Medical Policy

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Title: Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non–Orthopedic Conditions

Related Policies:	▪ *Orthopedic Applications of Platelet-Rich Plasma* ▪ *Negative Pressure Wound Therapy in the Outpatient Setting* ▪ *Bio-Engineered Skin and Soft Tissue Substitutes*

Professional / Institutional
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Populations	Interventions	Comparators	Outcomes
Individuals: • With diabetic lower-extremity ulcers	Interventions of interest are: • Recombinant platelet-derived growth factor	Comparators of interest are: • Standard wound care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity
Individuals:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include:

Populations	Interventions	Comparators	Outcomes
• With pressure ulcers	• Recombinant platelet-derived growth factor	• Standard wound care	• Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • With venous stasis leg ulcers	Interventions of interest are: • Recombinant platelet-derived growth factor	Comparators of interest are: • Standard wound care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • With acute surgical or traumatic wounds	Interventions of interest are: • Recombinant platelet-derived growth factor	Comparators of interest are: • Standard wound care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • With chronic wounds	Interventions of interest are: • Platelet-rich plasma	Comparators of interest are: • Standard wound care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • With acute surgical or traumatic wounds	Interventions of interest are: • Platelet-rich plasma	Comparators of interest are: • Standard wound care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity

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.

OBJECTIVE

The objective of this evidence review is to evaluate whether the use of recombinant platelet-derived growth factor or platelet-rich plasma improves health outcomes compared with standard

care for diabetic ulcers, pressure ulcers, venous stasis ulcers, and surgical and traumatic wounds.=

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. Recombinant PDGF also has been extensively investigated for clinical use in wound healing.

Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma (PRP), can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets (releasing 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 recombinant PDGF products and PRP for non-orthopedic 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;
- Time to complete wound closure (reflecting accelerated wound closure);
- Incidence of complete wound closure following surgical wound closure;
- Pain control.

REGULATORY STATUS

Becaplermin

In 1997, becaplermin gel (Regranex®; Smith & Nephew), a recombinant PDGF product, was approved by the FDA for the following labeled indication:

"Regranex Gel is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply. When used as an adjunct to, and not a substitute for, good ulcer care practices including initial sharp debridement, pressure relief and infection control, Regranex Gel increases the complete healing of diabetic ulcers.

The efficacy of Regranex Gel for the treatment of diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous tissue or ischemic diabetic ulcers … has not been evaluated…Regranex is not intended to be used in wounds that close by primary intention."

In 2008, the manufacturer added the following black box warning to the labeling for Regranex®: "An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex Gel in a postmarketing retrospective cohort study. Regranex Gel should only be used when the benefits can be expected to outweigh the risks. Regranex Gel should be used with caution in patients with known malignancy."

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

Platelet-Rich Plasma

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, 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.

POLICY

A. Recombinant platelet-derived growth factor (i.e., becaplermin) may be considered **medically necessary** when used as an adjunct to standard wound management for the following indications:

1. Neuropathic diabetic ulcers extending into the subcutaneous tissue
   Appropriate candidates for becaplermin gel for treatment of neuropathic ulcers should meet **ALL** of the following criteria:
   a. Adequate tissue oxygenation, as measured by a transcutaneous partial pressure of oxygen of 30 mm Hg or greater on the foot dorsum or at the margin of the ulcer **AND**
   b. Full-thickness ulcer (i.e., stage III or IV), extending through dermis into subcutaneous tissues **AND**
   c. Participation in a wound-management program, which includes sharp debridement, pressure relief (i.e., non-weight-bearing), and infection control

2. Pressure ulcers extending into the subcutaneous tissue
   Appropriate candidates for becaplermin gel for the treatment of pressure ulcers should meet **ALL** of the following criteria:
   a. Full-thickness ulcer (i.e., stage III or IV), extending through dermis into subcutaneous tissues **AND**
   b. Ulcer in an anatomic location that can be offloaded for the duration of treatment **AND**
   c. Albumin concentration >2.5 dL **AND**
   d. Total lymphocyte count >1000/uL **AND**
   e. Normal values of vitamins A and C

B. Other applications of recombinant platelet-derived growth factor (i.e., becaplermin) are considered **experimental / investigational**, including, but not limited to:
   1. Ischemic ulcers
   2. Venous stasis ulcers, and
   3. Ulcers not extending through the dermis into the subcutaneous tissue

C. Use of platelet-rich plasma (i.e., autologous blood-derived preparations) is considered **experimental / investigational** for the treatment of acute or chronic wounds, including surgical wounds and nonhealing ulcers.

