

PLATELET DERIVED GROWTH FACTORS FOR TREATMENT OF WOUNDS

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Related Policies

- [Apheresis](#)
- [Bone or Soft Tissue Healing and Fusion Enhancement Products](#)

Related Pharmacy Resource

- [Becaplermin Gel \(Regranex\)](#)

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General benefits package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes ¹
Precertification with Medical Director Review Required	Yes
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	All

Special Considerations

¹Precertification is required for services covered under the Member's General Benefits package when performed in the office of a participating provider. For Commercial plans, precertification is not required, but is encouraged for out-of-network services performed in the office that are covered under the Member's General Benefits package. If precertification is not obtained, Oxford may review for medical necessity after the service is rendered.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Recombinant-Human Platelet Derived Growth Factors

When used according to U.S. Food and Drug Administration (FDA) approved indications, becaplermin (Regranex[®] Gel) is proven and/or medically necessary for the treatment of lower extremity diabetic neuropathic ulcers.

In June 2008, the U.S. Food and Drug Administration (FDA) announced the addition of a boxed warning to the labeling of becaplermin (Regranex Gel). Please see the U.S. Food and Drug Administration section for more information.

Platelet Rich Plasma

Autologous platelet rich plasma (e.g., Procren[®], AutoloGel[®], or SafeBlood[®]) is unproven and/or not medically necessary for the treatment of wounds.

The better designed studies do not demonstrate that autologous platelet rich plasma such as Procren, AutoloGel or SafeBlood improves health outcomes in patients with wounds. The remaining studies have design flaws that do not allow confidence in analyzing final study results. The clinical utility of autologous platelet rich plasma remains to be determined in larger well-designed controlled clinical trials comparing their use with standard wound care.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

CPT Code	Description
0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed <i>CPT[®] is a registered trademark of the American Medical Association</i>

HCPCS Code	Description
G0460	Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment
S0157	Becaplermin gel 0.01%, 0.5 gm
S9055	Procren or other growth factor preparation to promote wound healing

DESCRIPTION OF SERVICES

Recombinant-Human Platelet-Derived Growth Factors

Platelet-derived growth factors are applied directly to the wound surface to promote growth of skin, soft tissue, and blood vessels. Recombinant DNA technology has been used to produce a recombinant human platelet-derived growth factor (rPDGF, rPDGF-BB, or rhPDGF-BB). Becaplermin (tradename Regranex Gel) is not an autologous product, but is a commercially prepared biotechnology product with recombinant PDGF as the active ingredient. The growth factor is produced in the laboratory by inserting a gene into yeast.

Platelet Rich Plasma

Platelet-rich plasma (also known as platelet-enriched plasma, platelet-rich concentrate, autogenous platelet gel, or platelet releasate) is being evaluated as an enhancement for soft-tissue healing by placing supraphysiologic concentrations of autologous platelets at the site of tissue damage. AutoloGel and SafeBlood are autologous preparations in which blood is drawn from the patient and centrifuged to create platelet-rich plasma that is applied to the wound. Procuren[®] an autologous product that has been used as treatment in the past for chronic wound healing, but it is no longer manufactured or commercially available.

CLINICAL EVIDENCE

Becaplermin

The earlier studies evaluating recombinant PDGF or becaplermin for chronic diabetic ulcers were well-designed with large sample sizes. Results of these studies demonstrate that becaplermin, in conjunction with good wound care, is efficacious in accelerating wound closure of chronic diabetic ulcers (Embil et al., 2000; Ehrlich and Freedman, 2002). Significant increases in the incidence of complete wound closure and decreases in the time to achieve complete wound healing were observed in patients receiving the study medication compared with those receiving placebo.

A total of 922 patients with full-thickness diabetic neuropathic ulcers were entered into 1 of 5 randomized prospective blinded clinical trials comparing treatment of recombinant PDGF with placebo gel. Results showed that patients treated with PDGF had a significant increase in complete healing and decreased time to complete healing compared with patients given placebo (Steed, 2006).

