Evaluation of the Effectiveness of Regranex (Becaplermin) Gel 0.01% on the Treatment of Wounds

Melissa Wood

University of North Dakota

Follow this and additional works at: https://commons.und.edu/pt-grad

Part of the Physical Therapy Commons

Recommended Citation
Wood, Melissa, "Evaluation of the Effectiveness of Regranex (Becaplermin) Gel 0.01% on the Treatment of Wounds" (2000). Physical Therapy Scholarly Projects. 485.
https://commons.und.edu/pt-grad/485
EVALUATION OF THE EFFECTIVENESS OF REGRANEX (BECAPLERMIN) GEL 0.01% ON THE TREATMENT OF WOUNDS

by

Melissa Wood
Bachelor of Science in Physical Therapy
University of North Dakota, 1999

An Independent Study
Submitted to the Graduate Faculty of the
Department of Physical Therapy
School of Medicine
University of North Dakota
in partial fulfillment of the requirements
for the degree of
Master of Physical Therapy

Grand Forks, North Dakota
May
2000
This Independent Study, submitted by Melissa Wood in partial fulfillment of the requirements for the degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

David Kelling
Faculty Preceptor

Peggy Mahr
Graduate School Advisor

Thomas Moen
Chairperson, Physical Therapy
PERMISSION

Title
Evaluation of the Effectiveness of REGRANEX (becaplermin) Gel 0.01% on the Treatment of Wounds

Department
Physical Therapy

Degree
Master of Physical Therapy

In presenting this Independent Study Report in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the Department of Physical Therapy shall make it freely available for inspection. I further agree that permission for extensive copying for scholarly purposes may be granted by the professor who supervised my work or, in his/her absence, by the Chairperson of the department. It is understood that any copying or publication or other use of this Independent Study Report or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and the University of North Dakota in any scholarly use which may be made of any material in my Independent Study Report.

Signature

Date

12/16/99
# TABLE OF CONTENTS

LIST OF TABLES ...................................................................................................................... v

ACKNOWLEDGMENTS .............................................................................................................. vi

ABSTRACT .................................................................................................................................. vii

CHAPTER

I  INTRODUCTION ....................................................................................................................... 1

II  LITERATURE REVIEW ............................................................................................................. 4

   The Wound Healing Process ................................................................................................. 8
   Impediments in Wound Healing ............................................................................................ 9
   Principles of Good Wound Care ........................................................................................... 11
   Platelet-Derived Growth Factor ............................................................................................ 12
   REGRANEX (becaplermin) Gel 0.01% .................................................................................. 13

III  METHODOLOGY .................................................................................................................. 19

   Subjects ................................................................................................................................. 19
   Instrumentation ..................................................................................................................... 21
   Procedure ............................................................................................................................... 21
   Data Analysis ......................................................................................................................... 21

IV   RESULTS ............................................................................................................................ 22

V    DISCUSSION ........................................................................................................................ 29

APPENDIX A .............................................................................................................................. 32

APPENDIX B .............................................................................................................................. 43

APPENDIX C .............................................................................................................................. 45