POLICY GUIDELINES

A. Becaplermin
   1. Individuals are typically treated once daily for up to 20 weeks or until completely healed. Application of the gel may be performed by the individual in the home.
   2. Becaplermin is available in 2-, 7.5-, and 15-g tubes and is applied in a thin continuous layer, about 1/16 of an inch thick (i.e., 1.6 mm or the thickness of a dime). The amount of the gel used will depend on the size of the ulcer, measured in square centimeters. However, an average-sized ulcer, measuring 3 cm^2, treated for an average length of time of 85 days, will require a little more than one 15-g tube. If the ulcer is treated for the maximum length of time of 140 days, 1.75 of the 15-g tubes would be required.

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.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through November 22, 2024.

The platelet-rich plasma (PRP) portion of this evidence review on the platelet-derived wound healing formulae was originally based on a 1992 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 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.[4,5,6,7,8,]

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 function¾including 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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

RECOMBINANT PLATELET-DERIVED GROWTH FACTOR FOR DIABETIC LOWER-EXTREMITY ULCERS

Clinical Context and Therapy Purpose

The purpose of recombinant platelet-derived growth factor (PDGF) is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with diabetic lower-extremity ulcers.

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

Populations

The relevant population of interest is individuals with diabetic lower-extremity ulcers.

Interventions

The therapy being considered is recombinant PDGF.

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 (QOL), and treatment-related morbidity.

Follow-up at 20 weeks is of interest for recombinant PDGF to monitor relevant outcomes.

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

The portion of this evidence review on the use of recombinant PDGF (becaplermin gel) was informed by a 1999 TEC Assessment, which found that the evidence supported the conclusion that becaplermin gel, in conjunction with good wound care, improves the health outcomes of patients with chronic neuropathic diabetic ulcers that met the patient selection criteria defined therein.[9,] Becaplermin gel plus good wound care resulted in a 43% complete wound closure rate, compared with 28% for patients treated with good wound care alone. Becaplermin gel also appeared to reduce the average time to complete wound closure.

Systematic Reviews

A 2014 systematic review identified 6 RCTs (N=992 patients) that compared recombinant PDGFs with placebo or standard care.[10,] There was a combined odds ratio of 1.53 (95% confidence interval [CI], 1.14 to 2.04; p=.004) favoring recombinant PDGF for complete healing rate.

Sridharan et al (2018) conducted a systematic review and meta-analysis of RCTs on topical growth factors compared with standard of care in patients with diabetic foot ulcers (DFUs). The

primary outcome of concern was complete healing and the second outcome of concern was the existence of adverse events. Rankogram was generated based on the surface under the cumulative ranking curve. In total, 26 studies with 2088 participants and 1018 adverse events were included. The pooled odds ratio estimates for recombinant human epidermal growth factor (rhEGF), autologous-PRP, and recombinant human platelet-derived growth factor were 5.7 [95% CI, 3. 34 to 10.37], 2.65 [95% CI, 1.65 to 4.54], and 1.97 [95% CI, 1.54 to 2.55] respectively. The surface under the cumulative ranking curve for rhEGF was 0.95; sensitivity analysis did not reveal significant changes from pooled estimates and rankogram. With regard to adverse events, no differences were observed for the overall risk of adverse events between the growth factors; however, the growth factors were observed to lower the risk of lower limb amputations compared to standard of care. The results lead the authors to conclude that rhEGF, recombinant human platelet-derived growth factor, and autologous PRP significantly improved the healing rate when used as adjuvants to the standard of care. Compared to other growth factors, rhEGF performed better. The limitations of this study include the following: the strength of most of the outcomes assessed was low, and the findings may not be applicable for DFU with infection or osteomyelitis.[11,]

Table 1. Systematic Reviews of Trials Assessing Recombinant Platelet-Derived Growth Factor for Diabetic Lower-Extremity Ulcers

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Sridharan et al (2018)	Dec 2016	RCTs	Patients with diabetic lower-extremity ulcers treated with platelet-derived growth factor	2088	RCTs	Pooled analysis estimated rhEGF, PRP, rhPDGF

PRP: autologous platelet-rich plasma; RCT: Randomized Controlled Trial; rhEGF: recombinant epidermal growth factor; rhPDGF: recombinant human platelet-derived growth factor

