FASTER HEALING OF DIABETIC NEUROPATHIC ULCERS

REGRANEX® Gel, when combined with good ulcer care, accelerated healing by ~6 weeks compared to placebo gel (12.3 wk vs 18.1 wk, respectively; P=0.013)*

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of REGRANEX® Gel in a postmarketing retrospective cohort study. REGRANEX® Gel should only be used when the benefits can be expected to outweigh the risks. REGRANEX® Gel should be used with caution in patients with known malignancy.

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.

*For study design and additional efficacy results, please see page 3.

FASTER HEALING—SEEN WITH ACCELERATED WOUND CLOSURE

A well-prepared wound bed is ready for REGRANEX® (becaplermin) Gel, 0.01%²

Good ulcer care checklist

- Wound bed is free of necrotic tissue³
- Infection has been controlled³
- Pressure has been redistributed (off-loading)³
- Adequate blood flow is present and wound extends into the subcutaneous tissue or beyond³
- Patient and/or caregiver has shown an understanding of good foot care⁴

REGRANEX® Gel is the first and only FDA-approved platelet-derived growth factor (PDGF) therapy for diabetic neuropathic ulcers⁵

- Endogenous PDGF initiates healing by attracting repair cells to revitalize wounds⁶

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.
In clinical trials, REGRANEX® Gel helped close diabetic neuropathic ulcers faster\(^1\)

- REGRANEX® Gel, when combined with good ulcer care, accelerated healing by ~6 weeks compared to placebo gel (12.3 wk vs 18.1 wk, respectively, \(P=0.013\))

REGRANEX® Gel significantly increased the incidence of healing in diabetic neuropathic ulcers\(^1\)

- Patients using REGRANEX® Gel demonstrated a 50% incidence of complete wound closure vs 35% with placebo gel (\(P=0.007\))
- More patients using REGRANEX® Gel achieved complete wound closure as early as 4 weeks into treatment compared with patients using placebo gel

**Study design:** The efficacy and safety of REGRANEX® Gel were studied in 382 patients with type 1 or type 2 diabetes in a multicenter, double-blind, parallel-group, placebo-controlled trial. Patients had at least one full-thickness chronic ulcer of the lower extremity. After sharp debridement of the ulcer, patients were randomized to receive REGRANEX® Gel or placebo gel, in conjunction with good ulcer care, until complete wound closure was achieved or for a maximum of 20 weeks. To assess rate of closure, study visits were scheduled weekly for Visits 2–6 and every other week after Visit 6. To assess incidence of closure, the area of the ulcer was measured and the target ulcer was assigned a functional assessment score based on whether the wound was completely closed without drainage or need of dressing, or <100% closed with drainage and requiring a dressing.\(^1\)

**IMPORTANT SAFETY INFORMATION**

**WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY**

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.
STRAIGHTFORWARD DOSING

Easy-to-calculate dosing for REGRANEX® (becaplermin) Gel, 0.01%:

- Calculating the amount of REGRANEX® Gel to use will depend on the size of the ulcer area.
  - In the event of multiple wounds, each ulcer should be assessed individually.
- Dose should be recalculated at weekly or biweekly intervals, based on the rate of change in the ulcer area.
- Applying more than the calculated amount of REGRANEX® Gel has not been shown to be beneficial.
- Please note that the estimates are only intended as a guide, contain rounded values where appropriate, and assume a constant wound size throughout the treatment period. Therefore, you should adjust these estimates based upon your own clinical experience and individual wound characteristics. Not intended to supersede independent clinical judgment or institutional protocols.

The dosing calculation:

\[
\text{(Ulcer length cm)} \times \text{(Ulcer width cm)} \div 4 = \text{Length of gel to be applied (cm)}
\]

Sample calculation for a 3 cm x 2 cm ulcer:

\[
(3 \text{ cm}) \times (2 \text{ cm}) \div 4 = 1.5 \text{ cm}
\]

Apply 1.5 cm of REGRANEX® Gel.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

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Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.
IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of REGRANEX® Gel in a postmarketing retrospective cohort study. REGRANEX® Gel should only be used when the benefits can be expected to outweigh the risks. REGRANEX® Gel should be used with caution in patients with known malignancy.

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.