REFERENCES ............................................................................................................................ 48
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Demographic Data of Patients Used in Chart Review</td>
<td>20</td>
</tr>
<tr>
<td>2.</td>
<td>Length of Ulcers At Each Time Interval Measured in Centimeters in Patients Treated with REGRANEX</td>
<td>23</td>
</tr>
<tr>
<td>3.</td>
<td>Length of Ulcers At Each Time Interval Measured in Centimeters in Patients Not Treated with REGRANEX</td>
<td>23</td>
</tr>
<tr>
<td>4.</td>
<td>Width of Ulcers At Each Time Interval Measured in Centimeters in Patients Treated with REGRANEX</td>
<td>24</td>
</tr>
<tr>
<td>5.</td>
<td>Width of Ulcers At Each Time Interval Measured in Centimeters in Patients Not Treated with REGRANEX</td>
<td>24</td>
</tr>
<tr>
<td>6.</td>
<td>Measurement of Percent (%)Eschar and Necrotic Tissue At Each Time Interval in Patients Treated with REGRANEX</td>
<td>25</td>
</tr>
<tr>
<td>7.</td>
<td>Measurement of Percent (%)Eschar and Necrotic Tissue At Each Time Interval in Patients Not Treated with REGRANEX</td>
<td>25</td>
</tr>
<tr>
<td>8.</td>
<td>The Mean and Standard Deviation of Percent Eschar of Each Treatment Group</td>
<td>27</td>
</tr>
<tr>
<td>9.</td>
<td>The Mean and Standard Deviation of Size (Area in Centimeters) for Each Treatment Group</td>
<td>27</td>
</tr>
<tr>
<td>10.</td>
<td>Total Number of Wounds with 0% Eschar at Each Time Interval</td>
<td>28</td>
</tr>
<tr>
<td>11.</td>
<td>Total Number of Healed Wounds Based on Size (Area in Centimeters) at Each Time Interval</td>
<td>28</td>
</tr>
</tbody>
</table>
ACKNOWLEDGMENTS

I would like to thank the Staff in the Physical Therapy Department at University of North Dakota, especially Dave Relling, my preceptor, for his instruction and guidance and Renee Mabey for her help with the statistics of this project. I would also like to thank Pat Guthmiller, RN at the Altru Wound Clinic, for her help with the chart review. This Independent Study would not have been possible without my Family for their support throughout my college career and my life, my Friends especially Suzanne Grant and Leslie Harris for their friendship and fun times through PT school without which I would not have kept my sanity, and to Sean Horne for his love, support and encouragement.
ABSTRACT

REGRANEX (becaplermin[rhPDGF-BB]) Gel 0.01% is a topical gel used for the treatment of chronic lower extremity diabetic neuropathic ulcers (8 weeks or longer). It contains growth factors to aid in healing by promoting the formation of granulation tissue. Becaplermin[rhPDGF-BB] is the only growth factor to show clinical efficacy and to be approved by the FDA. The purpose of this study is to evaluate the effectiveness of this topical gel to speed the closing of wounds and/or production of healthy granulation tissue.

To accomplish this evaluation, a chart review was done at Altru Health Systems. A list of names of patients who have been treated at the wound clinic was attained and a chart review was done on the basis of this list. Eight patient charts, 4 of which received REGRANEX and 4 that did not receive REGRANEX were reviewed. Objective data collected from the charts included: length, width and depth of the wound, percent granulation tissue, location, cleansing and dressing of the wound. A statistical analysis was performed to determine if REGRANEX was an effective wound topical gel. This study demonstrated REGRANEX is associated with less eschar and therefore more granulation tissue when viewed by the clinician. However, no significant difference was found with statistical analysis. Improvement in the formation of granulation tissue is a plus for patients with diabetes because it may prevent them from enduring the pain or other side effects that go along with debridement.
CHAPTER I
INTRODUCTION

REGRANEX (becaplermin) Gel 0.01% was approved by the Food and Drug Administration in December 1997 as a treatment for lower extremity diabetic neuropathic ulcers. It is a topical gel that contains growth factors to promote the formation of granulation tissue.

A common and serious complication of Diabetes Mellitus is lower extremity diabetic ulcers, which can lead to amputations. They are difficult to heal, may last for months and often become infected because they remain open. Patients with diabetes have decreased immunological systems that make it difficult for the body to fight infections. Ulcers result from a variety of etiological factors. Inability to heal is the main identifying factor of a chronic ulcer. Minor trauma has been sited as a major contributing factor to lower extremity ulcers and can lead to amputations. An example of this is trauma related to foot wear.

