Department of Veterans Affairs Medical Advisory Panel and
Pharmacy Benefits Management Strategic Healthcare Group

NON-FORMULARY USE OF BECAPLERMIN GEL IN VETERAN PATIENTS

The following information is based on current literature. These criteria are not intended to interfere with clinical judgement. Rather, they are intended to assist practitioners in providing cost effective, consistent, high quality care.

Becaplermin (Regranex®) is a recombinant human platelet-derived growth factor (rhPDGF) with biologic activity similar to endogenous platelet-derived growth factor (PDGF). Biologic activity of PGDF includes encouraging chemotaxis and proliferation of cells responsible for wound repair and augments production of granulation tissue. Becaplermin gel is FDA approved for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond (stage III or IV as defined by the International Association of Enterostomal Therapy, IAET, for staging chronic wounds) and possess an adequate blood supply. It is to be used as an adjunct to, not a replacement for, good ulcer care including sharp debridement, non-weight bearing, twice daily moist dressing changes, and prevention and treatment of infection. Becaplermin gel is **not** approved for the treatment of pressure, venous stasis or other types of non-diabetic related ulcers.

I. Indication for use of becaplermin gel in veterans: ***All of the following criteria must be met for use of becaplermin gel.***

a. Patients should have a recent glycosylated hemoglobin (hemoglobin A1c or HbA1c) less than 8. If not, aggressive control of their diabetes should be attempted.
b. Patients should be nonsmoking or enrolled in a smoking cessation plan.
c. Stage III or IV (International Association of Enterostomal Therapy for staging chronic wounds) lower extremity diabetic ulcers that extend through the dermis into the subcutaneous tissue or beyond.
d. The wound must have an adequate blood supply measured by oscillometry (at least 2 units), transcutaneous oxygen pressure (TcpO2 >30 mm Hg) or bleeding with debridement.
e. The wound must be free from infection.
f. If present, lower extremity edema should be treated.
g. The patient must have failed standard therapy for at least 2 months (careful-frequent debridement, moist dressing changes and non-weight bearing).
h. The provider must see the patient on a weekly to biweekly basis for debridement and assessment of ulcer response.
i. The provider must recalculate a new amount of becaplermin gel to be applied at every visit.

II. Education:

a. Patients and care providers must be educated regarding proper application of becaplermin gel, storage (must be refrigerated) and cost of the product. An assessment of their ability to properly apply becaplermin gel should be done.
b. Patients and care providers need to be educated on proper wound care including dressing changes not involving application of becaplermin gel (second dressing change of the day). They also need to be educated on the **importance** of non-weight bearing measures.

III. Length of Therapy:

a. Patient and providers must be committed to 10 weeks of becaplermin gel. The maximum duration of treatment is 20 weeks.

IV. When to Discontinue Therapy:

a. Becaplermin gel should be discontinued if there is <30% decrease in ulcer size after 10 weeks of treatment or the ulcer is not completely healed after 20 weeks.
b. If the patient or caregiver is unable to properly apply the becaplermin gel.
c. If the patient is non-compliant with non-weight bearing measures or moist dressing changes.
d. If the patient is non-compliant with weekly to biweekly follow up appointments (misses 2 consecutive appointments).

V. Restricted providers:

The decision to prescribe becaplermin gel should be made by providers who are experienced in chronic care of recalcitrant ulcers (Vascular/wound clinics, plastic surgery clinics, podiatry clinics, etc). In addition, providers should be able to see patients on a weekly to biweekly basis for debridement, reinforcement of non-weight bearing measures, assessment of ulcer response, and recalculation of the new amount of becaplermin gel to be applied.

VI. Dosage and Administration:

The amount of becaplermin gel applied will vary depending upon the size of the ulcer. To calculate an adequate dose of becaplermin gel, measure the greatest length multiplied by the greatest width of the ulcer in inches or centimeters.

To calculate the proper dose in inches (in): 0.65 g of becaplermin per inch

Tube Size	Formula
15 g tube	Length (in) **X** Width (in) **X** 0.6

To calculate the proper dose in centimeters (cm): 0.25 g of becaplermin per centimeter

Tube Size	Formula
15 g tube	Length (cm) **X** Width (cm) divide by 4

The calculated dose of becaplermin gel (in centimeters or inches) should be squeezed out onto a clean surface (wax paper) in a linear fashion. The measured dose can be transferred from this clean surface using an applicator (tongue blade or cotton swab) and spread over the ulcer's surface. The dose of becaplermin gel should be applied only once a day and spread evenly over the surface of the ulcer to produce a thin continuous layer about 1/16 of an inch in thickness. The gel should then be covered with saline moistened gauze and a secondary dressing and left for approximately 12 hours. For the second dressing change of the day, the gel can be gently rinsed off using saline or water and a saline moistened dressing applied to the ulcer without reapplication of becaplermin gel. It should be left for the remaining 12 hours of the day.

