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

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider recombinant platelet-derived growth factor (PDGF [i.e., becaplermin]) when used as an adjunct to standard wound management to be **eligible for coverage** for the following indications:

- Neuropathic diabetic ulcers extending into the subcutaneous tissue
- Pressure ulcers extending into the subcutaneous tissue

Patient Selection Criteria
Becaplermin
Appropriate candidates for becaplermin gel for treatment of neuropathic ulcers should meet ALL of the following criteria:

- 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
- Full-thickness ulcer (i.e., Stage III or IV), extending through dermis into subcutaneous tissues; AND
- Participation in a wound-management program, which includes sharp debridement, pressure relief (i.e., non-weight-bearing), and infection control.

Appropriate candidates for becaplermin gel for the treatment of pressure ulcers should meet ALL of the following criteria:

- Full-thickness ulcer (i.e., Stage III or IV), extending through dermis into subcutaneous tissues; AND
- Ulcer in an anatomic location that can be off-loaded for the duration of treatment; AND
- Albumin concentration > 2.5 dL; AND
- Total lymphocyte count > 1,000; AND
- Normal values of vitamins A and C.

Note: Patients are typically treated once daily for up to 20 weeks or until complete healing. Application of the gel may be performed by the patient in the home.

Note: 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., 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 the15-g tubes would be required.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers other applications of becaplermin including, but not limited to, ischemic ulcers, ulcers related to venous stasis, and ulcers not extending through the dermis into the subcutaneous tissue to be **investigational.***

Based on review of available data, the Company considers use of autologous blood-derived preparations (i.e., platelet-rich plasma [PRP]) for the treatment of acute or chronic wounds including, but not limited to surgical wounds and non-healing ulcers to be **investigational.***

Background/Overview

WOUND HEALING TREATMENT

A variety of growth factors have been found to play a role in wound healing, including PDGFs, 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, 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 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 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.

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) and Hemaseel®‡ are examples of commercially available fibrin sealants. Autologous fibrin sealants can be created from platelet-poor plasma. This policy does not address the use of fibrin sealants.

WOUND CLOSURE OUTCOMES

This review addresses the use of recombinant PDGF products and 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 U.S. Food and Drug Administration (FDA) for industry in developing products for treatment of chronic cutaneous ulcer and burn wounds:

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

FDA or Other Governmental Regulatory Approval

U.S. FDA

A recombinant PDGF product, becaplermin gel (Regranex®‡, Smith & nephew) was approved by the U.S. FDA in 1997. The labeled indication is as follows:

> "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 débridement, 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."
>
> In 2008, the manufacturer added this 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 post-marketing 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.”

Platelet-Rich Plasma
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 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, FDA has not attempted to regulate activated PRP.

Numerous PRP preparation systems have been cleared for marketing by FDA through the 510(k) process. 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.

Centers for Medicare and Medicaid Services (CMS)
In 2012, Medicare revised its national coverage decision on autologous blood-derived products for chronic nonhealing wounds. This replaces noncoverage decisions from 2004 and 2008.

The CMS covers autologous PRP only for patients who have chronic nonhealing diabetic, pressure, and/or venous wounds and when all of the following conditions are met:

- The patient is enrolled in a clinical research study that addresses the following questions using validated and reliable methods of evaluation. Clinical study applications for coverage pursuant to this National Coverage Determination (NCD) must be received by August 2, 2014.
- The clinical research study must meet the requirements specified below to assess the effect of PRP for the treatment of chronic non-healing diabetic, pressure, and/or venous wounds. The clinical study must prospectively address whether Medicare beneficiaries who have chronic non-healing diabetic, pressure, and/or venous wounds who receive well-defined optimal usual care, along with PRP therapy, experience clinically significant health outcomes compared to patients who receive well-defined optimal usual care for chronic non-healing diabetic, pressure, and/or venous wounds as indicated by addressing at least one of the following:
    a. Complete wound healing;
    b. Ability to return to previous function and resumption of normal activities; or
    c. Reduction of wound size or healing trajectory, which results in the patient's ability to return to previous function and resumption of normal activities.

Rationale/Source

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 patients 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 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.