Approximately 15% of people diagnosed with diabetes will develop a foot ulcer during their lifetime. Each year 2% to 3% of people with diabetes will develop a foot ulcer. There are approximately 162,000 annual hospitalizations for foot ulcers and 46% of them have been diagnosed with diabetes. In 1990, 2.8 million people with diabetes were hospitalized. Approximately 6% of those also had a diagnosis related to lower extremity ulcers. Of patients hospitalized with diabetes, the length of stay was 59% longer if they also had a foot ulcer.
If left untreated or treated incorrectly, ulcers may become infected and develop gangrene which is the leading cause of amputations in a patient with diabetes.\textsuperscript{1,3} Approximately 85\% of all nontraumatic lower limb amputations start out as a foot ulcer.\textsuperscript{2} Half of the amputations that are performed in the US are done on people with diabetes. In people with diabetes, the annual amputation rate is 15 to 40 times higher than the rate in nondiabetic people.\textsuperscript{1} Each year approximately 67,000 amputations are performed on people with diabetes.\textsuperscript{1,3,4,5} Nearly half of those people will have further amputations of the same leg or the opposite leg within 5 years.\textsuperscript{1,4} Survival rate for individuals with diabetes who have had a lower-limb amputation is 50\% after the first 3 years and about 40\% after 5 years.\textsuperscript{1,3}

Problem Statement

Social and economic burdens are associated with lower extremity ulcers.\textsuperscript{3} Some of these are loss of income and function and a decline in the patient’s quality of life. Some economic costs include costs of hospital care, doctor visits, operations, rehabilitation, artificial limbs, and long-term care.\textsuperscript{4} A rapid healing rate can have important social and economic advantages for patients and their caregivers.\textsuperscript{3} REGRANEX can provide a treatment for these ulcers which can decrease the cost by healing ulcers faster. Since REGRANEX is a fairly new product, only a small amount of literature has been published about the effectiveness of this topical ointment. This study will also provide information about ulcers, healing, REGRANEX and a review of previous clinical studies completed on REGRANEX.

Purpose of the Study

The purpose of this study is to evaluate the effectiveness of REGRANEX (becaplermin) topical gel to speed the closing of wounds and/or production of healthy granulation tissue. A retrospective chart review of patients that received REGRANEX as a treatment was performed to accomplish this purpose.
Significance of the Study

As Physical Therapists we are involved in the treatment of wounds. The significance of this study is to make healthcare employees aware of this type of product as another alternative in the treatment of lower extremity diabetic neuropathic ulcers. This product may be able to improve patient's lives so they continue as a productive citizen.

Research Questions

How does this growth factor effect wound healing?
What is a lower extremity diabetic neuropathic ulcer and how do you treat them?
What are the stages of wound healing and what is involved in each stage?
What is REGRANEX?
How safe and effective has REGRANEX been in previous clinical studies, including animal and human studies?

Hypotheses

This Independent Study investigates the ability of REGRANEX to speed the closing of wounds and/or increase the production of granulation tissue. Healing is defined as a decrease in the amount of percent eschar and area of the wound. Using statistical analysis, is there a significant difference in healing between treatment groups (REGRANEX and No REGRANEX) over a 3 month period?
CHAPTER II
LITERATURE REVIEW

There are five major factors which contribute to the development and persistence of chronic lower extremity ulcers. They are neuropathy, peripheral vascular disease, edema, metabolic factors and infection. When these factors are combined with normal mechanical stress during weight bearing, the lower extremity becomes vulnerable to the development of ulcers.

Neuropathy

Most patients with diabetic ulcers on the medial, lateral and plantar surfaces of the foot have some degree of neuropathy. Neuropathy effects more than 80% of patients with diabetic foot ulcers. Neuropathy is one of the causing factors in 60% of lower extremity amputations. Slow healing and resistance to traditional treatments are some of the characteristics of diabetic neuropathic ulcers. Other characteristics include loss of motor, sensory and autonomic neural function.

Motor neuropathy will reduce or eliminate nerve signals that are sent to muscle to keep proper tension and tone of the muscles. Muscle weakness, atrophy and paresis are some of the results of motor neuropathy. These structural changes make the foot vulnerable to injury from wearing shoes which do not fit properly, trauma or repetitive stress. Motor neuropathy can also cause foot deformities such as hammer toes, Charcot's joint or neuro-osteoarthropathy. The imbalance of muscles can lead to cavus or high arched foot.
The clawing of the toes can also cause alterations in the fat pads that protect the metatarsal heads.\textsuperscript{1,6} The muscles and fat pads may be thinner.\textsuperscript{1} This makes the plantar surface of the foot more susceptible to neuropathic ulcers especially under the metatarsal heads. The toes are unable to bear weight when they are severely clawed and the weight is then distributed to the metatarsal heads.\textsuperscript{6} It has been found that 90\% of diabetic ulcers occur on the foot where pressure from weight bearing is high.

