Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 7/1/24**
(See policy history boxes for previous effective dates)

Title: Platelet Rich Plasma Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Non-Orthopedic Conditions

Description/Background

WOUND HEALING TREATMENT

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factors (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 the 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 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.

Platelet-rich plasma 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 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 the purposes of this review, the primary end points of interest for studies of wound closure are as follows, consistent with guidance from the FDA for industry in developing products for treatment of chronic cutaneous ulcer and burn wounds:[1]

- Incidence of complete wound closure;
- Time to complete wound closure (reflecting accelerated wound closure);
- Incidence of complete wound closure following surgical wound closure;
- Pain control.

Regulatory Status:

The 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 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.[2]

Numerous PRP preparation systems that have been cleared for marketing by 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.

Medical Policy Statement

The use of platelet-rich plasma (ie, autologous blood-derived growth factor or autologous platelet gel [eg, AurixTM / AutologelTM and SafeBlood®]) for the treatment of acute or chronic wounds, including surgical wounds and nonhealing ulcers, has not been established. There is insufficient evidence to draw definitive conclusions regarding the clinical efficacy of autologous platelet concentrate or gel, therefore, they are considered experimental/investigational.

Inclusionary and Exclusionary Guidelines NA

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

NA

Other codes (investigational, not medically necessary, etc.):

G0460 G0465 P9020 S9055 0232T

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

This evidence review was originally based on a 1992 Blue Cross Blue Shield Association TEC Assessment that primarily focused on the Procuren process.[3] This preparation method is no longer commercially available. Currently, a large number of devices are available for the preparation of platelet-rich plasma (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 injection is necessary.[4,5,6,7,8]

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to individuals and to 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 balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 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 platelet-rich plasma is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with chronic wounds.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with chronic wounds.

Interventions
The therapy being considered is PRP.

Comparators
Comparators of interest include standard wound care.

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

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

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Diabetic Foot Ulcers

Systematic Reviews
A number of systematic reviews of the evidence on PRP have been published.[9,10,11,12,13,14,15,16] These reviews are heterogenous in whether they pooled data from studies reflecting a variety of wound types[11,10,9,12,23] or focused on specific wound types, primarily diabetic foot ulcers.[13,14,15,16] Results from the reviews that pooled data from a variety of wound types[11,10,9,12] are not discussed herein as their design precludes drawing conclusions about the applicability of the review findings to specific wound types. As the majority of the RCTs included in the systematic reviews were published post-2014, herein are summarized those systematic reviews that focused on specific wound types with search dates that extend to at least 2015.[14,15,16]

Three recent systematic reviews have evaluated studies of PRP for individuals with diabetic foot ulcers.[14,15,16] Table 1 provides a crosswalk of the studies included in the systematic reviews.

Table 1. Comparison of Trials of Platelet-Rich Plasma in Individuals with Diabetic Foot Ulcers Included in Systematic Reviews

Primary Study (Year)	Deng 2023[14]	Li 2019[15]	Qu 2020[16]

Ahmed 2017[17]	•	•	•
Chen 2008[a][18]	•	•	
Driver 2006[19]	•	•	•
Elsaid 2020[20]			•
Friese 2007 (conference proceeding)[21]	•	•	
Game 2018[22]			•
Gude 2019[24]			•
Kakagia 2007[25]	•	•	•
Karimi 2016[26]			•
Li 2015[27]	•	•	•
Liu 2016[a][28]	•	•	
Ma 2014[a][29]	•	•	
Milek 2017[30]			•
Qi 2014[a][31]	•	•	
Saad Setta 2011[32]	•	•	•
Saldalamacchia 2004[33]	•	•	•
Serra 2013[34]	•	•	•
Singh 2018[35]			•
Steed 1992[36]			
Steed 1996[37]			
Xie 2020[38]			•
Yang 2017[39]			•
Zhang 2016[a][40]	•	•	
Zhou 2015[a][41]	•	•	
Zhu 2012[a][42]	•	•	

[a] In Chinese

Tables 2 and 3 summarize the characteristics and results of the 3 systematic reviews that have evaluated studies of PRP for individuals with diabetic foot ulcers.[14,15,16]