Retrospective Studies

A 2005 industry-sponsored study assessed the effectiveness of recombinant PDGF for diabetic neuropathic foot ulcers in actual clinical practice.[12,] Among a cohort of 24,898 patients in wound care centers, those subjects whose wounds did not heal over an 8-week observation period were eligible for the study and were retrospectively assessed over 20 weeks or until they healed. Any subject with an open wound who was lost to follow-up was considered unhealed. Of the nearly 25000 patients treated for foot ulcers, 2394 (9.6%) received recombinant PDGF. A propensity score method with covariates to statistically model treatment selection was used to adjust for selection bias; results were stratified by 5 propensity score groups. Overall, the rate of healing was 26.5% in the control group and 33.5% in patients treated with recombinant PDGF. The relative risk (RR), controlling for the propensity to receive PDGF, was 1.32 (95% CI, 1.22 to 1.38) for healing and 0.65 (95% CI, 0.54 to 0.78) for amputation (6.4% in controls vs. 4.9% in the PDGF group). The analysis also indicated those who received PDGF were more likely to be younger, male, and have older wounds-factors not known to affect wound healing. These results support the clinical utility of recombinant PDGF for treatment of diabetic neuropathic foot ulcers in actual clinical practice.

Section Summary: Recombinant Platelet-Derived Growth Factor for Diabetic Lower-Extremity Ulcers
Published evidence includes an industry-sponsored study and 2 systematic reviews that showed an improvement in treatment over control for tested outcome measures.

RECOMBINANT PLATELET-DERIVED GROWTH FACTOR FOR PRESSURE ULCERS

Clinical Context and Therapy Purpose
The purpose of recombinant PDGF is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with pressure ulcers.

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

Populations
The relevant population of interest is individuals with pressure ulcers.

Interventions
The therapy being considered is recombinant PDGF.

Comparators
Comparators of interest include standard wound care.

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 pressure ulcer 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

Randomized Controlled Trials
Rees et al (1999) conducted an RCT focusing on the use of becaplermin gel as a treatment for pressure ulcers.[13,] Patient selection criteria included full-thickness ulcers and an anatomic location where pressure could be offloaded during treatment. This latter patient selection criterion might have limited the number of patients with pressure ulcers who would have been considered candidates for becaplermin therapy. Patients were randomized to 1 of 4 parallel treatment groups and received either a placebo or 1 of 3 dosages of becaplermin. All patients received a

standardized program of good wound care. In the 2 groups treated with the once-daily dosage (becaplermin 0.01% or 0.03%), the incidence of complete healing was significantly improved compared with the placebo group. There was no difference in outcome between the 0.01% and 0.03% groups, suggesting there is no clinical benefit in increasing the potency above 0.01%. A third group received becaplermin 0.01% twice daily. That group did not report improved outcomes compared with placebo, a finding that is unexplained.

Section Summary: Recombinant Platelet-Derived Growth Factor for Pressure Ulcers
Published evidence includes a multicenter, double-blind RCT that showed an improvement in treatment over control for tested outcome measures.

RECOMBINANT PLATELET-DERIVED GROWTH FACTOR FOR VENOUS STASIS LEG ULCERS

Clinical Context and Therapy Purpose
The purpose of recombinant PDGF is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with venous stasis leg ulcers.

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

Populations
The relevant population of interest is individuals with venous stasis leg ulcers.

Interventions
The therapy being considered is recombinant PDGF.

Comparators
Comparators of interest include standard wound care.

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 venous stasis leg ulcer 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

Randomized Controlled Trials

Senet et al (2011) in France, published a multicenter, double-blind RCT of becaplermin gel for venous leg ulcers.[14,] There was no significant difference between the becaplermin (n=28) and control hydrogel (n=31) groups for any of the outcome measures, which included complete closure rates after 8 and 12 weeks, changed ulcer area, and changed ulcer-related pain and QOL.

Section Summary: Recombinant Platelet-Derived Growth Factor for Venous Stasis Leg Ulcers

Published evidence includes a multicenter, double-blind RCT that showed no difference between treatment and control for tested outcome measures.

Recombinant Platelet-Derived Growth Factor for Acute Surgical or Traumatic Wounds

Clinical Context and Therapy Purpose

The purpose of recombinant PDGF 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 population of interest is individuals with acute surgical or traumatic wounds.

Interventions

The therapy being considered is recombinant PDGFs.

Comparators

Comparators of interest include standard wound care.

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 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

Topical recombinant PDGF has also been investigated for repair of work-related fingertip injuries. A 2005 prospective controlled trial alternately assigned 50 patients (fingertip wound area ≥1.5 cm, with or without phalangeal exposure) to daily treatment with PDGF (n=25) or surgical reconstruction (n=25).[15,] Statistical analysis showed that baseline characteristics of the 2 groups were similar for patient age, wound area (2.2 to 2.4 cm), and distribution of fingertip injuries across the digits. Assessment by an independent physician showed that, compared with the surgical intervention, treatment with recombinant PDGF resulted in faster return to work (10 days vs. 38 days) and wound healing (25 days vs. 35 days), less functional impairment (10% vs. 22%), and less need for physical therapy (20% vs. 56%), respectively. Fingertips treated with PDGF were also reported to have satisfactory aesthetic results, while surgically treated fingertips were shorter and often unsightly. These results, if confirmed in additional RCTs, could lead to improvement in health outcomes for patients with fingertip injuries. However, this trial was limited by its small sample size, method of randomization, and potential for investigator bias (although examining physicians were blinded to treatment allocation, actual treatment might have been obvious).