Sensory neuropathy in a person with diabetes will produce a loss of protective sensation. The person then becomes vulnerable to injury from pain, pressure and heat.\textsuperscript{2} Minor trauma may not be felt by the patient and may go unnoticed for a period of time. Examples of minor traumas leading to ulceration include foreign objects entering the body while barefoot, shoes that do not fit properly, trauma from nail trimming, and burns caused by hot water or warming feet on a radiator.\textsuperscript{4} When sensation is lost, the person may not even realize they have an ulcer.\textsuperscript{6} The smell, blood stained sock or another person's discovery may be the only way the person with diabetes becomes aware they have an ulcer. They may also have a loss of proprioceptive sensation.\textsuperscript{2} With this loss, the person is unable to judge what position their feet are in when they make contact with the ground.

Autonomic neuropathy will alter blood flow in the peripheral vessels and decrease perspiration.\textsuperscript{1} These conditions along with warm and overly dry feet contribute to skin breakdown, such as fissures and cracks.\textsuperscript{1,2,6} The patient with diabetes has a distinctive appearance to their foot with these neuropathic changes.\textsuperscript{6} This includes a cavus (high arched), dry, insensitive foot with dilated veins, good pulses, clawed toes, and hyperkeratosis under the forefoot and heel.
Peripheral Vascular Disease

Peripheral Vascular Disease (PVD) or ischemia as the only factor in ulcers is rare and occurs in about 10% to 15% of patients with diabetic foot ulcers. It is common, however, for patients to have some degree of decreased blood supply. About 15% to 20% have a mix of neuropathy and ischemia. PVD has been a factor in 62% of non-healing lower extremity diabetic ulcers. In 46% of amputations, PVD has been the causing factor. PVD is four times higher in patients with diabetes than patients without diabetes.

An early sign of PVD is claudication which presents as leg pain on walking distances. Patients with diabetes may not be able to describe the pain due to neuropathy. For this reason they may not realize they have the PVD until tissue loss and gangrene occur. Ninety percent of patients with diabetes have surgically correctable occlusions.

Most ulcers due to PVD or ischemia occur in distal parts of the foot (i.e. the toes). Patients with diabetes, who smoke, have hyperlipidemia, and hypertension are at risk for atherosclerosis. The most commonly affected vessels are the superficial femoral, tibial, and peroneal arteries. A single vessel is usually not the only involvement. In a person with diabetes and PVD the usual findings include a bounding popliteal pulse and no pulse in the foot.

Peripheral Vascular Disease contributes to limb ulceration, gangrene and it delays healing. It increases the chances of acquiring an infection and decreases the body’s ability to fight infection by decreasing the oxygen, nutrients and antibiotics to the area. In one study, it was shown that low (less than 30 mm Hg) transcutaneous oxygen tension is a risk factor for foot ulcers.
Ulcers can occur with a constant low pressure applied over a length of time in an ischemic foot. Shoes and especially new shoes have been shown to cause ulcers due to ischemia. People with diabetes are encouraged to wear new shoes for short periods of time to prevent ulceration from happening. If an ischemic ulcer is formed, the blood supply needed to heal the ulcer is greater than the blood supply needed for the intact skin.

**Edema**

Painful lower extremity edema may be present even in patients with neuropathy. It delays wound healing by decreasing the cutaneous blood supply. When the patient's shoes do not allow for edema, the increased pressure makes their feet vulnerable to minor trauma and ulcers. Treatment for edema includes control of infection, foot elevation, compression stockings, elastic leg wraps and pneumatic compression devices.