A meta-analysis by del Pino-Sedeno et al (2018) assessed 8 RCTs and 2 longitudinal-observational studies (N=525) to determine the safety and efficacy of PRP to treat diabetic foot ulcers.[14] Results indicated PRP significantly increased chronic wound healing compared with standard treatment (RR=1.41; 95% CI: 1.08 to 1.84; p=.01; 1^2=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=.02; allogenic RR=3.20; 95% CI: 1.14 to 9.03; p=.03). Platelet-rich plasma preparation method also influenced healing (homemade RR=1.22; 95% CI: 1.04 to 1.44; p=.02; commercial protocol RR=1.13; 95% CI: 0.58 to 2.20; p=.71; blood bank RR=3.20; 95% CI: 1.14 to 9.03; p=.03). 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=.02; I^2=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=.41; I^2=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.[15] 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. 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; 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. Further, 7 of the included trials are available only in the Chinese language. Finally, most of the trials were 8 to 12 weeks long and others only 2 to 5 weeks, making it difficult to analyze the relationship of time of observation to ulcer healing.

The Agency for Healthcare Research and Quality (AHRQ) (2020) published a Technology Assessment on Platelet-Rich Plasma for Wound Care in the Medicare Population. This Technology Assessment was requested by the Centers for Medicare & Medicaid Services to inform reconsideration of a National Coverage Decision on autologous blood-derived products for chronic non-healing wounds.[16] This Technology Assessment evaluates evidence in lower extremity diabetic ulcers, lower extremity venous ulcers and pressure ulcers. Separate meta-analyses were conducted for each wound type. Here the focus is on findings for lower extremity diabetic ulcers and those for the other populations are discussed below. Risk of bias of individual studies was assessed using the Cochrane Collaboration's Risk of Bias 2 tool and rated high in 8 RCTs (57.14%), moderate in 6 RCTs (42.86%) and high in the 1 observational study (100%). Strength of the body of evidence was rated based on the Evidence-based Practice Center methods guide. The findings of this Technology Assessment indicated that there is moderate-strength evidence that PRP modestly increases complete wound closure (see meta-analysis results in Table 4 below) and low-strength evidence that PRP may shorten time to wound closure (meta-analysis not feasible). However, due to risk of bias and severe imprecision, evidence is insufficient to draw conclusions about other important outcomes, including wound infection, amputation, pain reduction, and wound recurrence. Important limitations of the literature were described as "inadequate description of offloading and wound care procedures, wound characteristics, PRP formulation techniques, concentration and volume; inadequate length of follow-up, and lack of stratification by comorbidities and other patient characteristics, such as diabetes control, vascular perfusion, and under representation of older adults."

A meta-analysis by Deng et al (2023) assessed 22 RCTs (N=1559) to determine the safety and efficacy of PRP to treat diabetic foot ulcers.[14] Results indicated PRP significantly increased the overall healing rate of diabetic foot ulcers compared with standard treatment (risk ratio [RR]=1.42; 95% CI: 1.30 to 1.56; p<.001; I^2=55%). PRP increased the complete wound healing time of diabetic foot ulcers compared to conventional treatment (mean difference [MD]=-3.13; 95% CI: -5.86 to -0.39; p<.001; I^2=97.5%) and resulted in a greater

reduction in diabetic foot ulcer area (MD=1.02; 95% CI: 0.51 to 1.53; p<.001; I^2=36%). The rate of amputation, reported by 3 trials, significantly reduced risk for the autologous PRP group (RR=0.35; 95% CI, 0.15 to 0.83; p<.001; I^2=0%). Four studies reported adverse events, and pooled analysis revealed a similar rate of events between the PRP and control groups (RR=0.96; 95% CI, 0.57 to 1.61; p>0.05; 35%). The authors reported no significant publication bias was detected by funnel plot analysis; however, a sensitivity analysis suggested that the pooled outcome assessment for time to wound healing may be affected by considerable inter-study variability. The low number of high-quality of studies available on PRP for diabetic foot ulcers and the low number of studies reporting some outcomes of interest were limitations of this meta-analysis.

Table 2. Characteristics of Key Systematic Reviews with Meta-Analyses in Individuals with Diabetic Foot Ulcers

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Deng (2023)[14]	Inception-2023	22	Adults with diabetic foot ulcers	N=1559	RCTs	NR
Li (2019)[15]	2004-2017	15	Patients with diabetic chronic cutaneous wounds/ulcers that do not show signs of healing in 4 weeks	N=829 (14-117)	RCTs	NR
Qu (2020)[16]	Inception-2020	14	Adults with lower extremity diabetic ulcers, lower extremity venous ulcers, or pressure ulcers in any location, or a mix of these 3 etiologies	N=1,096 (range NR)	RCTs	Median = 6 wk (range, none to 11 months)

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

Table 3. Results of Key Systematic Reviews with Meta-Analyses In Individuals with Diabetic Foot Ulcers

