PLATELET-DERIVED GROWTH FACTORS FOR WOUND HEALING
RX501.034

COVERAGE:

Becaplermin (Regranex Gel), a recombinant, platelet-derived growth factor (PDGF) may be eligible for coverage when used as an adjunct to standard wound management and used according to the FDA-labeled indication (i.e., neuropathic diabetic ulcers extending into the subcutaneous tissue).

Other applications of becaplermin are considered investigational and are not eligible for coverage. These include, but are not limited to:

- Ischemic ulcers
- Ulcers related to venous stasis,
- Pressure ulcers
- Ulcers not extending through the dermis into the subcutaneous tissue

Platelet-derived wound healing formula (Procuren) is considered investigational and is not eligible for coverage.

DESCRIPTION:

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factor, epidermal growth factor, fibroblast growth factors, transforming growth factors and insulin-like growth factor. Topically applied platelet-derived growth factors (PDGF) have been most extensively investigated for clinical use in wound healing. The U.S. Food and Drug Administration (FDA) have recently approved a recombinant PDGF product, becaplermin (trade name Regranex Gel, McNeil Pharmaceutical). The labeled indication is as follows:

Becaplermin (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."

Appropriate candidates for Becaplermin (Regranex Gel) are selected by the following criteria:

1. 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

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

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.

Becapleromin is available in 2-g, 7.5-g, and 15-g tubes, and is applied in a thin continuous layer, about 1/16\(^{th}\) of an inch, 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, 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 15-g tubes would be required.

Platelet-derived wound healing formula (Procuren, Curative Technologies, Inc.) is an autologous product that is derived from the patients' own blood cells. This product has not undergone FDA approval. The patient's platelets are isolated by centrifugation, then exposed to thrombin, which prompts a release of a variety of growth factors. This platelet releasate is applied to the wound for a period of 12 hours, then rinsed away and followed by an application of topical antibiotics. Platelet-derived wound healing formula is often offered as part of a program of wound care management as offered by Wound Care Centers, which are operated by Curative Technologies, Inc.

Chronic nonhealing ulcers of the lower extremity are a common problem and may be related to venous stasis, peripheral neuropathy, local trauma, or ischemia—three factors that are common causes for ulcers in diabetics. Standard treatment for nonhealing ulcers includes debridement, treatment of infection, avoidance of weight bearing, and revascularization in those surgical candidates with ischemic ulcers.

RATIONAL:

**Becaplermin (Regranex Gel)**

This policy regarding the use of Becaplermin is based on a 1999 TEC assessment that offered the following conclusions:

- The evidence supports the conclusion that Becaplermin treatment, in conjunction with good wound care, improves the health outcomes of patients with chronic neuropathic diabetic ulcers that meet the patient selection criteria. Becaplermin gel plus good wound care resulted in a 43% complete wound-closure rate, compared to 28% for patients treated with good wound care alone. Becaplermin gel also appeared to reduce the average time to complete wound closure.

- There is insufficient evidence to determine the effect of Becaplermin gel in treatment of other types of ulcers, including ischemic, chronic venous or chronic pressure ulcers.

- It should be emphasized the beneficial effects of Becaplermin were achieved within the setting of a controlled clinical trial protocol. Results of the clinical trials clearly tied the efficacy of Becaplermin treatment to the overall intensity of the wound management effort. Variations in standard care, including infection
control, debridement type and frequency, non-weight bearing compliance and methods, and patients' glycemic control all influence ulcer healing. Whether this comprehensive degree of wound care is maintained in a community practice or home care setting is a concern. The magnitude of becaplermin effect, as demonstrated in clinical trials, can be expected only in settings that adhere to good wound care practices.

**Platelet Derived Wound Healing Formula (i.e., Platelet Releasate, Procuren)**

The policy on platelet derived wound healing formula is derived from a 1992 TEC assessment. The TEC assessment identified two randomized clinical trials that report conflicting results such that no conclusions could be reached regarding the health benefits of platelet-derived wound healing formula. A literature search extending from January 1992 to April 1999 was performed; no additional randomized studies were identified. Glover and colleagues published a 4-year retrospective study of wound healing using platelet-derived wound healing formula. Although the authors stated that patients in the treatment group reported higher healing rates compared to those treated with standard wound care alone, this uncontrolled study does not permit analysis of the independent contribution of platelet-derived wound healing formula.

**DISCLAIMER:**

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically. HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.

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