RECOMBINANT PLATELET-DERIVED GROWTH FACTOR

Diabetic Lower-Extremity Ulcers

The portion of this evidence review on the use of recombinant platelet-derived growth factor (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. 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. A 2014 systematic review identified 6 RCTs (total N=992 patients) that compared recombinant PDGFs with placebo or standard care. There was a combined odds ratio of 1.53 (95% confidence interval [CI], 1.14 to 2.04; p=0.004) favoring recombinant PDGF for complete healing rate.
A 2005 industry-sponsored study assessed the effectiveness of recombinant PDGF for diabetic neuropathic foot ulcers in actual clinical practice. 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 25,000 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 that 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: Diabetic Lower-Extremity Ulcers
Results from RCTs have shown improved rates of healing with use of recombinant PDGF for diabetic lower-extremity ulcers. The increase in the rate of healing must be balanced with the potential for increased risk from cancer. Overall the evidence is sufficient that use of recombinant PDGF improves health outcomes.

Pressure Ulcers
Rees et al (1999) conducted an RCT focusing on the use of becaplermin gel as a treatment for pressure ulcers. 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 oncedaily 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 that 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: Pressure Ulcers
Results from RCTs have shown improved rates of healing with use of recombinant PDGF for diabetic pressure ulcers. The increase in the rate of healing must be balanced with the potential for increased risk from cancer. Overall the evidence is sufficient that use of recombinant PDGF improves health outcomes.

Venous Leg Ulcers
In 2011, Senet et al in France published a multicenter, double-blind RCT of becaplermin gel for venous leg ulcers. 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 quality of life.

Section Summary: Venous Leg Ulcers
The evidence is insufficient to determine whether becaplermin gel improves health outcomes when used to treat venous leg ulcers.

Acute Surgical or Traumatic Wounds
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). Statistical analysis showed that baseline characteristics of the 2 groups were similar for patient age, wound area (2.2-2.4 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).

Section Summary: Acute Surgical or Traumatic Wounds
The evidence is insufficient to determine whether becaplermin gel improves health outcomes when used to treat acute or traumatic wounds.

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 that 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. FDA 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.

PLATELET-RICH PLASMA (IE, AUTOLOGOUS BLOOD-DERIVED PREPARATIONS)
The portion of this evidence review on platelet-derived wound healing formulae was informed by a 1992 TEC Assessment that primarily focused on the Procuren process. This preparation method is no longer commercially available. Currently, a large number of devices are available for the preparation of PRP or PRP gel. The amount and mixture of growth factors produced by different cell-separating systems vary, and it is unknown whether platelet activation before injection is necessary.

Mixed Wound Types (Chronic and Surgical)

Systematic Reviews

A number of systematic reviews of the evidence on PRP have been published. A 2012 Cochrane review included 9 RCTs (total N=325 participants) of PRP for treating chronic wounds. This review was restricted to trials comparing PRP with no additional treatment or placebo. Four RCTs included patients with mixed chronic wounds, three included patients with venous leg ulcers, and two included patients with diabetic foot ulcers. Only 1 trial was considered to be at low risk of bias. After a median treatment duration of 12 weeks, there was no significant difference between the PRP and control groups in complete healing of diabetic foot ulcers, venous leg ulcers, or mixed chronic wounds. There was no significant difference in the area epithelialized in 3 RCTs of mixed chronic wounds. In 2 RCTs of mixed chronic wounds, there was a significant difference favoring PRP in the wound area that was healed. Reviewers concluded that there was no current evidence to suggest that autologous PRP would be of value for treating chronic wounds, given the small number of RCTs included, most of which were either at high or unclear risk of bias.

This Cochrane review was updated in 2016; it added a new RCT, for a total of 10 RCTs (total N=442 patients). Conclusions about the quality of the overall body of evidence were similar to the 2012 review. For the outcome of overall wound healing, autologous PRP did not significantly increase healing compared with standard treatment (RR=1.19; 95% CI, 0.95 to 1.50; I^2=27%, low-quality evidence). For wound healing in foot ulcers in people with diabetes, the evidence suggested that autologous PRP might increase healing compared with standard care (RR=1.22; 95% CI, 1.01 to 1.49; I^2=0%, low-quality evidence). It was unclear whether autologous PRP increased wound healing compared with standard care for venous leg ulcers (RR=1.05; 95% CI, 0.29 to 3.88; I^2=0%, low-quality evidence).