Estimated tubes of REGRANEX® Gel based on ulcer area and length of treatment*5

Not intended to supersede independent clinical judgment or institutional protocols. While each 15-g tube of REGRANEX® Gel is estimated to dispense 60 cm of gel, the actual centimeters from each tube may vary based on user characteristics and application methods.

*If the ulcer does not decrease in size by approximately 30% after 10 weeks of treatment or complete healing has not occurred in 20 weeks, continued treatment with REGRANEX Gel should be reassessed.5

The number of tubes calculation5

\[
\text{Estimated number of tubes} = \frac{\text{(Length of gel per application cm)} \times \text{(Estimated length of therapy days)}}{\text{(60 cm/tube)}}
\]

Sample calculation for a 3 cm x 2 cm ulcer:

\[
\text{(1.5 cm) } \times \text{ (14 days) } \div \text{ 60 cm/tube } = 0.35 \text{ tubes}
\]

Order 1 tube of REGRANEX® Gel

In a clinical study, patients who healed with REGRANEX® Gel received an average of 1.5 tubes.7

Indicate total prescription refills based on the size of the wound area

REGRANEX® Gel is available in 15-g tubes.

* Indicate total prescription refills based on the size of the wound area.
AT-HOME APPLICATION

Flexible at-home application schedule:

- Decide with the patient who will apply REGRANEX® (becaplermin) Gel, 0.01% (patient or caregiver) and walk them through the application steps
- Make sure the patient and caregiver are informed about how much REGRANEX® Gel to apply
- Instruct patient and/or caregiver to review the Medication Guide that accompanies REGRANEX® Gel

Application schedule can work around daily foot checks

Apply in the AM, change dressing in the PM
or
Apply in the PM, change dressing in the AM

References:
5. REGRANEX® Gel Prescribing Information.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.
Applying REGRANEX® Gel

1. Prepare
   - Wash hands
   - Squeeze the calculated length of REGRANEX® Gel on a clean, firm, non-absorbent surface, such as wax paper

2. Apply
   - Use application aid to spread REGRANEX® Gel in a thin, even layer of approximately 1/16-inch thickness over the entire ulcer area
   - Thickness of gel to be applied is about the thickness of a penny.

3. Cover
   - Cover area with saline-moistened gauze dressing
   - After approximately 12 hours, gently remove the dressing and rinse ulcer with saline or water to remove remaining REGRANEX® Gel
   - Cover ulcer with new saline-moistened dressing (without REGRANEX® Gel) for the remainder of the day

Don’t Forget: Remind patients to refrigerate REGRANEX® Gel.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

Please see additional Important Safety Information on pages 8–9 and accompanying Full Prescribing Information in pocket.
IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of REGRANEX® (becaplermin) Gel, 0.01% in a postmarketing retrospective cohort study. REGRANEX® Gel should only be used when the benefits can be expected to outweigh the risks. REGRANEX® Gel should be used with caution in patients with known malignancy.

Indication and limitations of use

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. REGRANEX® Gel is indicated as an adjunct to, and not a substitute for, good ulcer care practices including initial sharp debridement, pressure relief and infection control.

- 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.
- The effects of REGRANEX® Gel on exposed joints, tendons, ligaments, and bone have not been established in humans.
- REGRANEX® Gel is a non-sterile, low bioburden preserved product. Therefore, it should not be used in wounds that close by primary intention.

Contraindications

REGRANEX® Gel is contraindicated in patients with known neoplasm(s) at the site(s) of application. REGRANEX® Gel is contraindicated in patients with known hypersensitivity to any component of the product (e.g., parabens).

Warnings and precautions

Malignancies distant from the site of application have been reported in both a clinical study and in postmarketing use. REGRANEX® Gel should be used with caution in patients with a known malignancy.

If application site reactions occur, the possibility of sensitization or irritation caused by parabens or m-cresol should be considered.

Commonly observed adverse reactions

In clinical trials, erythematous rashes occurred in 2% of patients treated with REGRANEX® Gel (and good ulcer care) or placebo (and good ulcer care), and none in patients receiving good ulcer care alone.

See warnings above regarding malignancy.

Burning sensation at the site of application and erythema have been reported during post-approval use of REGRANEX® Gel.