Study	Healing Rate	Healing Time	Complete Wound Healing	Risk of Infection	Wound complications	Pain Reduction	Recurrence
Deng (2023)[14]							
RR	1.42				.096		
MD		-3.13					
95% CI	1.30 to 1.56	-5.86 to -0.39			0.57 to 1.61		
P-value	<.001	<.001			.203		
Li (2019)[15]							
RR	1.39						
MD		-9.18					
OR				0.34			
95% CI	1.29 to 1.50	-11.32 to -7.05		0.15 to 0.77			
P-value	<.001	<.001		.009			
Qu (2020)[16]							

RR			1.20	0.77			2.09
WMD						-1.10[a]	
95% CI			1.09 to 1.32	0.54 to 1.11		-1.81 to -0.39	0.31 to 13.93
P-value							

[a] Visual analog scale
CI: confidence interval; MD: mean difference; OR: odds ratio; RR: risk ratio; Z: indicates overall effect

Randomized Controlled Trials

Key characteristics and results of several RCTs of diabetic foot ulcers published subsequent to the AHRQ review (2020) are summarized in Tables 4 and 5 below.

One RCT of PRP dressing with total-contact casting compared to standard saline dressing for diabetic foot ulcers (Gupta et al [2021])[52] did not find significant differences in rates of ulcer area reduction or absolute ulcer area reduction between groups over the 6-week study period. Another RCT of PRP versus standard wound care found accelerated rates of ulcer area reduction and decreased incidence of wound infections with PRP treatment; however, the difference in the percentage of healed surface between groups lost statistical significance at 6, 7, or 8 weeks of follow-up and it is unclear whether complete wound healing was achieved in either group. [53]

Table 4. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	Control
Gupta et al (2021) [52]	India	1	2016 to 2018	Individuals with diabetes mellitus with noninfected diabetic foot ulcers with total ulcer area of 20 cm^2 or less on the plantar surface	Autologous intralesional PRP therapy with total contact casting (n=30)	Saline dressing (n= 30)
Hossam et al (2022) [53]	Egypt	1	2018	Individuals with type 1 or 2 diabetes with non-ischemic revascularized chronic diabetic foot ulcers of more than 6 months duration with no clinical signs of infection, Wagner grade 1 or 2, and ASA physical status class 2	Autologous intralesional $CaCl_2$-activated PRP therapy (injection and/or gel) with saline gauze (n=40)	Standard wound care with moist dressing with or without collagenase ointment (n=40)

ASA: American Society of Anesthesiologists; PRP: platelet-rich plasma; RCT: randomized controlled trial.

Table 5. Summary of Key RCT Results

Study	Complete Healing	Percentage of Healed Surface Area[a]	Complete Healing Time	Pain	Quality of Life	Infection
Gupta et al (2021) [52]	NR	6 weeks: 85.98% vs 81.72%; p=NR	NR	NR	NR	NR
Hossam et al (2022) [53]	95% vs 77.8%[b]; p<.001	1 week: 23.1% vs 0%; p=.002 5 weeks: 89.2% vs 60.1%; p<.001 8 weeks: 96.7% vs 95.5%; p=.529	NR	NR	NR	PRP: 4 (10%) Control: 18 (45%) with 4 resulting in amputation p<.001

Other Chronic Wound Types

The AHRQ (2020) Technology Assessment on Platelet-Rich Plasma for Wound Care in the Medicare Population described above also evaluated evidence on use of PRP in individuals with lower extremity venous ulcers and individuals with pressure ulcers.[44]

For individuals with lower extremity venous ulcers, the evidence included 8 RCTs and 3 observational studies (N=615). The majority compared PRP to management without PRP. Risk of bias was described as moderate due to randomization and outcome measurement limitations. There were no significant differences between PRP versus management without PRP in complete wound closure (RR=1.49; 95% CI: 0.72 to 3.06; 5 studies, N=250; I^2=29.4%), wound recurrence (RR=0.38; 95% CI: 0.09 to 1.57), wound infection (RR=0.79; 95% CI: 0.22 to 2.81), or quality of life as measured by the Chronic Lower Limb Venous Insufficiency Questionnaire (WMD=10.99; 95% CI: -50.5 to 72.5). For the outcomes time to complete wound closure and pain, meta-analysis of 2 studies was not possible due to insufficient data and findings were mixed between studies on both outcomes. The strength of evidence was rated as 'insufficient' to draw conclusions on all outcomes. Oliveira et al (2020) also conducted a meta-analysis of cost and effectiveness of studies of PRP for venous ulcers.[45] Based on fewer studies identified from searches only through July 2018, although their findings indicated greater reductions in wound area for PRP, findings were consistent with the ARHQ review in finding no significant difference in complete wound closure (RR=2.54; 95% CI, 0.42 to 15.30; 4 studies, n=156; I^2=69%).