Buchberger et al. (2011) assessed the safety, efficacy and effectiveness of growth factors alone or in combination with other technologies in the treatment of diabetic foot ulcers (DFU). The authors identified 25 studies comparing becaplermin, rhEGF, bFGF and metabolically active skin grafts (Dermagraft and Apligraf) with standard wound care (SWC) alone or extracellular wound matrix. Study duration ranged from 12 to 20 weeks and the study population comprised between 17 and 382 patients. Treatment with becaplermin, rhEGF, Dermagraft and Apligraf resulted in a higher incidence of complete wound closure and shorter time to complete wound healing with statistically significant differences. The authors concluded that add-on therapy with growth factors for treating uncomplicated DFU could be an alternative to SWC alone.

Gilligan et al. (2015) sought to determine the long-term cost effectiveness of becaplermin gel plus good wound care (BGWC) vs. good wound care (GWC) alone in terms of wound healing and risk of amputation in patients with diabetic foot ulcers (DFUs). They conducted a 20-week retrospective study of subjects with DFU from the Curative Health Services database. A total of 24,898 subjects met the criteria for DFU, and were divided into two treatment groups: becaplermin (n=2,394) (i.e., becaplermin good wound care [BGWC]) and no becaplermin (n=22,504) (i.e., good wound care alone [GWC]). GWC included appropriate debridement of necrotic tissue, infection control, and local ulcer care with saline moistened gauze. A four-state Markov model was used to predict costs and outcomes of wound healing and risk of amputation for BGWC vs. GWC alone over 1 year in patients with DFU. Patients treated with BGWC had substantially more closed-wound weeks compared with GWC (16.1 vs. 12.5 weeks, respectively). More patients receiving BGWC had healed wounds at 1 year compared with those receiving GWC (48.1% vs. 38.3%). Risk of amputation was lower in the BGWC cohort (6.8% vs. 9.8%). Expected annual direct costs for DFU were \$21,920 for BGWC and \$24,640 for GWC. The authors concluded that the results of this study indicate that becaplermin gel is an effective adjunct therapy to GWC. DFU patients treated with BGWC had a higher healing rate and lower risk of amputation during the treatment period relative to GWC alone. BGWC was economically dominant over GWC, providing better outcomes at a lower cost in patients with DFU.

Platelet Rich Plasma

Sridharan and Sivarmakrishnan (2017) conducted a meta-analysis to compare the efficacy of various growth factors used topically in the management of diabetic foot ulcer (DFU). Randomized controlled trials were included if they provided data on the outcome measures, number of patients achieving complete healing (primary outcome) or adverse events (secondary outcomes). A total of 26 studies with 2088 participants and 1018 events were included. Ten eligible studies were obtained evaluating recombinant human platelet-derived growth factor (rhPDGF), six

assessed recombinant human epidermal growth factor (rhEGF), five compared autologous platelet rich plasma (PRP) and three evaluated recombinant human basic fibroblast growth factor. The growth factors were observed to lower the risk of wound infection, cellulitis, peripheral edema and lower limb amputation compared to standard of care and enhance wound healing rate. The authors concluded that rhEGF, rhPDGF and autologous PRP significantly improved the healing rate when used as adjuvants to standard of care. The strength of most of the outcomes assessed was low and the findings may not be applicable for DFU with infection or osteomyelitis. The authors observed a high risk of bias in most of the included studies.

A systematic review was performed by Miron et al. (2017) to analyze studies utilizing platelet-rich fibrin (PRF) for soft tissue regeneration, augmentation, and/or wound healing. Thirty one clinical studies were included; a total of 8 reported the effects of PRF in a randomized clinical trial, with 5 additional studies (13 total) reporting appropriate controls. Fifty-eight percent of clinical studies reported positive wound healing events associated with the use of PRF. Twenty-seven of the 31 clinical studies (87%) supported the use of PRF for soft tissue regeneration and wound healing for a variety of procedures in medicine and dentistry. The authors concluded that the results from the systematic review highlight the positive effects of PRF on wound healing after regenerative therapy for the management of various soft tissue defects found in medicine and dentistry.

