Protocol

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

(20116)

Medical Benefit		**Effective Date**: 08/01/22	**Next Review Date**: 07/23
Preauthorization	No	**Review Dates**: 09/10, 07/11, 07/12, 05/13, 05/14, 05/15, 07/15, 07/16, 07/17, 07/18, 07/19, 07/20, 07/21, 07/22	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

RELATED PROTOCOLS

Bioengineered Skin and Soft Tissue Substitutes

Electrostimulation and Electromagnetic Therapy for Treating Wounds

Negative Pressure Wound Therapy in the Outpatient Setting

Orthopedic Applications of Platelet-Rich Plasma

Populations	Interventions	Comparators	Outcomes
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.

SUMMARY OF EVIDENCE

PLATELET-RICH PLASMA

For individuals who have chronic wounds who receive PRP, the evidence includes meta-analyses of a number of small controlled trials. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity. In individuals with lower extremity diabetic ulcers, PRP demonstrated an improvement over the control groups in complete wound closure and healing time, but moderate to high risk of bias and imprecision preclude drawing conclusions on other important outcomes such as recurrence, infection, amputation, and quality of life. In individuals with venous ulcers, PRP did not demonstrate an improvement over the control groups in complete wound closure, recurrence, wound infection or quality of life, although imprecision likely precluded identifying differences on these outcomes. In individuals with pressure ulcers, although PRP reduced wound size, other important outcomes such as complete wound closure were not measured. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have acute surgical or traumatic wounds who receive PRP, the evidence includes a systematic review and a number of small controlled trials. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and treatment-related morbidity. Current results of trials using PRP are mixed and the studies are limited in both size and quality. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY

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

POLICY GUIDELINES

Note: This protocol does not address becaplermin.

MEDICARE ADVANTAGE

Autologous PRP for the treatment of chronic non-healing diabetic wounds may be considered **medically necessary** for a duration of 20 weeks, when prepared by devices whose FDA-cleared indications include the management of exuding cutaneous wounds, such as diabetic ulcers.

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 fibrino-

gen, 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

For this protocol, 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

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.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced

procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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