



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

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Subject **Becaplermin (Regranex®)**

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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2009 CIGNA

Coverage Policy

CIGNA covers becaplermin (Regranex®) as medically necessary to be used as an adjunct treatment for a diabetic neuropathic ulcer of the lower extremity extending into the subcutaneous tissue or beyond.

CIGNA does not cover becaplermin (Regranex®) for the following indications because it is considered experimental, investigational or unproven (this list may not be all-inclusive):

- pressure ulcers
- venous stasis ulcers
- diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous tissue (Stage I or II, International Association Enterostomal Therapy (IAET) staging classification)
- ischemic diabetic ulcer

General Background

FDA Approved Indications

Regranex (becaplermin) 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 incidence of complete healing of diabetic ulcers. The efficacy of Regranex Gel has not been established for the treatment of pressure ulcers and venous stasis ulcers and has

not been evaluated for the treatment of diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous tissue (Stage I or II, IAET staging classification) or ischemic diabetic ulcers.

FDA Recommended Dosing

The amount of Regranex Gel to be applied will vary depending upon the size of the ulcer area. To calculate the length of gel to apply to the ulcer, measure the greatest length of the ulcer by the greatest width of the ulcer in either inches or centimeters and use the following table:

Tube Size	Formula	
	Inches of Gel	Centimeters of Gel
7.5 or 15 g tube	length x width x 0.6	length x width ÷ 4
2 g tube	length x width x 1.3	length x width ÷ 2

Becaplermin gel is a recombinant human platelet-derived growth factor (rhPDGF-BB) for topical administration. Becaplermin is produced by recombinant deoxyribonucleic acid (DNA) technology by insertion of the gene for the B chain of platelet-derived growth factor (PDGF) into the yeast, *Saccharomyces cerevisiae*. Becaplermin is a homodimer composed of two identical polypeptide chains that are bound together by disulfide bonds. Becaplermin has biological activity similar to that of endogenous platelet-derived growth factor, which includes promoting the chemotactic recruitment and proliferation of cells involved in wound repair and enhancing the formation of granulation tissue.

The effects of becaplermin on the incidence of and time to complete healing in lower extremity diabetic ulcers were assessed in four randomized controlled studies. Of 922 patients studied, 478 received either becaplermin 0.003% or 0.01%. All study participants had lower extremity diabetic neuropathic ulcers that extended into the subcutaneous tissue or beyond (Stages III and IV of the IAET guide to chronic wound staging). Ninety-three percent (93%) of the patients enrolled in these four trials had foot ulcers. The remaining 7% of the patients had ankle or leg ulcers. The diabetic ulcers were of at least eight weeks duration and had an adequate blood supply (defined as $T_{c}pO_2 > 30$ mm Hg). In the four trials, 95% of the ulcers measured in area up to 10 cm², and the median ulcer size at baseline ranged from 1.4–3.5 cm². All treatment groups received a program of good ulcer care consisting of initial complete sharp debridement; a nonweight-bearing regimen; systemic treatment for wound-related infection, if present; moist saline dressings changed twice a day; and additional debridement as necessary. Becaplermin gel 0.003% or 0.01% or placebo gel was applied once a day and covered with a saline moistened dressing. After approximately 12 hours, the gel was gently rinsed off, and a saline moistened dressing was then applied for the remainder of the day. Patients were treated until complete healing or for a period of up to 20 weeks. Patients were considered a treatment failure if their ulcer did not show an approximate 30% reduction in initial ulcer area after eight to ten weeks of becaplermin therapy.

In a multicenter, double-blind, placebo-controlled trial of 118 patients, the incidence of complete ulcer closure for becaplermin 0.003% (n=61) was 48% versus 25% for placebo gel (n=57; p=0.02). The median percentage reduction in wound area was 98.8% with the becaplermin gel and 82.1% with placebo gel (p=0.09). The recurrence rate was 26% after 8.6 weeks in the becaplermin gel group and 46% after 8.5 weeks in the placebo group.

In another multicenter, double-blind, placebo-controlled study, the incidence of complete ulcer closure for becaplermin 0.01% (n=123) was 50% versus 36% for becaplermin 0.003% (n=132), and 35% for placebo gel (n=127). Only the difference between the healing rate with 0.01% gel and placebo was significant (p=0.01).

The safety of vehicle gel (placebo, n=70) compared to good ulcer care alone (n=68) and becaplermin 0.01% (n=34) was assessed in a multicenter-controlled trial. Incidences of complete ulcer closure were 44% for becaplermin, 36% for placebo gel, and 22% for good ulcer care alone.

In general, where becaplermin was associated with higher incidences of complete ulcer closure, differences in the incidence first became apparent after approximately 10 weeks and increased with continued treatment. Becaplermin gel is well tolerated. The only increased risk associated with becaplermin gel is the development of a rash.

In two small, randomized, double-blinded studies of becaplermin gel (100mcg/g once daily for 16 weeks) in patients with venous stasis ulcers, the combined incidence of complete ulcer closure was 46% (30/65) in the becaplermin group and 39% (26/67) in the vehicle control group. This difference was not statistically significant.

Coding/Billing Information

Note: This section is currently unavailable.

References

1. McEvoy GK, ed. AHFS 2009 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2009.
2. Mustoe TA, Cutler NR, Allman RM, et al. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg. 1994;129:213-9.
3. OMJ Pharmaceuticals, Inc. Regranex® (Becaplermin) package insert. San Gennan, Puerto Rico: OMJ Pharmaceuticals, May 2008.
4. Steed DL, 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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