In a meta-analysis, Martinez-Zapata et al (2016) examined whether autologous platelet-rich plasma (PRP) promotes the healing of chronic wounds. Ten randomized controlled trials (RCTs) that compared autologous PRP with placebo or alternative treatments for any type of chronic wound in adults were included (442 participants,). Four RCTs recruited people with a range of chronic wounds; three RCTs recruited people with venous leg ulcers, and three RCTs considered foot ulcers in people with diabetes. The median length of treatment was 12 weeks. The authors concluded that the results were non-conclusive as to whether autologous PRP improves the healing of chronic wounds generally compared with standard treatment. Autologous PRP may increase the healing of foot ulcers in people with diabetes compared with standard care, but it is unclear if autologous PRP has an effect on other types of chronic wounds. Three studies reported wound complications such as infection or dermatitis, but results showed no difference in the risk of adverse events in people treated with PRP or standard care. These findings are based on low quality evidence due to the small number of studies and patients included, and their poor methodological quality.

A Cochrane Database systematic review was performed by Marti-Carvajal et al. (2015) to assess the benefits and harms of growth factors for foot ulcers in patients with type 1 or type 2 diabetes mellitus. They identified 28 randomized clinical trials involving 2365 participants. The cause of foot ulcer (neurologic, vascular, or combined) was poorly defined in all trials. The trials evaluated 11 different experimental growth factors compared with several different control interventions. The authors found that any growth factor compared with placebo or no growth factor increased the number of participants with complete wound healing (345/657 (52.51%) versus 167/482 (34.64%). Data on quality of life was not reported. Safety data was poorly reported. The authors concluded that they found evidence suggesting that growth factors may increase complete healing of foot ulcers in people with diabetes. However, this conclusion is based on randomized clinical trials with high risk of systematic errors (bias). Half of the trials were sponsored by the pharmaceutical industry that produces these growth factors. Well-designed trials are required to assess the benefits and harms of growth factors in the treatment of diabetic foot ulcers. The studies should report how many of the participants' ulcers healed and how long the healing took; any level of amputation in the foot; quality of life; ulcer-free days following treatment; and harms caused by treatment.

Escamilla Cardenosa et al. (2016) conducted an unblinded randomized control trial to analyze the efficacy and safety of using platelet rich in growth factor (PRGF) as a local treatment for venous ulcers. The study included 58 patients (n=102 ulcers) who were randomly assigned to the study group (application of PRGF) or the control group (wet-to-dry dressing changes with saline) over a 24-week period. The average percentage healed area in the platelet rich plasma (PRP) group was 67.7% (vs 11.2% in the control group). PRP group members had greater reduction in pain. No adverse effects were observed in either of the two treatment groups. The authors concluded that the study results reveal that application of plasma rich in platelets is an effective and safe method to speed up healing and reduce pain in venous ulcers. The small sample size and lack of blinded assessment are factors compromising the quality of the evidence.

Carter et al. (2011) conducted a systematic review and meta-analysis to evaluate the use platelet rich plasma (PRP) for the treatment of cutaneous wounds compared to standard wound care. Twenty-four studies met inclusion criteria. These studies included 3 systematic reviews, 12 randomized controlled trials, 2 prospective cohort studies, 3 prospective comparative studies and 4 retrospective reviews. The results of the meta-analysis suggested that PRP therapy can positively impact wound healing and associated factors such as pain and infection in cutaneous wounds. Limitations of the studies included heterogeneous patient populations, lack of long-term follow-up, and pooling of data on different types of PFG products and regimens. Several of the studies included in the meta-analysis had conflicting results.

Litmathe et al. (2009) performed a prospective, double-blind study in 44 high-risk patients for wound healing complications (e.g., obesity, diabetes, smokers, peripheral vascular disease, heart failure) after cardiac surgery. The study group was treated with autologous platelet gel (APG). The control group underwent conventional wound treatment. The incidence of major and minor wound complications at the thoracotomy, as well as in the area of saphenous vein harvesting, was not pronounced in either of the groups. The authors concluded that despite promising results in other fields of surgery, APG shows no beneficial effect in high-risk patients undergoing cardiac surgery.

Saad Setta et al. (2011) investigated the efficiency of platelet releasate on the healing of chronic diabetic ulcers in comparison with platelet-poor plasma (PPP). This study included 24 patients with chronic diabetic ulcers. They were systematically randomized into two groups: PRP group (n = 12) and PPP group (n = 12). The results showed that healing in PRP group was significantly faster. The authors concluded that PRP enhances healing of chronic diabetic foot ulcers. These findings require confirmation in a larger study.