For individuals with pressure ulcers, the AHRQ Technology Assessment (2020)[44] included 1 RCT and 1 comparative observational study (Total N not reported). The comparator was serum physiological dressing in the RCT and saline dressing in the observational study. Risk of bias of the primary studies was described as moderate, due to limitations in the randomization process and outcome measurement, deviations from intended interventions, and selective outcome reporting. Although both studies found that PRP significantly reduced

wound size (strength of evidence=insufficient), neither study evaluated other important outcomes, such as complete wound closure.

A meta-analysis by Fang et al (2023) pooled data from 6 studies on patients treated for lower extremity venous ulcers with PRP.[46] A total of 294 patients were included, with 148 patients in the PRP group and 146 in the control group. PRP was found to have a greater reduction in elliptical area at the end of treatment compared to the control group (Mean difference [MD], -1.19; 95% CI, -1.8 to -.058; P=.0001) with a moderate quality of evidence. The healing rate also favored PRP over the control group (RR=5.73; 95% CI, 3.29 to 9.99; P<.00001) with a moderate quality to the evidence base. The authors suggest there may be publication bias in the calculation of these pooled estimates according to Egger's test.

Randomized Controlled Trials

Two RCTs of PRP for chronic wounds (Saha et al [2020])[47] were identified as published subsequent to the AHRQ review (2020).[44] Key characteristics and results of selected RCTs are reported in Tables 6 and 7 below.

Saha et al.'s analyses included 91.5% (n=108) of randomized individuals. Participants were mostly males in their late 40s with trophic ulcer duration of 13.4 months. Reduction in ulcer surface area, the primary outcome, was significantly greater for the PRP group from the first week (38.96% vs 12.46%; p<.001) through the fifth (and last) week of follow-up (91.10% vs 79.77%; p<.001). However, healing time and recurrence were not reported and there was no significant difference in complete healing rate.

Shehab et al (2023) conducted an RCT of adjunct PRP in addition to compression therapy in individuals with post-phlebitic venous ulcers.[48] Forty patients were randomized 1:1 to either PRP and compression therapy or placebo. The median number of treatments was 6 (range 3 to 6). Both participants and outcome assessors were blinded to treatment allocation. The median ulcer surface area, the primary outcome, was significantly lower for the PRP group (4 cm^2 vs 10 cm^2; p=.036) as well as the median volume of ulcers (1 cm^3 vs 3 cm^3; p=.008). This translated to individuals in the PRP group experiencing a larger drop in ulcer area (74% vs 40%; p=.008) and volume (81% vs 48%; p=.013) compared to placebo. Differences in VAS pain scores were observed in favor of the PRP group at both the 3-month and 6-month follow-ups. Nine patients in the PRP group had complete wound healing, but the authors did not report the rate of complete healing in the control group, and healing time and recurrence were not reported.

Table 6. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Intervention	Control
Saha et al (2020)[47]	Iran	1	2016 to 2018	Individuals with clinically diagnosed trophic ulcers due to leprosy	Autologous PRP therapy with total contact casting (n=59)	Only total contact casting (n=59)
Shehab et al (2023)[48]	Egypt	1	2019 to 2020	Adults with chronic post-phlebitic lower limb venous ulcers	Autologous PRP therapy with compression therapy (n=20)	Placebo plus compression therapy (n=20)

PRP: Platelet-rich plasma; RCT: randomized controlled trial

Table 7. Summary of Key RCT Results

Study	Complete Healing	Healing Time	Pain	Quality of Life	Infection	Recurrence
Saha et al (2020)[47]	22 (39.29%) vs 11 (21.15%); p NR	NR	NR	NR	0 vs 0; p=.773	NR

NR: Not reported; RCT: randomized controlled trial.
[a] Percentage of healed surface area in study and control groups at 6 weeks.