Please see accompanying Full Prescribing Information in pocket.
Compliance checklist for REGRANEX® Gel

At the office

- ✔ Determine who is going to apply REGRANEX® Gel (patient or caregiver)
- ✔ Schedule weekly or biweekly physician appointments
- ✔ Set patient or caregiver cell phone alarm for daily application and dressing change reminders
- ✔ Remind patient and/or caregiver to review the Medication Guide that accompanies the product

At home

- ✔ Maintain off-loading
- ✔ Examine feet every day
- ✔ Apply REGRANEX® Gel as directed
- ✔ Refrigerate REGRANEX® Gel
- ✔ Contact clinician with any concerns or side effects

Other important information

The amount of REGRANEX® Gel to be applied should be recalculated by the physician or wound caregiver at weekly or biweekly intervals depending upon the rate of change in ulcer area.

If the ulcer does not decrease in size by approximately 30% after 10 weeks of treatment or complete healing has not occurred in 20 weeks, continued treatment with REGRANEX® Gel should be reassessed.

Pregnancy & Nursing Mothers: Pregnancy Category C. REGRANEX® Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether becaplermin is excreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when REGRANEX® Gel is administered to nursing women.

Safety and effectiveness of REGRANEX® Gel in pediatric patients below the age of 16 years have not been established.

Counsel patients to review the Medication Guide and to discuss any questions or concerns with their healthcare provider before starting REGRANEX® Gel and at regular intervals during treatment, including when their prescription is refilled.

To report suspected adverse reactions, contact Smith & Nephew at 1-800-441-8227 or contact FDA at www.fda.gov/medwatch or at 1-800-FDA-1088.
Financial support and information

REGRANEX® Gel is covered by many commercial payers, Medicare Part D plans, and Medicaid plans, with varying coverage requirements. Regranex360® provides both patients and healthcare professionals direct access to comprehensive support services throughout the entire treatment process.

For more information on REGRANEX® Gel, including information on reimbursement, visit www.Regranex.com or call 1-888-REGRANEX (734-7263).

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED RATE OF MORTALITY SECONDARY TO MALIGNANCY

An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of REGRANEX® Gel in a postmarketing retrospective cohort study. REGRANEX® Gel should only be used when the benefits can be expected to outweigh the risks. REGRANEX® Gel should be used with caution in patients with known malignancy.

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. REGRANEX® Gel is indicated as an adjunct to, and not a substitute for, good ulcer care practices.

Limitations of use

- The efficacy of REGRANEX® Gel has not been established for the treatment of pressure ulcers and venous stasis ulcers.
- The effects of REGRANEX® Gel on exposed joints, tendons, ligaments, and bone have not been established in humans.
- REGRANEX® Gel is a non-sterile, low bioburden preserved product that should not be used in wounds that close by primary intention.
- REGRANEX® Gel is contraindicated in patients with known neoplasm(s) at the site(s) of application. REGRANEX® Gel is contraindicated in patients with known hypersensitivity to any component of the product (e.g., parabens).

Malignancies distant from the site of application have been reported in both a clinical study and in postmarketing use.

In clinical trials, erythematous rashes occurred in 2% of patients treated with REGRANEX® Gel or placebo; none occurred in patients receiving good ulcer care alone. Burning sensation at the site of application and erythema have been reported during post-approval use of REGRANEX® Gel.

Please see accompanying Full Prescribing Information.
REGRANEX Gel contains becaplermin, a recombinant human platelet-derived growth factor for topical administration. Becaplermin is produced by recombinant DNA technology by the insertion of the gene for the growth factor (PDGF) into the yeast, Saccharomyces cerevisiae. Becaplermin has a molecular weight of approximately 25 KD and is a homodimer composed of two identical polypeptide chains that are bound together by disulfide bonds. REGRANEX Gel is a non-sterile, tear-formulation containing becaplermin and the following inactive ingredients: carbonated water, cetyl alcohol, decyl alcohol, glycine, hydrogenated castor oil, methylparaben, propylparaben, sodium acetate trihydrate, sodium chloride, and water for injection. Each gram of REGRANEX Gel contains 100 mcg of becaplermin.