Adverse Events

Growth factors cause cells to divide more rapidly. For this reason, the manufacturer of Regranex continued to monitor studies that started before its approval (in December 1997) for any evidence of adverse events, such as increased numbers of cancers. In a long-term safety study completed in 2001, more deaths from cancer occurred among patients who used Regranex than in those who did not. A subsequent study was performed using a health insurance database that covered the period from January 1998 through June 2003. This trial identified 2 groups of patients with similar diagnoses, drug use, and use of health services: 1 group used Regranex, and the other group did not. Results showed there were more deaths from cancer among patients who were given 3 or more prescriptions for Regranex than deaths for those not treated with Regranex. No single type of cancer was identified; deaths from all types of cancer were observed. In 2008, the U.S. Food and Drug Administration concluded that the increased risk of death from cancer in patients who used 3 or more tubes of Regranex was 5 times higher compared with those who did not use Regranex, prompting the manufacturer to add a black box warning to the labeling for Regranex. The risk of new cancers among Regranex users was not increased compared with nonusers, although the duration of follow-up of patients in this study was not long enough to detect new cancers.

Section Summary: Recombinant Platelet-Derived Growth Factor for Acute Surgical or Traumatic Wounds

Published evidence includes nonrandomized controlled trials reporting satisfactory aesthetic results. Larger RCTs are required to confirm and expound on these results.

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 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, QOL, 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.[16,17,18,19,20,21,22,23,]These reviews are heterogenous in whether they pooled data from studies reflecting a variety of wound types[16,17,24,18,25,]or focused on specific wound types, primarily diabetic foot ulcers.[19,20,21,22,] Results from the reviews that pooled data from a variety of wound types[16,17,24,18,25,] 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. [21,22,23,]
Four recent systematic reviews have evaluated studies of PRP for individuals with diabetic foot ulcers. [21,22,23,26,] Table 2 provides a crosswalk of the studies included in the systematic reviews.

Table 2. Comparison of Trials of Platelet-Rich Plasma in Individuals with Diabetic Foot Ulcers Included in Systematic Reviews

Primary Study (Year)	Li 2019[21,]	Qu 2021[22,]	Deng 2023[23,]	Platini 2024[26,]
Ahmed 2017[27,]	●	●	●	●
Alamdari 2021[28,]			●	●
Chen 2008[a29,]	●			
Driver 2006[30,]	●	●	●	
Elsaid 2020[31,]		●	●	
Friese 2007 (conference proceeding)[32,]	●		●	
Game 2018[33,]		●		
Gude 2019[34,]		●		●
Goda 2018[35,]				
Habeeb 2020[36,]			●	
Helmy 2021[37,]			●	
Hossam 2021[38,]			●	
Jeong 2010[39,]			●	
Kakagia 2007[40,]	●	●	●	
Karimi 2016[41,]		●	●	
Li 2012[a 42,]			●	
Li 2015[43,]	●	●	●	●
Liu 2016[a44,]	●		●	
Liao 2020[45,]			●	
Meamar 2021[46,]			●	
Ma 2014[a47,]	●			
Milek 2017[48,]		●		
Qi 2014[a49,]	●			
Rainys 2019[50,]			●	●
Saad Setta 2011[51,]	●	●	●	
Saldalamacchia 2004[52,]	●	●	●	
Serra 2013[53,]	●	●		●
Singh 2018[54,]		●	●	

Primary Study (Year)	Li 2019[21,]	Qu 2021[22,]	Deng 2023[23,]	Platini 2024[26,]
Steed 1992[55,]			●	
Steed 1996[56,]			●	
Tofign 2022[57,]			●	
Xie 2020[58,]		●		●
Yang 2017[59,]		●		
Zhang 2016[a60,]	●			
Zhou 2015[a61,]	●			
Zhu 2012[a62,]	●			

[a] In Chinese

Tables 3 and 4 summarize the characteristics and results of the 3 systematic reviews that have evaluated studies of PRP for individuals with diabetic foot ulcers.][21,22,23,]

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[21,] 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 [OR]=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.[63,] 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.[23,] 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.