Table 8. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Saha et al (2020)[47]	4. Single site in Iran	4. Short duration of treatment; 8 weeks		1. Recurrence, quality of life not addressed 5. Clinical significance of difference in wound surface area not prespecified	1. 4 weeks follow-up post-treatment insufficient to assess long-term efficacy
Hossam et al (2022) [53]	4. Single site in Egypt	1. Frequency and type of PRP treatment (injection and/or gel) not standardized 4. Short duration of treatment; 8 weeks		1. Complete wound healing, recurrence, quality of life not addressed 5. Primary outcome differences and timepoints were not prespecified	1. 8 week study period insufficient to assess long-term efficacy

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 9. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Saha et al (2020)[47]						
Hossam et al (2022) [53]	4. Single site in Egypt	1. Frequency and type of PRP treatment (injection and/or gel) not standardized 4. Short duration of treatment; 8 weeks		1. Complete wound healing, recurrence, quality of life not addressed 5. Primary outcome differences and timepoints were not prespecified	1. 8 week study period insufficient to assess long-term efficacy	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Platelet-Rich Plasma 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. In individuals with lower extremity diabetic ulcers, PRP demonstrated an improvement over the control groups in complete wound closure and healing time, but moderate to high risk of bias and imprecision preclude drawing conclusions on other important outcomes such as recurrence, infection, amputation, and quality of life. In individuals with venous ulcers, PRP did not demonstrate an improvement over the control groups in complete wound closure, recurrence, wound infection or quality of life, although imprecision likely precluded identifying differences on these outcomes. In individuals with pressure ulcers, although PRP reduced wound size, other important outcomes such as complete wound closure were not measured. 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 individuals with acute surgical or traumatic wounds.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are individuals with acute surgical or traumatic wounds.

Interventions

The therapy being considered is PRP.

Comparators

Comparators of interest include standard wound care.

Outcomes

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

Though not completely standardized, follow-up for acute surgical or traumatic wound 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.

REVIEW OF EVIDENCE

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.[49] 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<.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 (1 patient in each group) and no significant difference 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 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.[50] The 2 groups were comparable at baseline. At the end of cardiac surgery, PRP gel was applied on the sternum 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 this study is limited by likely differences in treatments over time. RCTs are needed to evaluate this potential use of PRP.

Zhu et al (2023) published a meta-analysis of the effect of PRP on sternal wound healing.[51] Eleven studies with a total of 8961 cardiac surgery patients were included. Patients were either treated with PRP (n=3663) or control therapies (n=5298), with sample sizes ranging from 44 to 2000 participants. PRP was found to have a significantly lower rate of sternal wound infection (Odds ratio [OR], 0.11; 95% CI, 0.03 to 0.34; p<.001; I^2, 0%), deep sternal wound infection (OR, 0.29; 95% CI, 0.16 to0.51; p<.001; I^2, 32%) and superficial sternal wound infection (OR, 0.20; 95% CI, 0.13 to 0.33; p<.001; I^2, 0%) compared to patients in the control cardiac surgery groups. All pooled estimates at no to low heterogeneity (0% to 32%). The poor quality of included studies, heterogeneous PRP preparations, and heterogeneous cardiac surgeries limit the interpretation of the results.

Otolaryngology
El-Anwar et al (2016) reported on an RCT that evaluated PRP in 44 children (age range, 12 to 23 months) undergoing repair of a complete cleft palate.[51] 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 perceptal assessment (p=.024) and better velopharyngeal closure on endoscopy (p=.016).

A 2008 double-blind RCT assessed the efficacy of PRP following tonsillectomy in 70 children (age range, 4 to 15 years).[54] 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 either the patient or 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 the patients showed no differences in pain, medication doses, activity, and days eating solid foods between the 2 conditions.

Other Surgical 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.[55]

Alamdari et al (2018) published a clinical trial evaluating the efficacy of pleurodesis with a combination of PRP and fibrin glue compared with a 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, 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=.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 < .001). The study was limited due to the fact the procedure for randomization was not described and, thus, its efficacy cannot be evaluated.[57]

Mohamadi et al (2019) reported on an RCT of 110 participants in Tehran that evaluated the efficacy of PRP gel in wound healing time following pilonidal sinus surgery.[58] Each group included 55 participants. Follow-up duration was 9 weeks. In the treatment group, PRP was both injected into the wound weekly, as well as applied to the wound surface and covered with latex. In the control group, wound dressing was described as "classic", but no other details were provided. Little to no detail was provided about specific outcome assessment methods (ie, "pain duration was inquired from participants"). All patients completed the study and were included in the outcome assessments. PRP significantly shortened mean healing time (4.8 vs 8.7 weeks; p<.001), pain duration (1.3 vs 3.4 weeks; p<.001), and antibiotic consumption duration (0.57 vs 1.74 weeks; p<.001). This RCT also performed regression analyses to evaluate the correlation between different factors in wound healing activity. Significant negative associations were found between healing time and wound volume and pain duration and angiogenesis. Notable limitations of this study included unclearly defined wound dressing in the comparator group, unblinded and poorly defined outcome assessment, short-term follow-up and lack of assessment of other important health outcomes.