1 INDICATIONS AND USAGE

1.1 Indication

The efficacy of REGRANEX Gel is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and are not managed by a diabetic blood supply. The effects of becaplermin on exposed joints, tendons, ligaments, and bone have not been established in humans. (1.2)

1.2 Limitations of Use

The efficacy of REGRANEX Gel has not been established for the treatment of pressure ulcers and venous stasis ulcers. (1.2)

The effects of REGRANEX Gel on exposed joints, tendons, ligaments, and bone have not been established in humans. (1.2)

REGRANEX Gel is a non-sterile, low bioburden preserved product. Therefore, it should not be used in wounds that close by primary intention. (1.2)

2 DOSAGE AND ADMINISTRATION

2.1 Topical Use

For topical use, not for oral, ophthalmic or intranasal use. (2)

To calculate the length of REGRANEX Gel to apply, measure the greatest length of the ulcer by the greatest width of the ulcer in either inches or centimeters. (2)

Formula to Calculate Length of Gel to Be Applied Daily

\[
\text{Inches} = \text{Length of Gel} \times \frac{1}{2}
\]

\[
\text{Centimeters} = \text{Length of Gel} \times \frac{25.4}{100}
\]

To calculate the length of gel to be applied, use the formula shown below in Table 1, and to calculate the length of REGRANEX Gel in centimeters, use the formula shown in Table 2.

Table 1: Formula to Calculate Length of Gel in Inches to Be Applied Daily

<table>
<thead>
<tr>
<th>Tube Size</th>
<th>Gel length × width = 6.0</th>
<th>Tube Size</th>
<th>Gel length × width = 4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>15g tube</td>
<td>15 g tube length × width ÷ 4</td>
<td>15g tube</td>
<td>15 g tube length × width ÷ 4</td>
</tr>
<tr>
<td>5g tube</td>
<td>5 g tube length × width ÷ 4</td>
<td>5g tube</td>
<td>5 g tube length × width ÷ 4</td>
</tr>
<tr>
<td>2g tube</td>
<td>2 g tube length × width ÷ 2</td>
<td>2g tube</td>
<td>2 g tube length × width ÷ 2</td>
</tr>
<tr>
<td>0.5g tube</td>
<td>0.5 g tube length × width ÷ 1</td>
<td>0.5g tube</td>
<td>0.5 g tube length × width ÷ 1</td>
</tr>
</tbody>
</table>

Using the calculation, each square inch of ulcer surface will require approximately 2/3 inch length of gel squeezed from a 15g tube, approximately 0.57 inch length of gel from a 5g tube, or approximately 0.28 inch length of gel from a 2g tube.

To calculate the length of gel to be applied, use the formula shown below in Table 2.

\[
\text{Inches} = \text{Ulcer length} \times \frac{1}{2}
\]

\[
\text{Centimeters} = \text{Ulcer length} \times \frac{25.4}{100}
\]

To apply, calculate the length of gel to be squeezed on a clean measuring surface, e.g., wax paper. The measured REGRANEX Gel is transferred from the application aid and then spread over the entire ulcer area to yield a thin continuous layer of approximately 1/16 inch on thickness. The desired thickness of application varies by a safety factor depending on the left in place for approximately 12 hours. The dressing should then be removed and the ulcer site cleaned. If a dressing change is desired every other day a second dressing (without REGRANEX Gel) for the remainder of the day. REGRANEX Gel should be used only once daily, after complete healing has occurred. If the ulcer does not decrease in size by approximately 30% after 10 weeks of treatment or if complete healing has not occurred in 12 weeks, continued treatment with REGRANEX Gel should be reassessed. The step-by-step instructions for applying REGRANEX Gel for home application are provided in “Patient Counseling Information.” (2.1)

3 DOSAGE FORMS AND STRENGTHS

REGRANEX Gel (6.1)

4 CONTRAINDICATIONS

4.1 General

REGRANEX Gel is contraindicated in patients with known malignancy. (4.1)

5 WARNINGS AND PRECAUTIONS

5.1 Cancer and Cancer Mortality

An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of REGRANEX Gel in a postmarketing retrospective cohort study. REGRANEX Gel should only be used when the benefits can be expected to outweigh the risks. REGRANEX Gel should be used with caution in patients with known malignancy. (5.1)

6.1 Clinical Trials

In a nonclinical study, rats injected at the metatarsals with 3 or 10 mcg/site of becaplermin for 14 days had an increased rate of mortality secondary to malignancy. The adjusted rate ratio was 1.8 (95% confidence interval 0.7–4.9). (6.1)