**Metabolic factors**

Hyperglycemia, or high glucose levels, is common in patients with diabetes. The effects of hyperglycemia influence the development of complications in diabetic patients. These complications usually appear 15 years after hyperglycemia develops. With hyperglycemia, sorbitol accumulates on nerves and attributes to neuropathy. Another possible metabolic disturbance is in the glycation of proteins including collagen and fibrin. Glycated proteins contribute to the microvascular and macrovascular derangements of diabetes. This causes problems because an essential part of wound healing is the synthesis of proteins such as fibroblasts and collagen.

**Infection**

Some factors that predispose patients to infection include poor granulation tissue formation, prolonged persistence of abscesses and impaired wound healing. Abnormal leukocyte function develops from high glucose and low oxygen levels, which increases a patient's risk for developing infections once the skin is broken. The possibility of infection is increased in areas where bacteria is high (i.e. the foot). Some complications
of infection that may develop include cellulitis, osteomyelitis and gangrene. These often lead to amputations.

Once infection has occurred, it can delay wound healing. It has been shown that wounds with greater than $10^5$ colonies of bacteria per gram of tissue have a lower healing rate than those with fewer bacterial colonies. Infection prolongs inflammation which delays wound healing and contributes to chronic lower extremity diabetic ulcers.

The Wound Healing Process

Normal wound healing happens in an orderly progression. The injury occurs, platelets arrive and release coagulation factors and growth factors. Homeostasis is achieved by intense vasoconstriction for 5 to 10 minutes after injury. The wound is cleared of dead tissue and foreign material. The wound is then ready for healing and regeneration. There are 3 phases involved in normal wound healing: Inflammation, Proliferation and Remodeling.

The inflammation phase lasts 4 to 6 days after injury. After the initial vasoconstriction, vasodilation occurs to allow capillary permeability. During this time cells are recruited into the wound in an orderly fashion. This is regulated by growth factors, including platelet-derived growth factor (PDGF), which are released by the platelets during coagulation. An influx of cells occur including neutrophils, macrophages and fibroblasts. Neutrophils are among the first to arrive. Macrophages job is to kill bacteria and ingest debris. There must be adequate tissue oxygen tension for the killing of bacteria to occur. During the first 3 hours it is important to kill the bacteria to prevent colonization. Macrophages are also a significant source of growth factors, such as PDGF which play a key role in migration and activation of wound fibroblasts.

The proliferative phase begins 4-6 days after injury and lasts approximately 3 weeks. Neovascularization occurs with the creation of an extracellular matrix, including collagen, in the wound bed and epithelialization. This phase is regulated by growth factors
that are secreted by macrophages and fibroblasts. Fibroblasts produce substances essential for wound repair. They are the main source of collagen and wound connective tissue. With no infection present, there is a continual decrease in the number of inflammatory cells.

The remodeling phase begins 3-4 weeks after injury and it may continue for up to 2 years. There is a balance of collagen deposition and degradation. There is a reorganization of collagen fibers into a more organized structure. The collagen continues to increase in tensile strength to withstand outside forces better than tissue prior to remodeling. It eventually reaches a plateau which is only 80% as strong as normal tissue.

Impediments in Wound Healing

A chronic wound does not heal in an orderly progression and it has decreased structural integrity. Skin ulcers are the most common chronic wound. Seventy percent are due to pressure ulcers, diabetic foot ulcers and venous ulcers. Some factors which impede healing include wound hypoxia, infection, presence of debris and necrotic tissue, use of anti-inflammatory medications, a diet deficient in vitamins or minerals, or general nutritional deficiencies, tumors, environmental factors and metabolic disorders. If factors that impede wound healing are identified and controlled the wound will heal faster. Studies have suggested that growth factors may stimulate healing. Growth factors will work more efficiently in an environment free of these factors.