Platini et al. (2024) conducted a systematic review and meta-analysis to assess the efficacy and safety of autologous platelet-rich plasma gel for managing diabetic foot ulcers in older adults (N=598) across 8 RCTs.[26,] Compared with standard care, autologous PRP gel significantly improved wound healing rates (Relative Risk [RR]=1.32; 95% CI: 1.22 to 1.57; p<.0001; I^2=23%) and reduced the time to complete healing (MD= -16.97 days; 95% CI: -32.64 to -1.29; p<.0001; I^2=93%). PRP also shortened hospital stays (MD=-20.11 days; 95% CI: -38.02 to -2.20; p=.03) and decreased the amputation rate (RR=0.36; 95% CI: 0.16 to 0.84; p=.02; I^2=0%) when compared to conventional treatments. The authors also noted its infection prevention efficacy during early treatment was significant at one week (RR=0.56; 95% CI: 0.34 to 0.91; p=.02) and two weeks (p=.01), but when assessed from week 4 to 12, no significant differences were observed. No improvements in the reduction of wound surface area were noted in the included studies. Heterogeneity across outcomes varied but was particularly high in healing duration outcomes. Funnel plot analyses revealed minimal publication bias. Limitations included non-standardized dosages of PRP, high heterogeneity for some pooled estimates, and insufficient reporting of some clinical outcomes.

Table 3. Characteristics of Key Systematic Reviews with Meta-Analyses in Individuals with Diabetic Foot Ulcers

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Li (2019)[21,]	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 (2021)[22,]	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)
Deng (2023)[23,]	Inception-2023	22	Adults with diabetic foot ulcers	N=1559	RCTs	NR
Platini (2024)[26,]	Inception-2024	8	Older adults with diabetic foot ulcers	N=598	RCTs	NR

NR: not reported; RCT: randomized controlled trial; wk: week(s); y: year(s).

Table 4. 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
Li (2019)[21,]							
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 (2021)[22,]							
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							
Deng (2023)[23,]							
RR	1.42				.096		
MD		-3.13					

Study	Healing Rate	Healing Time	Complete Wound Healing	Risk of Infection	Wound complications	Pain Reduction	Recurrence
95% CI	1.30 to 1.56	-5.86 to -0.39			0.57 to 1.61		
P-value	<.001	<.001			.203		
Platini (2024)[26,]							
RR	1.32	-16.97		0.56			
MD							
95% CI	1.22 to 1.57	-32.64 to -1.29		0.34 to 0.91			
P-value	<.0001	<.0001		.02			

[a] Visual Analog Scale
CI: confidence interval; MD: mean difference; OR: odds ratio; RR: risk ratio; WMD: weighted mean difference; 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 5 and 6 below.

One RCT of PRP dressing with total-contact casting compared to standard saline dressing for diabetic foot ulcers (Gupta et al [2021])[64,] 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.[38,]

Table 5. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Intervention	Control
Gupta et al (2021)[64,]	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)[38,]	Egypt	1	2018	Individuals with type 1 or 2 diabetes with non-ischemic revascularized chronic diabetic foot ulcers of	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)

Study	Countries	Sites	Dates	Participants	Intervention	Control
				more than 6 months duration with no clinical signs of infection, Wagner grade 1 or 2, and ASA physical status class 2		

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

Table 6. Summary of Key RCT Results

Study	Complete Healing	Percentage of Healed Surface Area[a]	Complete Healing Time	Pain	Quality of Life	Infection	Recurrence
Gupta et al (2021)[64,]	NR	6 weeks: 85.98% vs 81.72%; p=NR	NR	NR	NR	NR	NR
Hossam et al (2022)[38,]	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	NR

NR: not reported; PRP: platelet-rich plasma; RCT: randomized controlled trial.
[a] Percentage of healed surface area in treatment vs. control groups.
[b] Proportion of patients with complete healing in treatment (n=38) vs. control groups (n=28) at 6 and 9 weeks, respectively.

Study relevance, design, and conduct limitations are summarized below in Tables 9 and 10.

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.[65,]

For individuals with lower extremity venous ulcers, the evidence included 8 RCTs and 3 observational studies (total 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 (weighted mean difference [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.[66,] 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)[22,] 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.[67,] 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.