6.2 Postmarketing Experience

Treatment of 3 or more tubes of REGRANEX Gel should be stopped if the ulcer is not decreasing in size. If the ulcer is not decreasing in size by approximately 30% after 10 weeks of treatment or if complete healing has not occurred in 12 weeks, continued treatment with REGRANEX Gel should be reassessed. The step-by-step instructions for applying REGRANEX Gel for home application are provided in “Patient Counseling Information.” (6.2)

7 DRUG INTERACTIONS

It is not known whether becaplermin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when REGRANEX Gel is administered to nursing women. (7)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There are no adequate and well-controlled studies in pregnant women treated with REGRANEX Gel. REGRANEX Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Animal reproduction studies have not been conducted with REGRANEX Gel. (8.1)

8.4 Pediatric Use

Safety and effectiveness of REGRANEX Gel in pediatric patients below the age of 16 years has not been established. (8.4)

9 OVERDOSAGE

There are no data on the effects of becaplermin overdose. (9)

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

REGRANEX Gel has biological activity similar to that of endogenous platelet-derived growth factor (PDGF) into the yeast, Saccharomyces cerevisiae. Becaplermin has a molecular weight of approximately 25 KD and is a homodimer composed of two identical polypeptide chains that are bound together by disulfide bonds. REGRANEX Gel is a non-sterile, tear-formulation containing becaplermin and the following inactive ingredients: carbonated water, cetyl alcohol, decyl alcohol, glycine, hydrogenated castor oil, methylparaben, propylparaben, sodium acetate trihydrate, sodium chloride, and water for injection. Each gram of REGRANEX Gel contains 100 mcg of becaplermin.

11 DESCRIPTION

11.1 Constituent of the Metallic Impurity of Ferocity

Becaplermin was not genotoxic in a battery of in vitro assays [including those for bacterial mammalian cell proliferation, chromosomal aberration, and DNA damage/regap]. Becaplermin was also not mutagenic in an in vitro assay for the induction of recombinant bacteria. (11.1)

11.2 Animal Toxicology and/or Pharmacology

No clinical studies of REGRANEX Gel in animals were conducted. (11.2)

12 CLINICAL STUDIES

12.1 Animal Toxicology

No clinical studies of REGRANEX Gel in animals were conducted. (12.1)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Becaplermin was not genotoxic in a battery of in vitro assays [including those for bacterial mammalian cell proliferation, chromosomal aberration, and DNA damage/regap]. Becaplermin was also not mutagenic in an in vitro assay for the induction of recombinant bacteria. (13.1)

13.2 Animal Toxicology and/or Pharmacology

No clinical studies of REGRANEX Gel in animals were conducted. (13.2)

14 CLINICAL STUDIES

14.1 Animal Toxicology

No clinical studies of REGRANEX Gel in animals were conducted. (14.1)
In general, where REGRANEX Gel was associated with higher incidences of complete ulcer closure in Study 2, the incidence of complete ulcer closure for REGRANEX Gel 0.01% (n=125) was 35% versus 16% for placebo gel (n=57; p=0.01, logistic regression analysis). In Study 3, a multicenter, double-blind, placebo-controlled trial of 362 patients, the incidence of complete ulcer closure for REGRANEX Gel 0.01% (n=125) was 35% versus 36% for REGRANEX Gel 0.001% (n=120) and 35% for placebo gel (n=127). The REGRANEX Gel 0.01% was significantly different from placebo gel (p=0.01, logistic regression analysis).

The primary goal of Study 3, a multicenter controlled trial of 362 patients, was to assess the safety of vehicle gel (placebo; n=75) compared to good ulcer care alone (n=69). The study included a blinded arm (n=125) where patients with Stage II pressure ulcers were randomized to receive either: Sniff: Smell: See: Image: REGRANEX Gel 0.01% applied to re-HEAL Your Wound

MEDICATION GUIDE

REGRANEX® (RE-GRAN-IX) (bepicamelin) Gel

Read this Medication Guide before you start using REGRANEX and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about REGRANEX?

People who use 3 or more tubes of REGRANEX may have an increased risk of death from cancer.

If you already have cancer, you and your healthcare provider should consider whether you will use REGRANEX.

If you decide to use REGRANEX, your healthcare provider will tell you how to use REGRANEX. See the section "How should I use REGRANEX?" below.

What is REGRANEX?

