Smith+Nephew

# REGRANEX◊
(becaplermin) gel 0.01%

**REGRANEX (becaplermin) gel, for topical use**

**Prescription Only.**

**Initial U.S. Approval: 1997**

**Brief Summary of Prescribing Information**

For complete Prescribing Information, consult official package insert.

## 1 INDICATIONS AND USAGE
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.

**Limitations of Use:**
The efficacy of REGRANEX gel has not been established for the treatment of pressure ulcers and venous stasis ulcers [see Clinical Studies (14.2)] 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, International Association of Enterostomal Therapy (IAET) staging classification] or ischemic diabetic ulcers. The effects of becaplermin on exposed joints, tendons, ligaments, and bone have not been established in humans [see Nonclinical Toxicology (13.2)]. REGRANEX gel is a non-sterile, low bioburden preserved product. Therefore, it should not be used in wounds that close by primary intention.

## 4 CONTRAINDICATIONS
REGRANEX gel is contraindicated in patients with known neoplasm(s) at the site(s) of application.

## 5 WARNINGS AND PRECAUTIONS
### 5.1 Risk of Cancer
Malignancies distant from the site of application have occurred in REGRANEX gel users in a clinical study and in postmarketing use [see Adverse Reactions ( 6.1) and Clinical Studies (14.3)]. REGRANEX gel contains becaplermin, a recombinant human platelet-derived growth factor, which promotes cellular proliferation and angiogenesis [see Clinical Pharmacology (12.1)]. The benefits and risks of REGRANEX gel treatment should be carefully evaluated before prescribing in patients with known malignancy.

### 5.2 Application Site Reactions
If application site reactions occur, the possibility of sensitization or irritation caused by parabens or m-cresol should be considered. Consider interruption or discontinuation and further evaluation (e.g. patch testing) as dictated by clinical circumstances.

## 6 ADVERSE REACTIONS
### 6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, erythematous rashes occurred in 2% of subjects treated with REGRANEX gel (and good ulcer care) or placebo (and good ulcer care), and none in subjects receiving good ulcer care alone. Subjects treated with REGRANEX Gel did not develop neutralizing antibodies against becaplermin.

In a retrospective follow-up study of 491 of 651 subjects (75%) from two randomized, controlled trials of another formulation of becaplermin gel 0.01%, the subjects were followed for a median of approximately 20 months to evaluate safety and recurrence of healed diabetic lower extremity ulcers. Eight of 291 subjects (2.7%) from the becaplermin gel group and two of 200 subjects (1%) from the vehicle/standard of care group were diagnosed with cancers during the follow-up period, a relative risk of 2.7 (95% confidence interval [CI], 0.6-12.8). The types of cancers varied and all were remote from the treatment site [see Warnings and Precautions (5.1)].

### 6.2 Postmarketing Experience
Because post-approval adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the drug. The following adverse reactions have been identified during postapproval use of REGRANEX gel. Increased rate of death from systemic malignancies in patients dispensed 3 or more tubes of REGRANEX gel, observed in one of three retrospective postmarketing studies [see Clinical Studies (14.3)]. Burning sensation at the site of application and erythema.

## 7 DRUG INTERACTIONS
It is not known if REGRANEX gel interacts with other topical medications applied to the ulcer site. The use of REGRANEX gel with other topical drugs has not been studied.

## 8 USE IN SPECIFIC POPULATIONS
### 8.1 Pregnancy
**Risk Summary**
There are no available data on REGRANEX gel use in pregnant women to inform a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with REGRANEX gel. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

### 8.2 Lactation
There are no data on the presence of becaplermin in human milk, the effects on the breastfed infant, or the effects on milk production after topical application of REGRANEX gel to lactating women. The developmental and health benefits of breastfeeding should be considered along with the lactating woman's clinical need for REGRANEX gel and any potential adverse effects on the breastfed child from becaplermin.

### 8.4 Pediatric Use
Safety and effectiveness of REGRANEX gel in pediatric patients below the age of 16 years have not been established.

### 8.5 Geriatric Use
Among patients receiving any dose of REGRANEX gel in clinical studies of diabetic lower extremity ulcers, 150 patients were 65 years of age and older. No overall differences in safety or effectiveness were observed between patients < 65 years of age and patients ≥ 65 years of age. The number of patients aged 75 and older were insufficient (n=34) to determine whether they respond differently from younger patients.

## 10 OVERDOSAGE
There are no data on the effects of REGRANEX gel overdose.

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