Smith+Nephew

Patient Assistance Program

What is the Patient Assitance Program (PAP)?

- The Smith+Nephew Patient Assistance Program (PAP) provides prescription drugs at no cost to eligible patients who are low-income and uninsured or underinsured. With our dedicated team to handle the PAP, healthcare professionals can focus on prescribing medications to patients without regard for their ability to pay.
- To qualify for our program, patients must be a permanent US resident (includes Puerto Rico), meet low-income financial requirements, be uninsured or underinsured and not eligible or enrolled in Medicare or any other type of commercial insurance plan. Patients must also have a valid prescription for an FDA approved indication.

How can I enroll my patients?

- A Smith+Nephew Patient Assistance Program (PAP) application can be initiated by anyone including but not limited to a PCP, Traveling Physician Group, Case Manager, Social Worker, Patient or Patient Caregiver.
- For the PAP application to be processed quickly, each application should include complete and accurate information of the patient and the prescriber as well as a valid prescription.
- The application must include both the prescriber's and the patient's (or authorized representative) signatures. Applicants will only be evaluated for eligibility upon receipt of a completed and signed Smith+Nephew Patient Assistance Program (PAP) application.
- Our dedicated team will inform the healthcare professional when the PAP application is approved, denied or if additional information is needed.
- When approved, the product will be sent directly to the patient via FedEx®. Packages are delivered within 2 business days throughout the United States.

Where do I start?

- Visit our website **santyl.com/PAP** to learn more about our program and to download the PAP application.
- After completing and signing (both prescriber's and patient's signatures required) you can fax the application to (833) 965-1621 or email it to: PatientAssistanceProgram.us@PAP.smith-nephew.com.

PAP Eligibility Requirements

☐	Must be a U.S. Resident (includes Puerto Rico)
☐	Patient must be uninsured (no insurance) or underinsured (no coverage)
☐	Patient must meet financial requirements to qualify for Medicaid or have Medicaid coverage where the product is not covered
☐	Patient must be under the care of a licensed medical professional and have a prescription for SANTYL◊ Ointment or REGRANEX◊ gel
☐	Patients 65 and above will be excluded as low-income seniors are covered by Medicare Part D

*Images of tubes is for illustration purposes only - not actual size.

Advanced Wound Management
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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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RGEE31-32428-0622

RX Only

Collagenase SANTYL◊

Ointment 250 units/gram

DESCRIPTION

Collagenase SANTYL◊ Ointment is a sterile enzymatic debriding ointment which contains 250 collagenase units per gram of white petrolatum USP. The enzyme collagenase is derived from the fermentation by *Clostridium histolyticum*. It possesses the unique ability to digest collagen in necrotic tissue.

CLINICAL PHARMACOLOGY

Since collagen accounts for 75% of the dry weight of skin tissue, the ability of collagenase to digest collagen in the physiological pH and temperature range makes it particularly effective in the removal of detritus.[1]

Collagenase thus contributes towards the formation of granulation tissue and subsequent epithelization of dermal ulcers and severely burned areas.[2,3,4,5,6] Collagen in healthy tissue or in newly formed granulation tissue is not attacked.[2,3,4,5,6,7,8]

There is no information available on collagenase absorption through skin or its concentration in body fluids associated with therapeutic and/or toxic effects, degree of binding to plasma proteins, degree of uptake by a particular organ or in the fetus, and passage across the blood brain barrier.

INDICATIONS AND USAGE

Collagenase SANTYL◊ Ointment is indicated for debriding chronic dermal ulcers[2,3,4,5,6,8,9,10,11,12,13,14,15,16,17,18] and severely burned areas.[3,4,5,7,16,19,20,21]

CONTRAINDICATIONS

Collagenase SANTYL◊ Ointment is contraindicated in patients who have shown local or systemic hypersensitivity to collagenase.

PRECAUTIONS

The optimal pH range of collagenase is 6 to 8. Higher or lower pH conditions will decrease the enzyme's activity and appropriate precautions should be taken. The enzymatic activity is also adversely affected by certain detergents, and heavy metal ions such as mercury and silver which are used in some antiseptics.

When it is suspected such materials have been used, the site should be carefully cleansed by repeated washings with normal saline before Collagenase SANTYL◊ Ointment is applied. Soaks containing metal ions or acidic solutions should be avoided because of the metal ion and low pH. Cleansing materials such as Dakin's solution and normal saline are compatible with Collagenase SANTYL◊ Ointment.

Debilitated patients should be closely monitored for systemic bacterial infections because of the theoretical possibility that debriding enzymes may increase the risk of bacteremia.

A slight transient erythema has been noted occasionally in the surrounding tissue, particularly when Collagenase SANTYL◊ Ointment was not confined to the wound. Therefore, the ointment should be applied carefully within the area of the wound. Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

No allergic sensitivity or toxic reactions have been noted in clinical use when used as directed. However, one case of systemic manifestations of hypersensitivity to collagenase in a patient treated for more than one year with a combination of collagenase and cortisone has been reported.

OVERDOSAGE

No systemic or local reaction attributed to overdose has been observed in clinical investigations and clinical use. If deemed necessary the enzyme may be inactivated by washing the area with povidone iodine.

DOSAGE AND ADMINISTRATION

Collagenase SANTYL◊ Ointment should be applied once daily (or more frequently if the dressing becomes soiled, as from incontinence). When clinically indicated, crosshatching thick eschar with a #10 blade allows Collagenase SANTYL◊ Ointment more surface contact with necrotic debris. It is also desirable to remove, with forceps and scissors, as much loosened detritus as can be done readily. Use Collagenase SANTYL◊ Ointment in the following manner:

1. Prior to application the wound should be cleansed of debris and digested material by gently rubbing with a gauze pad saturated with normal saline solution, or with the desired cleansing agent compatible with Collagenase SANTYL◊ Ointment (See **PRECAUTIONS**), followed by a normal saline solution rinse.
2. Whenever infection is present, it is desirable to use an appropriate topical antibiotic powder. The antibiotic should be applied to the wound prior to the application of Collagenase SANTYL◊ Ointment. Should the infection not respond, therapy with Collagenase SANTYL◊ Ointment should be discontinued until remission of the infection.
3. Collagenase SANTYL◊ Ointment may be applied directly to the wound or to a sterile gauze pad which is then applied to the wound and properly secured.
4. Use of Collagenase SANTYL◊ Ointment should be terminated when debridement of necrotic tissue is complete and granulation tissue is well established.

HOW SUPPLIED

Collagenase SANTYL◊ Ointment contains 250 units of collagenase enzyme per gram of white petrolatum USP.

Do not store above 25°c (77° F) Sterility guaranteed until tube is opened.

Collagenase SANTYL◊ Ointment is available in the following sizes:

- 30 g tube NDC 50484-010-30
- 90 g tube NDC 50484-010-90

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SAPE72-38468-1123