Hu et al. (2024) conducted a systematic review and meta-analysis of 16 RCTs (N=699) to evaluate the efficacy and safety of PRP for venous ulcer treatment.[68,] PRP demonstrated a significant improvement in complete ulcer healing (Odds Ratio [OR]=5.06; 95% CI: 2.35 to 10.89; p<.01; I^2=58%) and a 47% greater reduction in ulcer size compared with standard therapy (MD=47%; 95% CI: 32% to 62%; p<.05; I^2=75%). PRP also significantly shortened healing time by an average of 3.25 months (MD=-3.25; 95% CI: -4.06 to -2.43; p<.05; I^2=49%). Recurrence rates were markedly reduced (OR=0.16; 95% CI: 0.05 to 0.50; I^2=18%), with no significant differences in infection (OR=0.89; 95% CI: 0.38 to 2.07; I^2=0%), VAS Pain scores (MD=1.19; 95% CI: -0.67 to 3.04; I^2=52%), or irritative dermatitis rates (OR=0.38; 95% CI: 0.08 to 1.90; I^2=0%). Funnel plot analysis and Egger's test (p=.0079) suggested the potential for publication bias. Limitations included heterogeneity in PRP preparation, inconsistency in ulcer measurement methods, the potential for publicatin bias, moderate to high heterogeneity for some outcome estimates, and limited sample sizes.

Randomized Controlled Trials

Two RCTs of PRP for chronic wounds (Saha et al [2020])[69,70,] were identified as published subsequent to the AHRQ review (2020).[22,] Key characteristics and results of selected RCTs are reported in Tables 7 and 8 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.[70,] 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 7. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Intervention	Control
Saha et al (2020)[69,]	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)[70,]	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.

Table8. Summary of Key RCT Results

Study	Complete Healing	Healing Time	Pain	Quality of Life	Infection	Recurrence
Saha et al (2020)[69,]	22 (39.29%) vs 11 (21.15%); p NR	NR	NR	NR	0 vs 0; p=.773	NR
Shehab et al (2023)[70,]	9 (45%) vs NR	NR	BL: 6.5 vs 6.4; p=.43 3 mos: 1	NR	NR	NR

Study	Complete Healing	Healing Time	Pain	Quality of Life	Infection	Recurrence
			vs 4.5; p<.0001 6 mos: 0.5 vs 2.2; p<.0001			

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

Tables 9 and 10 summarize the relevance and design and conduct limitations of selected RCTs.

Table 9. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Saha et al (2020)[69,]	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
Gupta et al (2021)[64,]	4. Single site in India	4. Short duration of treatment; 6 weeks	3. Total-contact casting not used in control group	1. Complete wound healing, recurrence, quality of life not addressed 5. Clinical significance of difference in wound surface area not prespecified	1. 6 week study period insufficient to assess long-term efficacy
Hossam et al (2022)[38,]	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

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Shehab et al (2023)[70,]	4. Single site in Egypt	1. Frequency and type of PRP treatment (injection and/or gel) not standardized 4. Short duration of treatment; 6 weeks	1. Placebo treatment not clearly defined	1. Recurrence, quality of life not addressed	

PRP: platelet-rich plasma.
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 10. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Saha et al (2020)[69,]						
Gupta et al (2021)[64,]		1-3. Blinding not described			1. Power calculations not reported	3. Confidence intervals and/or p values not reported
Hossam et al (2022)[38,]		1-3. Blinding not described		1. High loss to follow-up or missing data; reasons for and extent of missingness unclear at all timepoints	1. Power calculations not reported	3. Confidence intervals not reported
Shehab et al (2023)[70,]					1. Power calculations not reported	4. Complete healing rate not reported

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
						for the control group

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 meta-analyses of individuals with lower extremity diabetic ulcers, PRP demonstrated an improvement over the control groups in complete wound closure, recurrence rate, 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 population of interest is 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, QOL, 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 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

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.[71,] 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 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 to 2012, 422 consecutive patients) or without (2007 to 2009, 671 consecutive patients) application of PRP.[72,] The 2 groups were comparable at baseline. At the end of cardiac surgery, PRP gel was applied to the sternum before the closure of subcutaneous tissue. Rates of both deep and superficial wound infections 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.

Zhu et al (2023) published a meta-analysis of the effect of PRP on sternal wound healing.[73,] 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

A 2008 double-blind RCT assessed the efficacy of PRP following tonsillectomy in 70 children (age range, 4 to 15 years).[74,] 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.

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.[75,] 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=.024) and better velopharyngeal closure on endoscopy (p=.016).

Dinaki et al. (2024) conducted an RCT evaluating submucosal PRP injection on wound healing after endoscopic sinus surgery in 30 patients with chronic rhinosinusitis.[76,] Patients were randomized 1:1 to PRP (2.5 ml on each side) or control (no additional treatment with no placebo). PRP significantly reduced moderate crusting on endoscopy at 1 week (36.6% vs. 80%; p<.00001) through 12 weeks post-surgery (0% vs. 16.6%; p=.021). Bleeding was lower in the PRP group during the first 2 weeks (minimal bleeding: 33.3% vs. 66.6%; p=.004 at 1 week; 10% vs. 50%, p=.0003 at 2 weeks) but not significantly different between groups thereafter. Granulation tissue formation was reduced at 8 and 12 weeks in the PRP group (mild granulation: 30% vs. 60%; p=.021 at 8 weeks; 26.6% vs. 46.6%; p=.005 at 12 weeks). VAS scores improved significantly in the PRP group across all time points, with a median score of 0 (interquartile range [IQR]: 0 to 1) at 12 weeks compared to 2 (IQR: 1 to 2) in controls (p=.001). No significant differences were observed for adhesion or infection rates (p>.05). Limitations included the small sample size with an absence of power calculations, lack of double blinding, and absence of follow-up beyond 3 months.

