**Protocol**

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

(2016)

(Formerly Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Non-Orthopedic Conditions)

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective Date: 10/01/15</th>
<th>Next Review Date: 07/17</th>
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</thead>
<tbody>
<tr>
<td>Preauthorization</td>
<td>No</td>
<td>Review Dates: 09/10, 07/11, 07/12, 05/13, 05/14, 05/15, 07/15, 07/16</td>
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**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.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Individuals: • With nonhealing wounds</td>
<td>Interventions of interest are: • Platelet-rich plasma</td>
<td>Comparators of interest are: • Standard wound care</td>
<td>Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity</td>
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<tr>
<td>Individuals: • With acute surgical or traumatic wounds</td>
<td>Interventions of interest are: • Platelet-rich plasma</td>
<td>Comparators of interest are: • Standard wound care</td>
<td>Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Quality of life • Treatment-related morbidity</td>
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**Summary of Evidence**

This protocol addresses the use of blood-derived growth factor platelet-rich plasma (PRP) as a treatment of wounds or other miscellaneous non-orthopedic conditions, including but not limited to treatment of diabetic ulcers, pressure ulcers, and ulcers related to venous stasis.

The evidence for PRP in individuals who have nonhealing wounds or acute surgical or traumatic wounds includes a number of small controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. The potential benefit of PRP has received considerable interest due to its appeal as a simple, safe, low-cost, and minimally invasive method of applying growth factors. 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.

**Policy**

Use of autologous blood-derived preparations (i.e., platelet-rich plasma) is considered investigational for the treatment of acute or chronic wounds, including surgical wounds and nonhealing ulcers.
Medicare Advantage
For Medicare Advantage members there may be potential for benefit under coverage with evidence development (CED).

Background
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, osteoblasts), and vascular endothelial growth factors.

Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma (PRP), can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets, releasing various growth factors, and results in the polymerization of fibrin from fibrinogen, creating a platelet gel. The platelet gel can then be applied to wounds or may be used as an adjunct to surgery to promote hemostasis and accelerate healing. In the operating room setting, PRP has been investigated as an adjunct to a variety of periodontal, reconstructive, and orthopedic procedures. For example, bone morphogenetic proteins are a type of 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 be created from platelet-poor plasma. This protocol does not address the use of fibrin sealants.

Regulatory Status
Blood products such as platelet-rich plasma (PRP) are regulated by the Center for Biologics Evaluation and Research (CBER). CBER is responsible for regulating human cells, tissues, and cellular and tissue-based products. The regulation process for these products is described in FDA’s 21 CFR 1271 of the Code of Federal 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.

There are numerous PRP preparation systems on the market today with FDA clearance. For example, Aurix™ System (previously AutoloGel®; Cytomedix) and SafeBlood® (SafeBlood Technologies) are two related but distinct autologous blood-derived preparations that can be prepared at the bedside for immediate application. Both AutoloGel and SafeBlood have been specifically marketed for wound healing. Other devices may be used in the operating room setting, such as Medtronic Electromedics Elmd-500 autotransfusion system, the Plasma Saver device, or the Smart PreP device. The Magellan Autologous Platelet Separator System® (Medtronic) includes a disposable kit designed for use with the Magellan Autologous Platelet Separator portable tabletop centrifuge. BioMet Biologics was cleared for marketing by FDA through the 510(k) process for a gravitational platelet separation system (GPS® II), which uses a disposable separation tube for centrifugation and a dual cannula tip to mix the platelets and thrombin at the surgical site. Filtration or plasmapheresis may also be used to produce platelet-rich concentrates. 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.

Related Protocols
Electrostimulation and Electromagnetic Therapy for Treating Wounds
Negative Pressure Wound Therapy in the Outpatient Setting
Orthopedic Applications of Platelet-Rich Plasma

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