REGRANEX is a man-made protein medicine that is used with other ulcer care practices (such as good wound care) to treat diabetic sores (ulcers) of your legs or feet that are deeper than just your skin, in people who have good blood supply to the legs. It is not known if REGRANEX is effective for the treatment of pressure ulcers or ulcers that are due to poor blood circulation. It is not known if REGRANEX is safe and effective in children under 16 years of age.

Who should not use REGRANEX?

Do not use REGRANEX if you have a skin tumor at the area where you apply REGRANEX.

What should I tell my healthcare provider before using REGRANEX?

Before you use REGRANEX tell your healthcare provider if you:

• have cancer
• have poor blood flow to your lower legs and feet
• have allergies to any of the ingredients in REGRANEX.

If you are allergic to any ingredients in this Medication Guide for a complete list of ingredients in REGRANEX.

• have any other medical conditions
• are pregnant or plan to become pregnant. It is not known if REGRANEX will harm your unborn baby.
• are breast-feeding or plan to breast-feed. It is not known if REGRANEX passes into your breast milk.

Tell your healthcare provider about all the medicines you buy, including prescription and non-prescription medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you apply other medicines to diabetic ulcers of your legs or feet. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use REGRANEX?

Use REGRANEX together with good ulcer care, as prescribed by your healthcare provider. This includes follow your healthcare provider's instructions about not putting weight on the affected leg and foot (non-weight-bearing).

Use REGRANEX exactly as your healthcare provider tells you to use it.

REGRANEX is for use on skin ulcers only. Do not use REGRANEX in your mouth, eyes, or vagina.

REGRANEX comes as a gel. Your healthcare provider should tell you how often to use REGRANEX and how much REGRANEX to use.

Your healthcare provider may change the amount of REGRANEX to be applied to your ulcer as the size of your ulcer changes. The amount of REGRANEX to be squeezed from the tube may change as the size of your ulcer changes.

Close your REGRANEX tube tightly after each use.

Put the REGRANEX tube back in the refrigerator after each use.

Use a cotton swab, tongue depressor, or similar application aid, to spread the REGRANEX gel in a thin layer over the surface of the ulcer on your foot or leg.

Cover the area with a saline-moistened gauze dressing.

MEDICATION GUIDE

REGRANEX® (RE-GRAN-IX) (bepicamelin) Gel

REGRANEX is a registered trademark of Smith & Nephew, Inc.

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For complete information, including CONTRAINDICATIONS and WARNINGS, see full Prescribing Information.

REGRANEX is for external use only. Do not use REGRANEX in your mouth, eyes, or vagina.

REGRANEX is a man-made protein medicine. REGRANEX can cause allergic reactions in some people, including life-threatening reactions. CALL YOUR DOCTOR FOR MEDICAL ADVICE ABOUT SIDE EFFECTS.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. REGRANEX may cause serious side effects.

See the section, "What is the most important information I should know about REGRANEX?"

Common side effects of REGRANEX include:

• Red skin rash
• Burning at the application site

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of REGRANEX gel. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

How should I store REGRANEX?

• Store REGRANEX in the refrigerator at 36°F to 46°F (2°C to 8°C).
• Do not freeze REGRANEX.
• Do not use REGRANEX after the expiration date on the bottom (sealed end) of the tube.
• Throw away your REGRANEX that is out of date or no longer needed for your treatment.

Keep REGRANEX and all medicines out of the reach of children.

General information about REGRANEX

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use REGRANEX for a condition for which it was not prescribed. Do not give REGRANEX to other people, even if they have the same symptoms that you have. It may harm other people.

This Medication Guide summarizes the most important information about REGRANEX. If you would like more information about REGRANEX, talk to your healthcare provider. You can ask your healthcare provider or pharmacist for information about REGRANEX that is written for healthcare professionals.

The ingredients are in REGRANEX:

Active ingredient: bepicamelin

Inactive ingredients: carboxymethylcellulose sodium, glacial acetic acid, l-lysine hydrochloride, m-cresol, methylparaben, propylparaben, sodium acetate trihydrate, sodium chloride, and water for injection.

Manufactured by: Smith & Nephew, Inc.
Fort Worth, TX 76107
U.S. Gov’t License # 2004
Marketed by: Smith & Nephew, Inc.
Fort Worth, TX 76107
REGRANEX is a registered trademark of Smith & Nephew, Inc.
Part No. 140384-0814
Revised: August 2014
This Medication Guide has been approved by the U.S. Food and Drug Administration.