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

Chronic Wounds

Since the publication of the 2015 update to the Cochrane review on PRP for wounds, Escamilla Cardenosa et al (2017) reported on an unblinded RCT comparing PRP and saline for venous ulcer treatment. The trial included 61 patients (102 ulcers) who were randomized to the weekly application of a PRP dressing (31 patients, 55 ulcers) or weekly wet-to-dry dressing changes with saline (30 patients, 47 ulcers) over a 24-week period. The average percentage healed area in the PRP group was 67.7% and 11.2% in the control group ($p<0.001$). PRP group members had greater reductions in pain with the intervention.

Section Summary: Chronic Wounds

The evidence for autologous PRP for a variety of chronic wounds includes RCTs, which have been summarized in a systematic review. For chronic wounds, including diabetic ulcers, pressure ulcers, and vascular ulcers, the systematic review of RCTs did not find that PRP was associated with improved outcomes.

Acute Surgical or Traumatic Wounds

Surgical Wounds

Aortic Arch Repair

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

In 2015, Serraino et al reported on a large series with historical controls that assessed the occurrence of deep sternal wound infections in patients who underwent cardiac surgery either with (2010-2012, 422 consecutive patients) or without (2007-2009, 671 consecutive patients) application of PRP. The 2 groups were comparable at baseline. At the end of cardiac surgery, PRP gel was applied on the 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 these results is limited by likely differences in treatments over time. RCTs are needed to evaluate this potential use of PRP.

Otolaryngology

In 2016, El-Anwar et al reported on an RCT that evaluated PRP in 44 children (age range, 12-23 months) undergoing repair of a complete cleft palate. Speech and velopharyngeal valve movement on follow-up were evaluated by 3 judges who “usually assessed every patient blindly,” physical examination, video

nasoendoscopy, and audio recording of audio perceptual assessment. At 6 months, PRP-treated patients had better nasality grade on audio perceptual assessment (p=0.024) and better velopharyngeal closure on endoscopy (p=0.016).

A 2008 double-blind RCT assessed the efficacy of PRP following tonsillectomy in 70 children (age range, 4-15 years). PRP was placed into the tonsil beds of half of the children, where it was directly visible. To compare pain symptoms and recovery, a daily diary was completed by the patient or a family member for 10 days after surgery. A FACES Pain Scale was used for children ages 4 to 7 years, while a numeric pain rating scale was used for children older than 7 years. Diaries from 83% of patients showed no differences in pain, medication doses, activity, and days eating solid foods between the 2conditions.

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

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

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

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

SUMMARY OF EVIDENCE

Recombinant PDGFs

For individuals who have diabetic lower-extremity ulcers or pressure ulcers who receive recombinant PDGF, the evidence includes randomized controlled trials and systematic reviews. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. Results have shown improved rates of healing with use of recombinant PDGF for diabetic neuropathic ulcers and pressure ulcers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have venous stasis leg ulcers or acute surgical or traumatic wounds who receive recombinant PDGF, the evidence includes small randomized controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. The level of evidence does not permit conclusions whether recombinant PDGF is effective in treating other wound types, including chronic venous ulcers or acute traumatic wounds. The evidence is insufficient to determine the effects of the technology on health outcomes.

Platelet-Rich Plasma

For individuals who have chronic wounds or acute surgical or traumatic wounds who receive PRP, the evidence includes 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 the effects of the technology on health outcomes.

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Policy History

Original Effective Date: 06/16/2010
Current Effective Date: 09/19/2018

06/03/2010	Medical Policy Committee approval
06/16/2010	Medical Policy Implementation Committee approval. New policy.
05/05/2011	Medical Policy Committee approval
05/18/2011	Medical Policy Implementation Committee approval. No change to coverage.
05/03/2012	Medical Policy Committee review
05/16/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2013	Coding revised
05/02/2013	Medical Policy Committee review
05/22/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. Removed orthopedic applications of platelet rich plasma from the policy. Title change.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 09/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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

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information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code			
CPT	0232T, 36513			
HCPCS	G0460, P9020, S0157, S9055			
ICD-10 Diagnosis	E11.40-E11.49	E11.610	E11.618	E11.620-E11.628
	E11.630	E11.638	E11.649	E11.65
	E11.69	E13.40-E13.49	E13.610	E13.618
	E13.620-E13.628	E13.630	E13.638	E13.649
	E13.65	E13.69	I70.25	I70.35
	I70.45	I70.55	I70.65	I70.75
	L72.0-L72.9	L89.90-L89.95	L98.411-L98.419	L98.421-L98.429
	L98.491-L98.499			

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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