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.[77,]

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 interventions. 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.[28,]

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.[78,] 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.[79,] Indications for skin grafts were primarily hard-to-heal lower leg wounds. PRP was applied to 1 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 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).[80,] 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 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.[81,] 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 RCT 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 LPRP group received the intervention (n=15) and the control group received a placebo application (n=12). A concentration of 1.0×10^7 platelets/cm^2 (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 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. [82,]

Huang et al (2021) published a meta-analysis of 8 RCTs representing 539 patients with burn wounds.[83,] The healing rate of burn wounds was improved with PRP (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) 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.[84,] 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.

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.[85,] 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 on December 1, 2020 found that this 2015 guideline is now listed as 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)[86,] and venous ulcers (2015)[87,]:

- Pressure ulcer: "Growth factors are not indicated for PU [pressure ulcers] at this time." (level C evidence - no randomized controlled trials (RCTs) available comparing growth factors with A-level dressings)[86,]
- Venous ulcer: "Platelet-derived growth factor has shown no significant effects on VU [venous ulcer healing or recurrence]." (level A evidence)[87,]

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.[88,] 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 9. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05850611	The Effect of Combination Therapy of Oral Methylene Blue and Platelet-rich Plasma-fibrin Glue in Patients With Non-healing Diabetic Foot Ulcer: a Pilot Study	20	Sept 2024
NCT05996614	Evaluation of Platelet Rich Plasma in Skin Graft Take for Patients With Post Burn Raw Areas	40	Feb 2025
NCT06281483	Efficacy of Platelet-rich Plasma Versus Platelet-rich Fibrin Versus Conventional Treatment in Chronic Non-healing Skin Ulcers: A Comparative Study	36	Jan 2026
NCT06298110	The Effect of PRP on Wound Healing in High Risk Patients Undergoing Abdominal Hysterectomy	80	Sep 2024
NCT05979584	Platelet Rich Plasma VS Platelet Fibrin Plasma in Treatment of Diabetes Foot Ulcer: a Randomized Controlled Trial	56	Aug 2025
Unpublished			
NCT02071979[a]	Registry Trial of the Effectiveness of Platelet Rich Plasma for Chronic Non-Healing Wounds (CMS)	1500	Jan 2018 (terminated; updated 01/18)
NCT02312596[a]	A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Non-Healing Diabetic Foot Ulcers	200	Dec 2021 (unknown)
NCT02312570[a]	A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers	200	Dec 2021 (unknown)
NCT02307448[a]	Effectiveness of Autologous Platelet Rich Plasma in the Treatment of Chronic Non-Healing Wounds	80	Dec 2022 (terminated)
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)

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

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
86999	Unlisted transfusion medicine procedure
0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed
G0460	Autologous platelet rich plasma for non-diabetic chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment
G0465	Autologous platelet rich plasma (prp) for diabetic chronic wounds/ulcers, using an fda-cleared device (includes administration, dressings, phlebotomy, centrifugation, and all other preparatory procedures, per treatment)
P9020	Platelet rich plasma, each unit
S0157	Becaplermin gel 0.01%, 0.5 gm
S9055	Procuren or other growth factor preparation to promote wound healing

REVISIONS	
06-05-2012	Policy added to the bcbsks.com web site. A stand alone policy was developed based on policy language previously contained in the Wound Care: Skin Substitutes and Growth Factors medical policy.
	In Policy section: ▪ The new stand-alone policy adds the following: "C. Use of autologous blood-derived preparations (i.e., platelet-rich plasma) is considered experimental / investigational. This includes, but is not limited to, use in the following situations: 1. Treatment of acute or chronic wounds including nonhealing ulcers 2. Adjunctive use in surgical procedures 3. Primary use (injection) for other conditions such as epicondylitis (i.e., tennis elbow), plantar fasciitis, or Dupuytren's contracture"
02-05-2014	Description section updated
	Policy section reformatted – no policy statement changes made.
	Rationale section updated
	In Coding section: ▪ HCPCS Code added: G0460 ▪ Coding information bullets updated ▪ ICD-10 Diagnoses Codes added