Slaninka et al (2020) published an RCT that evaluated PRP in 24 individuals in the Czech Republic who had undergone dermo-epidermal skin grafts taken from the thigh area.[59] Indications for skin grafts were primarily hard-to-heal lower leg wounds. PRP was applied to one thigh and covered with Vaseline-impregnated, open-weave gauze and gauze. The control

was the other thigh, which was also covered with open-weave gauze and gauze, but without PRP. Of the 24 included individuals, 3 (12.5%) were excluded after developing infections. The infections were described as first occurring on the non-PRP wound and only subsequently occurring on the PRP wound after several days. PRP significantly shortened median healing time (14 days vs 18 days; p=.026). No other outcomes were reported. Notable limitations of the RCT include its small sample size and that it did not address important health outcomes and harms.

Traumatic Wounds

Kazakos et al (2009) reported 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).[60] Conventional treatment consisted of topical washing and cleaning of the wounds, removal of the necrotic tissue, and dressing with 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 debridement 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.[61] The study randomized 52 patients, 50 of whom received the allocated PRP intervention. There were no significant differences in short term (5 to 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 randomized controlled trial to test the efficacy of lyophilized platelet-rich plasma powder (LPRP) on the healing rate of wounds in patients with deep, second-degree burn injuries in comparison with a control group using a placebo. LPRP was dissolved in a solution and applied on deep second-degree burn 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 LRPR group received the intervention (n=15) and the control group received a placebo application (n=12). A concentration of 1.0×10^7 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 cm^2 and 99.73 ± 70.17 cm^2 (p=.0013), respectively. In the control group, the original wound area was 25.49 cm^2 at baseline, 23.79 cm^2 (6.67% healed) at week 2, and 4.34 cm^2 (86.40% healed) at week 3. In the LPRP group, the original wound area was 84.36 cm^2, followed by 23.96 cm^2 (71.59% healed) at week 2, and 0.63 cm^2 (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<.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 for 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.[62]

Huang et al (2021) published a meta-analysis of 8 RCTs representing 539 patients with burn wounds.[63] The healing rate of burn wounds was improved with PRP (odds ratio [OR], 4.43; 95% CI, 2.13 to 9.22), yielding a significantly shorter wound healing time (OR, -4.23; 95% CI, -5.48 to -2.98) compared to conventional dressings for both superficial and deep burn groups. Incidence of adverse events, pain scores, and scar scores was also all improved in the PRP treatment group. Interpretation of results is limited by risks of bias arising from lack of blinding, small study size, heterogenous PRP preparations, and short follow-up durations.

Imam et al (2023)[64] published a meta-analysis of 13 comparative studies, including 808 individuals with burn wounds who were treated with PRP (n=413) or standard wound therapy (n=395) with sample sizes ranging from 25 to 100 individuals.[80.] PRP had a shorter healing time than compared to standard therapy (Mean difference [MD], -5.80; 95% CI, -7.73 to -3.88; p<.001) as well as a higher healing rate (OR, 3.14; 95% CI, 2.05 to 4.8; p<.001) although these pooled estimates had substantial (I^2=93%) and moderate heterogeneity (I^2=42%), respectively. Individuals treated with PRP also had a higher percentage of graft take area (MD, 4.39; 95% CI, 1.51 to 7.26; p<.001) and higher percent of area healed (MD, 12.67; 95% CI, 9.79 to 15.55, p<.001) compared to standard therapy for burn wounds with a low level of heterogeneity. No differences were observed in the graft take ratio or infection rates which showed low heterogeneity across studies in the pooled estimates. Interpretation of results is limited by risks of bias arising from low overall study quality, small study sizes, heterogenous PRP preparations, limited number of studies included for some comparisons, and short follow-up durations.