Warn patients that application of excessive becaplermin gel has not been shown to be of greater benefit in ulcer healing.

VII. Warnings/Adverse Effects:

Becaplermin gel is contraindicated in patients with known hypersensitivity to parabens and patients with a known neoplasm(s) at application sites.

Adverse effects seen in clinical trials were similar to those seen with placebo gel. Erythematous rash was the only adverse effect that occurred to a greater extent with

becaplermin and placebo gel compared to good ulcer care alone (2% versus none, respectively).

VIII. Monitoring Parameters:

At each appointment, assessment of ulcer response and patient compliance with good ulcer care should be determined (non-weight bearing, no smoking, dressing changes, ability to properly apply becaplermin gel).

If the ulcer does not decrease by approximately 30% in size after 10 weeks of therapy, continued treatment with becaplermin should be reassessed. Treatment with becaplermin gel should continue until the ulcer is completely healed or a **maximum** of 20 weeks. If the ulcer has not completely healed after 20 weeks, continued treatment with becaplermin should be reassessed.

IX. Cost:

Becaplermin gel 15 g tube: $ 233.42
Cost of 20 weeks of therapy: $ 1,167.10

X. Outcomes:

To date, two investigators (Steed, et al, and Weiman, et al) have shown becaplermin gel to be statistically more effective than placebo or good wound care alone in healing chronic, full-thickness, neuropathic diabetic ulcers. In the study by Steed, et al, complete wound healing occurred in 48% of those receiving becaplermin 30mcg/g compared to 25% of those receiving placebo gel (p=0.02). However, in the study by Weiman, et al, the ulcer healing benefit was statistically significant (p=0.01) in the group receiving becaplermin 100 mcg/g gel (50%), but not the 30 mcg/g gel (36%), which was equal to placebo gel (35%). In both of these studies, the time to complete ulcer healing was decreased in the becaplermin groups compared to placebo gel or good ulcer care groups by approximately 30-40 days. A third study by D'Hemecourt, et al, compared placebo gel (NaCMC-vehicle contained in becaplermin) to good ulcer care alone. They also included a becaplermin 100mcg/g arm that was not powered for statistical significance. Although no statistical analysis was provided, authors noted that the placebo gel appeared to have a beneficial effect on ulcer healing compared to good wound care alone (complete healing 36% versus 22%, respectively). The final study, available only in abstract form, compared becaplermin 100 mcg/g gel to good ulcer care alone. Complete ulcer closure occurred in 36% of patients in the becaplermin group compared to 32% of patients receiving good ulcer care alone, which was not statistically different. Explanations for the conflicting data regarding the use of becaplermin gel may include non-compliance with good ulcer care on the part of the patient and/or provider; inadequate education on the proper use of becaplermin gel; and insufficient follow up care for ulcer assessment and debridement. Compliance with these factors is extremely important to the success of complete ulcer healing.

As a result of the limited and modest results of the published data regarding the use of becaplermin gel in diabetic patients with non-healing, full-thickness, neuropathic, lower extremity ulcers, it is recommended that becaplermin use be restricted to those patients meeting the above listed criteria.

XI. References:

1. Product information: Becaplermin Gel, McNeil Pharmaceuticals, Raritan, NJ, 1998.
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3. Steed DL and the Diabetic Ulcer Study Group. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. J Vasc Surg 1995;21:71-81
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7. Steed DL. Foundations of Good Ulcer Care. Am J Surg. 1998;176(suppl 2A):20S-25S)
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16. Pressure Ulcers Prevalence, Cost and Risk Assessment: Consensus Development Conference Statement: The National Pressure Ulcer Advisory Panel. Decubitus 1989;2:24-28.

Becaplermin Gel Monitoring Sheet

- For appropriate becaplermin gel candidates, refer to the criteria for nonformulary use.
- A new amount of becaplermin gel to be applied should be recalculated at each visit.
- Becaplermin should be discontinued if the ulcer has not decreased in size by 30% after 10 weeks or has not completely healed after 20 weeks of treatment.

Calculation of dosage: (15 g tube size)

Inches: Length (in) **X** Width (in) **X** 0.6 (0.65 gram of becaplermin per inch length)

Centimeters: Length (cm) **X** Width (cm) divided by 4 (0.25 gram of becaplermin per centimeter length)

Patient Name_____SSN_____

Duration and location of ulcer:_____

HGB A1C_____Date taken:_____

Date/week	**Ulcer size** (length)	**Ulcer size** (width)	**Ulcer size** (depth)	**Becaplermin Dose** (cm or inches)	**Comments**