Lawlor et al. (2011) evaluated whether incision application of platelet-rich plasma (PRP) decreased postoperative wound complications in vascular surgery patients. A prospective, randomized trial randomized 81 incisions in 51 patients who underwent femoral artery exposure for elective revascularization procedures or endovascular abdominal aneurysm repairs. Using the ASEPSIS wound classification system, the researchers found no difference in incidence of wound infection. Wound complications occurred in 9 (23%) of 40 of PRP group and 9 (22%) of 41 of non-PRP. Severe wound complications developed in 5 (13%) PRP and 6 (5%) of non-PRP. In multivariate analysis, there were no predictors for wound infection. According to the researchers, platelet-rich plasma did not decrease the incidence of groin wound complications in these patients.

A prospective, randomized, controlled, blinded multicenter study initially included 72 patients with diabetic foot ulcers who were treated with autologous platelet-rich plasma gel or control (saline gel). Thirty-two patients were excluded from the final protocol because of protocol violations and failure to complete treatment. Significantly more wounds healed in patients treated with platelet-rich plasma gel (13 out of 16 or 81.3%) than patients treated with control gel (8 out of 19 or 42.1%) (Driver, 2006). Study limitations include small sample size, study supported by manufacturer, protocol violations occurring during the study period, and high rate of patient dropouts.

Within a prospective randomized study, Buchwald et al. (2008) evaluated whether intraoperative use of autologous platelet gel on the leg during a coronary artery bypass graft (CABG) could reduce the incidence of postoperative wound healing disturbances. The application group (AG) included 35 patients and was compared to a control group (CG) that also had 35 patients. The platelet gel, as well as the thrombin required to activate the platelets, was prepared from autologous patient blood during the operation. Wound healing was photographically documented after surgery, and the patients were contacted by telephone on day 50 after surgery to obtain information on wound healing status. During the primary clinical stay, no statistically significant differences were recorded in the number of hematomas, postoperative leg swelling, or pain level. Large-area hematomas were less frequent in the application group. In the follow-up 51 days after surgery, 17.6% (6/34) of the patients from the AG and 31.4% (11/35) of the patients from the CG showed leg wound healing disturbances. The investigators concluded that despite optimum application of the autologous platelet gel to the wound, no clinically relevant differences were found between the groups, either during the primary clinic stay or in the follow-up period.

Kazakos et al. (2008) conducted a study to assess the benefits of using autologous platelet-rich plasma (PRP) gel in the treatment of acute limb soft tissue wounds. Fifty-nine patients with acute wounds (open fractures, closed fractures with skin necrosis and friction burns) were randomized into two groups. Group A (32 patients) were treated with conventional dressings and Group B (27 patients) were managed with local application of PRP gel. The rate of wound healing rate was significantly faster in Group B at week 1, 2 and 3. The investigators concluded that PRP gel treatment can be a valuable and effective aid in the management of acute trauma wounds. The value of this study is limited by the small sample size.

Almdahl et al. (2010) evaluated if spraying of wounds after open long saphenous vein harvesting with platelet-rich plasma might reduce the frequency of harvest site infections. A total of 140 patients undergoing first-time coronary artery bypass grafting were randomized into two groups of 70 patients. Both groups had standard surgical leg wound closure and care except topical application of platelet-rich plasma as adjunctive treatment in the active treatment group. End points were wound infection and cosmetic result at 6 weeks. The follow-up was 100% complete. Nine patients (13%) in the treatment group and eight (11%) in the control group experienced harvest site infection. The overall cosmetic result was also similar between the groups, but the top score was borderline and more frequent in the treatment group. The investigators concluded that topical application of autologous platelet-rich plasma on vein harvest wounds did not reduce the rate of surgical site infection.

Villela and Santos (2010) systematically reviewed evidence regarding the use of platelet-rich plasma (PRP) for the topical treatment of chronic leg ulcers. The systematic review of the literature was performed according to the steps recommended by the Cochrane Collaboration with studies published until July 2008. Among 18 selected studies, 7

(39%) of these studies were randomized clinical trials. Five of the seven randomized clinical trials studied ulcers of diabetic etiology. The results of meta-analysis showed that PRP favors the healing process (95% CI: 2.94-20.31). According to the reviewers, the present systematic review and meta-analysis show that there is scientific evidence regarding favorable outcomes of the use of PRP for the treatment of diabetic ulcer. The reviewers stated that the sample size of the studies analyzed was small.

