For a variety of other conditions, studies have either not demonstrated a benefit or have demonstrated small benefits in studies with methodologic limitations.

Summary of Evidence
Platelet-Rich Plasma
For individuals who have chronic wounds or acute surgical or traumatic wounds who receive PRP, the evidence includes meta-analyses of a number of small controlled trials. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity. Current results of trials using PRP are mixed, and the studies are limited in both size and quality. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have chronic wounds who receive PRP, the evidence includes a number of small controlled trials. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity. Current results of trials using PRP are mixed and the studies are limited in both size and quality. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Practice Guidelines and Position Statements
Association for the Advancement of Wound Care
The Association for the Advancement of Wound Care developed guideline recommendations for the management of pressure ulcers (2010)24 and venous ulcers (2015)29:
- Pressure ulcer: “Growth factors are not indicated for PU [pressure ulcers] at this time” (level C evidence - no RCTs available comparing growth factors with A-level dressings)24
- Venous ulcer: “Platelet-derived growth factor has shown no significant effects on VU [venous ulcer healing or recurrence].” (level A evidence)29

National Institute for Health and Care Excellence

U.S. Preventive Services Task Force Recommendations
Not applicable.
Medicare National Coverage
The Centers for Medicare & Medicaid Services (CMS) (2012) revised its national coverage decision on autologous blood-derived products for chronic non-healing wounds. This revision replaces prior noncoverage decisions. The Centers for Medicare & Medicaid Services covers autologous PRP only for patients who have chronic non-healing diabetic, pressure, and/or venous wounds and when all of the following conditions are met:

- The patient is enrolled in a clinical research study that addresses the following questions using validated and reliable methods of evaluation...

The clinical research study must meet the requirements specified below to assess the effect of PRP for the treatment of chronic non-healing diabetic, pressure, and/or venous wounds.

The clinical study must address:

- Prospectively, do Medicare beneficiaries that have chronic non-healing diabetic, pressure, and/or venous wounds who receive well-defined optimal usual care, along with PRP therapy, experience clinically significant health outcomes compared to patients who receive well-defined optimal usual care for chronic non-healing diabetic, pressure, and/or venous wounds as indicated by addressing at least one of the following:
  - Complete wound healing
  - Ability to return to previous function and resumption of normal activities
  - Reduction of wound size or healing trajectory, which results in the patient’s ability to return to previous function and resumption of normal activities?

Ongoing and Unpublished Clinical Trials
Some larger studies that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tbody>
<tr>
<td>Ongoing</td>
<td></td>
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<tr>
<td>NCT02312596a</td>
<td>A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers</td>
<td>250</td>
<td>Jul 2021</td>
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<td>NCT02312570a</td>
<td>A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers</td>
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<td>Jul 2021</td>
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<td>NCT02307448a</td>
<td>Effectiveness of Autologous Platelet Rich Plasma in the Treatment of Chronic Non-Healing Wounds</td>
<td>1500</td>
<td>Dec 2020</td>
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<tr>
<td>NCT02402374a</td>
<td>Randomized, Placebo-controlled, Blinded-observer Study to Evaluate the Safety and Efficacy of Autologous Platelet Rich Plasma Gel Prepared With the RegenKit-BCT Plus Family of Kits for the Treatment of Diabetic Foot Ulcer</td>
<td>192</td>
<td>Sep 2019</td>
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<tr>
<td>NCT02213952</td>
<td>Efficacy of Autologous Platelet-Rich Plasma in the Treatment of Vascular Ulcers in Primary Care: Clinical Trial Phase III</td>
<td>150</td>
<td>Dec 2017</td>
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<tr>
<td>Unpublished</td>
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</tbody>
</table>
# references


**Documentation for Clinical Review**

- No records required

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

### The following services may be considered investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>0232T</td>
<td>Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed</td>
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<tr>
<td>CPT®</td>
<td>20926</td>
<td>Tissue graft, other (e.g., paratenon, fat, demis) <em>(Deleted code effective 1/1/2020)</em></td>
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<tr>
<td></td>
<td>86999</td>
<td>Unlisted transfusion medicine procedure</td>
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<tr>
<td>HCPCS</td>
<td>G0460</td>
<td>Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment</td>
</tr>
<tr>
<td></td>
<td>P9020</td>
<td>Platelet rich plasma, each unit</td>
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<tr>
<td></td>
<td>S9055</td>
<td>Procuren or other growth factor preparation to promote wound healing</td>
</tr>
</tbody>
</table>

**Policy History**

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>09/12/2008</td>
<td>BCBSA Medical Policy adoption 2.01.16. References updated. Coding updated</td>
</tr>
<tr>
<td>12/13/2010</td>
<td>Coding Update</td>
</tr>
<tr>
<td>07/01/2011</td>
<td>Policy title change from Recombinant and Autologous Platelet-Derived Growth Factors as a Primary Treatment of Wound Healing and Other Miscellaneous Conditions in the Outpatient Setting without position change</td>
</tr>
<tr>
<td>06/13/2012</td>
<td>Coding Update</td>
</tr>
<tr>
<td>06/28/2013</td>
<td>Coding Update</td>
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</tbody>
</table>
Definitions of Decision Determinations

**Medically Necessary:** Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member’s illness, injury, or disease.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements (as applicable to your plan)**

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.