Section Summary: Platelet-Rich Plasma for Acute Surgical or Traumatic Wounds
The evidence for autologous PRP for a variety of acute surgical or traumatic wounds includes systematic reviews and 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 who receive PRP, the evidence includes meta-analyses of a number of small controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. In individuals with lower extremity diabetic ulcers, PRP demonstrated an improvement over the control groups in complete wound closure and healing time, but moderate to high risk of bias and imprecision preclude drawing conclusions on other important outcomes such as recurrence, infection, amputation, and quality of life. In individuals with venous ulcers, PRP did not demonstrate an improvement over the control groups in complete wound closure, recurrence, wound infection or quality of life, although imprecision likely precluded identifying differences on these outcomes. In individuals with pressure ulcers, although PRP reduced wound size, other important outcomes such as complete wound closure were not measured. The evidence

is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have acute surgical or traumatic wounds who receive PRP, the evidence includes a systematic review and a number of small controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, 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 that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

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 College of Physicians

In 2015, the American College of Physicians (ACP) published guidelines on treatment of pressure ulcers.[65] The guidelines noted that "although low quality evidence suggests that dressings containing PDGF [platelet-derived growth factors] promote healing, ACP supports the use of other dressings such as hydrocolloid and foam dressings, which are effective at promoting healing and cost less than PDGF dressings." A search of the ACP website found that this 2015 guideline is listed an inactive.

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)[66] and on venous ulcers (2015)[67]:

- 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)[66]
- Venous ulcer: "Platelet derived growth factor has shown no significant effects on VU [venous ulcer healing or recurrence]" (level A evidence).[67]

National Institute for Health and Care Excellence

In 2019, the National Institute for Health and Care Excellence updated its guidance on the prevention and management of diabetic foot problems.[68] The guidance stated that neither autologous platelet-rich plasma gel nor platelet-derived growth factors should be offered in the treatment of diabetic foot ulcers.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some larger studies that might influence this review are listed in Table 9.

Table 8. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05979584	Platelet Rich Plasma VS Platelet Fibrin Plasma in Treatment of Diabetes Foot Ulcer: a Randomized Controlled Trial	56	Dec 2024
NCT02312596[a]	A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers	250	Dec 2021
NCT02312570[a]	A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers	250	Dec 2021
NCT02307448[a]	Effectiveness of Autologous Platelet Rich Plasma in the Treatment of Chronic Non-Healing Wounds	80	Dec 2022
NCT02402374[a]	Randomized, Placebo-controlled, Blind-assessor 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	192	Dec 2020 (unknown)
Unpublished			
NCT02071979[a]	Registry Trial of the Effectiveness of Platelet Rich Plasma for Chronic Non-Healing Wounds (CMS)	1500	Jan 2018 (terminated; updated 01/16/18)

NCT: national clinical trial; PRP autologous platelet-rich plasma
[a] Denotes industry-sponsored or cosponsored trial

Government Regulations
National/Local:

National Coverage Determination (NCD) for Blood-Derived Products for Chronic Non-Healing Wounds (270.3)[69]
Effective Date of this Version: 04/13/21
Implementation Date: 11/09/2021

Indications and Limitations of Coverage
B. Nationally Covered Indications

Item/Service Description

A. General
Wound healing is a dynamic, interactive process that involves multiple cells and proteins. There are three progressive stages of normal wound healing, and the typical wound healing duration is about 4 weeks. While cutaneous wounds are a disruption of the normal, anatomic structure and function of the skin, subcutaneous wounds involve tissue below the skin's surface. Wounds are categorized as either acute, where the normal wound healing stages are not yet completed but it is presumed they will be, resulting in orderly and timely wound repair, or chronic, where a wound has failed to progress through the normal wound healing stages and repair itself within a sufficient time period.
Platelet-rich plasma (PRP) is produced in an autologous or homologous manner. Autologous PRP is comprised of blood from the patient who will ultimately receive the PRP. Alternatively, homologous PRP is derived from blood from multiple donors.

Blood is donated by the patient and centrifuged to produce an autologous gel for treatment of chronic, nonhealing cutaneous wounds that persist for 30 days or longer and fail to properly complete the healing process. Autologous blood derived products for chronic, non-healing wounds includes both: (1) platelet derived growth factor (PDGF) products, and (2) PRP (such as AutoloGel).

The PRP is different from previous products in that it contains whole cells including white cells, red cells, plasma, platelets, fibrin, stem cells, and fibrocyte precursors.
The PRP is used by physicians in clinical settings in treating chronic, non-healing wounds, open, cutaneous wounds, soft tissue and bone. Alternatively, PDGF does not contain cells and was previously marketed as a product to be used by patients at home.
Indications and Limitations of Coverage

B. Nationally Covered Indications
Effective for services performed on or after April 13, 2021, the Centers for Medicare & Medicaid Services (CMS) will cover autologous PRP for the treatment of chronic non-healing diabetic wounds under section 1862(a)(1)(A) of the Social Security Act (the Act) for a duration of 20 weeks, when prepared by devices whose Food and Drug Administration-cleared indications include the management of exuding cutaneous wounds, such as diabetic ulcers.