REVISIONS	
	References updated
10-29-2015	Description section updated
	In Policy section: ▪ In Item C added "surgical sounds and" and removed "This includes, but is not limited to, use in the following situations:", "Adjunctive use in surgical procedures", and "Primary use (injection) for other condition such as epicondylitis(i.e. tennis elbow), plantar fasciitis, or Dupuytren's contracture" to read, "Use of autologous blood-derived preparations (i.e., platelet-rich plasma) is considered experimental / investigational for the treatment of acute or chronic wounds, including surgical wounds and nonhealing ulcers."
	Rationale section updated
	In Coding section: ▪ Updated coding notations.
	References updated
04-25-2016	Description section updated
	Rationale section updated
	In Coding section: ▪ Coding notations updated
	References updated
03-01-2017	Title changed to "Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non–Orthopedic Conditions" from "Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Non–Orthopedic Conditions"
	Description section updated
	In Policy section: ▪ In Item A 2 d added "/uL" to correctly read "Total lymphocyte count >1000/uL" – no change in policy intent.
	Rationale section updated
	In Coding section: ▪ Removed ICD-10 Codes: E10.610, E10.618, E10.69, E11.610, E11.618, E11.69, I70.331, I70.332, I70.333, I70.334, I70.335, I70.338, I70.341, I70.342, I70.343, I70.344, I70.345, I70.348, I70.35, I70.731, I70.732, I70.733, I70.734, I70.735, I70.738, I70.741, I70.742, I70.743, I70.744, I70.745, I70.748, I70.75 ▪ Added ICD-10 Codes: L97.121, L97.122, L97.123, L97.124, L97.211, L97.212, L97.213, L97.214, L97.221, L97.222, L97.223, L97.224, L97.311, L97.312, L97.313, L97.314, L97.321, L97.322, L97.323, L97.324, L97.411, L97.412, L97.413, L97.414, L97.421, L97.422, L97.423, L97.424, L97.511, L97.512, L97.513, L97.514, L97.521, L97.522, L97.523, L97.524, L97.811, L97.812, L97.813, L97.814, L97.821, L97.822, L97.823, L97.824, L98.491, L98.492, L98.493, L98.494
	References updated
03-01-2018	Description section updated
	In Policy section: ▪ In Item B added "recombinant platelet-derived growth factor" to read "Other applications of recombinant platelet-derived growth factor (i.e., becaplermin) are considered experimental / investigational, including, but not limited to:" ▪ Updated Policy Guidelines
	Rationale section updated
	References updated
04-10-2019	Description section updated
	Rationale section updated
	References updated
03-23-2021	Description section updated

REVISIONS	
	Rationale section updated
	References updated
01-01-2022	In Coding section: Revised nomenclature G0460 Autologous platelet rich plasma (prp) for diabetic chronic wounds/ulcers, using an fda-cleared device (includes administration, dressings, phlebotomy, centrifugation, and all other preparatory procedures, per treatment) effective 01-01-22
03-08-2022	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Added CPT code G0465 ▪ Changed ICD-10 Diagnoses to code ranges ▪ Removed ICD-10 codes E10.41, E10.42, E10.43, E10.44, E10.49, E10.621, E10.622, E10.628, E11.44, E11.621, E11.622, E11.628, I70.231, I70.232, I70.233, I70.234, I70.235, I70.238, I70.241, I70.242, I70.243, I70.244, I70.245, I70.248, I70.25, I70.431, I70.432, I70.433, I70.434, I70.435, I70.438, I70.441, I70.442, I70.443, I70.444, I70.445, I70.448, I70.45, I70.531, I70.532, I70.533, I70.534, I70.535, I70.538, I70.541, I70.542, I70.543, I70.544, I70.545, I70.548, I70.55, I70.631, I70.632, I70.633, I70.634, I70.635, I70.638, I70.641, I70.642, I70.643, I70.644, I70.645, I70.648, I70.65 ▪ Removed Coding bullets o There is a CPT category III code for injections of platelet-rich plasma: 0232T. o 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 and 86965. o Code 0232T includes the harvesting and preparation of the platelet-rich plasma. o For situations other than injection (when 0232T would be reported), no specific CPT codes describe the preparation of autologous blood-derived products but CPT code 86999 can be used. It has been reported that providers have used CPT code 20926 (tissue graft, other) to describe the overall procedure. It is questionable whether platelet-rich plasma is appropriately considered a tissue graft. o 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. o There is also a HCPCS code for this treatment: G0460.
	Updated References Section
02-28-2023	Updated Description Section
	Updated Rationale Section
	Updated References Section
03-12-2024	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Removed ICD-10 Codes
	Updated References Section
02-25-2025	Updated Description Section
	Updated Rationale Section
	Updated Reference Section

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