Frykberg et al. (2010) conducted a prospective case series to evaluate how a physiologically relevant concentration of an autologous platelet-rich plasma (PRP) gel affects initial wound healing trajectories of chronic, nonhealing wounds of various etiologies. Using convenience sampling methods, 49 patients with 65 nonhealing wounds (mean duration 47.8 weeks) were prescribed PRP gel. The most common wounds were pressure ulcers (n = 21), venous ulcers (n = 16) and diabetic foot ulcers (n = 14). Mean wound area and volume were 19 cm² and 36.2 cm³, respectively. Following a mean of 2.8 weeks with 3.2 applications, reductions in wound volume (mean 51%, SD 43.1), area (39.5%, SD 41.2), undermining (77.8%, SD 28.9), and sinus tract/tunneling (45.8%, SD 40.2) were observed. For all wound etiologies, 97% of wounds improved. According to the investigators, the results of this study suggest the application of this PRP gel can reverse nonhealing trends in chronic wounds. These findings require confirmation in a statistically robust randomized controlled trial.

Marquez De Aracena Del Cid et al. (2009) evaluated the efficiency of the subconjunctival application of autologous regenerative factor-rich plasma (RFRP) in a study of 35 patients with different degrees of ocular alkali burns. The patients were classified into moderate and relevance groups according to the severity of the burn. A control group underwent conventional topical medical treatment. A further group was added to the severe chemical burn group, which received autohemotherapy. The clinical evolution of the lesions and the period in which the pathology prevented the patient from working were studied; monitoring was carried out until the patient had healed. In the moderate chemical burns, there was a significant reduction in corneal and conjunctival epithelization times, sick leave duration, and healing time when the patients were treated with RFRP in comparison to the control group. With regard to the severe burns, significant reduction in time to corneal scarring in those treated with RFRP in comparison to traditional treatment was reported. RFRP showed, at least as effective and less side effects than the autohemotherapy. The limitation of this study is small sample size.

Spyridakis et al. (2009) evaluated 52 patients with pilonidal sinus disease who underwent open excision and secondary closure of the surgical wound (n = 22) or additional local postoperative infusion of platelet-derived growth factors (n = 30). Duration of total wound healing and time to return to normal activities were evaluated. Wound-healing rates were much greater for the platelet group. Complete healing of the surgical wound required 24 days for the platelet group while the respective time for the control group was more than 30 days. According to the investigators, the study provides evidence that the use of platelet-derived growth factors directly to the surgical wound enhances the healing process resulting in faster recovery of patients surgically treated for pilonidal sinus disease. Study limitations include lack of blinding or randomization.

de Leon et al. (2011) investigated clinical outcomes in chronic nonhealing wounds following the short-term use of a platelet-rich plasma (PRP) gel (AutoloGel System). The study design was a large, observational case series using a multicenter registry database (all wounds included), which compared different populations within the database. Thirty-nine centers contributed to the registry. The target population included 285 chronic wounds (patient n = 200). Wound etiologies included diabetic, pressure, or venous ulcer; dehisced, surgical, or traumatic wound; and wounds of other etiologies. Clinical relevance was determined by analyzing outcomes in wounds that responded to treatment. A positive response occurred in 96.5% of wounds within 2.2 weeks with 2.8 treatments. In 86.3% of wounds, 47.5% area reduction occurred, and 90.5% of wounds had a 63.6% volume reduction. The authors concluded that in chronic wounds recalcitrant to other treatments, utilization of PRP gel can restart the healing process. The lack of a comparison group limits the conclusions that can be reached from this study.

In a diabetic inpatient clinical guideline, the National Institute for Health and Clinical Excellence (NICE) recommends that autologous platelet-rich plasma gel and platelet-derived growth factor (PDGF) should not be offered as treatment for diabetic foot problems unless part of a clinical trial (NICE, 2016).