C. Nationally Non-Covered Indications Autologous PDGF for the treatment of chronic, non-healing cutaneous wounds, and,Becaplermin, a non-autologous growth factor for chronic, non-healing subcutaneous wounds, and, Autologous PRP for the treatment of acute surgical wounds when the autologous PRP is applied directly to the closed incision, or for dehiscent wounds.
D. Other Effective for services performed on or after April 13, 2021:
Coverage of autologous PRP for the treatment of chronic non-healing diabetic wounds beyond 20 weeks will be determined by the local Medicare Administrative Contractors (MACs).
Coverage of autologous PRP for the treatment of all other chronic non-healing wounds will be determined by the local MACs under section 1862(a)(1)(A) of the Act.

National Coverage Analysis (NCA): Autologous Blood-Derived Products for Chronic Non-Healing Wounds CAG-00190R4
Decision Memo: 04/13/2021[70]

Decision Summary
The Centers for Medicare & Medicaid Services (CMS) will cover autologous platelet-rich plasma (PRP) for the treatment of chronic non-healing diabetic wounds under section 1862(a)(1)(A) of the Social Security Act (the Act) for a duration of 20 weeks, when prepared by devices whose FDA cleared indications include the management of exuding cutaneous wounds, such as diabetic ulcers. Coverage of autologous PRP for the treatment of chronic non-healing diabetic wounds beyond 20 weeks will be determined by local Medicare Administrative Contractors (MACs).

Coverage of autologous PRP for the treatment of all other chronic non-healing wounds will be determined by local Medicare Administrative Contractors (MACs) under section 1862(a)(1)(A) of the Act.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Orthopedic Applications of Platelet-Rich Plasma
Orthopedic Applications of Stem Cell Therapy (Including autologous stem cells used with Allografts and Bone Substitutes)
Prolotherapy
Wound Therapy (BCN Only)

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 1/24/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/22/02	11/22/02	11/25/02	Joint policy established
2/16/04	2/16/04	2/13/04	Routine maintenance
5/19/05	5/19/05	5/21/05	Routine maintenance, policy retired
5/1/07	3/1/07	5/1/08	Routine maintenance
7/1/10	5/13/10	4/20/10	Policy position changed from experimental/investigational to established for recombinant platelet derived growth factors. Deleted the word, “Preparations” from policy title.
3/1/11	12/13/11	12/21/11	Routine maintenance
7/1/13	4/16/13	4/22/13	Routine maintenance; title changed from “Platelet Derived Growth Factors used for Wound Healing” to “Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions”.
11/1/14	8/21/14	8/25/14	Routine maintenance Added HCPCS procedure code G0460
5/1/16	2/16/16	2/16/16	Routine maintenance Removed orthopedic indications from this policy. Refer to policy titled “Orthopedic Applications of Platelet-Rich Plasma.” Added “non-orthopedic” to policy title.
5/1/17	2/21/17	2/21/17	Routine maintenance
5/1/18	2/20/18	2/20/18	Routine maintenance
5/1/19	2/19/19		Routine maintenance

5/1/20	2/18/20		Routine maintenance; MPS, Inclusions and Exclusions language clarified. Ref 22, 23 added. Wound specialists added to physicians who manage care. “Regranex” added to MPS and inclusions.
5/1/21	2/16/21		Routine maintenance. Ref 23-51,58,59,68 added
5/1/22	2/15/22		Routine maintenance. G0465 added; G0460 revised Ref 50,52,54,66 added Change in S0157: no longer a medical benefit as of April 2021. Remove “Recombinant” from title, remove all references to Regranex from body, codes and rationale sections of policy.
7/1/22	4/19/22		Routine maintenance
7/1/23	4/18/23		Routine maintenance (jf) Vendor Managed: NA Reference Added: 23,51, & 52 removed 47 no longer a medical benefit as of April 2021. 2022 Removed all references to Regranex from body, codes and rationale sections of policy.
7/1/24	4/16/24		Routine maintenance (jf) Vendor Managed: NA References added: 14,46,48,51,64

Next Review Date: 2nd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PLATELET RICH PLASMA AUTOLOGOUS PLATELET-DERIVED GROWTH FACTORS AS A TREATMENT OF WOUND HEALING AND OTHER NON-ORTHOPEDIC CONDITIONS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	See the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.