An interventional clinical trial is in progress to evaluate the safety and efficacy of autologous platelet rich plasma (PRP) injection in combination with topical application of PRP gel in treating chronic or non-healing ulcers on lower extremity using a rapid, intra-operative, point of care technology at the patient's bedside.

<https://clinicaltrials.gov/ct2/show/NCT03026855>

Professional Societies

Wound Healing Society

In guidelines for the treatment of diabetic ulcers, the Wound healing Society states that Platelet-derived growth factor (PDGF) is effective in treating diabetic neurotrophic foot ulcers (Level 1) (Lavery et al. 2016).

In guidelines for the treatment of pressure ulcers, the Wound Healing Society states that the use of growth factor therapy [this includes platelet-derived growth factor] should be considered for pressure ulcers that are not responsive to initial comprehensive therapy and/or before surgical repair (Level II) (Gould et al. 2016).

In guidelines for the treatment of venous ulcers, the Wound Healing Society states that cytokine growth factors [includes platelet-derived growth factor] have yet to be shown to demonstrate sufficient statistically significant results of effectiveness to recommend any of them for treatment of venous ulcers, although isolated reports suggest their potential usefulness (Level I) (Marston et al. 2016).

American College of Physicians (ACP)

ACP published 2015 guidelines on the treatment of pressure ulcers. The guidelines noted that “although low quality evidence suggests that dressings containing Platelet derived growth factors (PDGF) 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.”

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

In December 1997, the FDA approved becaplermin for the treatment of patients with lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have adequate blood supply. According to FDA labeled indications, Becaplermin should be used in combination with standard ulcer wound care. This is the first FDA-approved biotechnology product to treat deep diabetic foot and leg ulcers. See the following Web site for more information: https://www.accessdata.fda.gov/drugsatfda_docs/applletter/1997/becaomj121697l.htm. (Accessed December 17, 2017)

In June 2008, the FDA announced the addition of a boxed warning to the labeling of Regranex Gel 0.01% (becaplermin). The new labeling indicates that Regranex (becaplermin) Gel is contraindicated in patients with a known hypersensitivity to any component of this product (e.g., parabens) or a known neoplasm(s) at the site(s) of application. The warnings in the new labeling indicate that Regranex Gel contains becaplermin, a recombinant human platelet-derived growth factor, which promotes cellular proliferation and angiogenesis. The benefits and risks of becaplermin treatment should be carefully evaluated before prescribing. Becaplermin should be used with caution in patients with a known malignancy. Malignancies distant from the site of application have occurred in becaplermin users in both a clinical study and in postmarketing use, and an increased rate of death from systemic malignancies was seen in patients who have received 3 or more tubes of Regranex Gel. See the following Web site for more information: <https://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM142821.pdf>. (Accessed January 14, 2018)

The AutoloGel Process Centrifuge is one of several devices cleared for marketing by FDA for point-of-care preparation of platelet-rich plasma (PRP) from a sample of a patient’s blood (see listings under product code JQC for additional devices). See the following Web site for more information: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnm.cfm>. (Accessed December 17, 2017)

In April 2003, the FDA approved the use of the GPS™ Platelet Separation Kit. The GPS™ separation kit aids separation of the patient’s own blood components by density through the use of the GPS™-Thermo International Equipment Company (IEC) centrifuge. The GPS separation kit permits platelet rich plasma to be rapidly prepared from a small volume of the patient’s blood that is drawn at the time of treatment. The GPS Platelet Separation Kit is designed for use in the clinical laboratory or intraoperatively at point of care, for the safe and effective preparation of platelet poor plasma and platelet concentrate from a small sample (50-60 ml) of whole blood. See the following Web site for more information: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmnm.cfm?ID=K030555>. (Accessed January 14, 2018)

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The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2018T0523N]

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2018	<ul style="list-style-type: none">• Updated coverage rationale; replaced language indicating:<ul style="list-style-type: none">○ “[The listed service] is proven <i>and</i> medically necessary” with “[the listed service] is proven <i>and/or</i> medically necessary”○ “[The listed service] is unproven <i>and</i> not medically necessary” with “[the listed service] is unproven <i>and/or</i> not medically necessary”• Updated supporting information to reflect the most current clinical evidence, FDA information, and references• Archived previous policy version DERMATOLOGY 010.14 T2