Wound hypoxia is the lack of oxygen to a wound. If there is only 30 to 40 mm Hg of oxygen present, fibroblasts cannot replicate and collagen production is limited. Wound hypoxia also leaves the wound vulnerable to bacteria. Possible causes of hypoxia are scar tissue around the vessels which decrease diffusion of oxygen and nutrients. This is the case with venous ulcers. Compressive therapy is used to treat this condition. In the case of arterial insufficiency, treatment should include bypass grafting to increase the amount of oxygen delivered to the area.
Infection of a wound may decrease healing by releasing bacterial enzymes that lessen the effects of fibrin and growth factors. All wounds have some bacteria present. As stated before if there is more than $10^5$ bacteria per gram of tissue present, the wound is considered infected. When foreign debris is present in a wound, it does not take as many bacteria to cause an infection. Bacteria are able to grow in the dead tissue. Debridement is the main way to rid bacteria from the wound.

The use of anti-inflammatory drugs impedes wound healing. Steroids, an example of these, reduce wound healing by delaying inflammation. These effects can be reversed by the administration of vitamin A. Nonsteroidal anti-inflammatory drugs also impede wound healing. Examples of these are aspirin and ibuprofen. They decrease collagen production and the exact mechanism is unknown. Patients may need to change pain medication until the wound shows signs of healing.

Tobacco is another impeding factor. It increases hypoxia or decreases oxygen to the wound. This occurs because the blood vessels are vasoconstricted. The patient should be encouraged to limit tobacco use, including nicotine patches. Vitamin and mineral deficiencies can also play a large role in impeding wound healing. If there is any doubt as to the patient’s nutritional status, supplements should be given.

Tumors should be considered as a differential diagnosis when evaluating a wound. Chronic skin cancer may result in tumors. A chronic wound is also at risk of developing a Marjolin’s ulcer which is aggressive squamous cell carcinoma. A tissue biopsy should be performed if etiology is in doubt. The use of topical growth factors is contraindicated if malignancy is present.

Some environmental factors which delay wound healing include pressure and wound temperature. Pressure must be relieved from the wound for it to heal. Wound temperature of less than 30 degrees Celsius reduces the wound’s strength after healing. This is most likely due to vasoconstriction and decreased perfusion.
The metabolic disorder diabetes mellitus is one of the most common diseases in patient with chronic wounds. It impairs wound healing in all 3 phases. Patients with diabetes have a decreased inflammatory response, fibroblast proliferation, and collagen accumulation, due to the high glucose concentrations. This decreases the tensile strength of the wound. The healed wound will only be approximately 80% the original strength which leaves them vulnerable to reinjury.

Poor blood glucose control also impairs leukocyte function which increases susceptibility to infection. The macrophages’ ability to kill bacteria is reduced and makes chronic wounds more difficult to heal. Disease management should be implemented to prevent and heal ulcers.

Principles of Good Wound Care

Growth factors, such as rhPDGF, are more effective when combined with good wound care. Good wound care includes first assessing the wound and then determining the extent of damage and the cause of the wound. The most important components of good wound care include debridement, infection control, pressure relief and maintaining a moist wound bed.

In one study it was determined that debridement plays a vital role in the care of chronic diabetic foot ulcers. Debridement removes useless and dead tissue, which includes callus, necrotic tissue and infected tissue. This tissue impedes healing and increases the risk of infection. Debridement has many advantages. The examiner is able to inspect the wound easier for infection. When removing calluses, excess pressure on the wound may be relieved. The examiner can view any other sources of pressure (i.e. bony prominences) and relieve the pressure point by removing it. Tissue with excessively high bacterial count can be removed to increase healing. Aging or old cells, which may have lost their ability to produce granulation tissue, can be removed from the wound, which may stimulate the production and release of growth factors.
Debridement also enhances the effects of REGRANEX by allowing it access to viable tissue and cell receptor sites.¹

Infection of the wound needs to be controlled due to the fact that it delays healing by prolonging the inflammatory phase of wound healing, destroys healthy tissue and prohibits new tissue from being deposited.¹ Local infection can be prevented by sharp debridement of infected tissue and applying saline moistened gauze dressings. If not prevented, infection of the bone may occur which is known as osteomyelitis.⁴ The most effective way to treat it, is by removing the infected bone. The patient will require antibiotics also.

Non-weight bearing is critically important.⁴ This should be maintained at all times. The use of crutches, a walker, a wheelchair, walking casts, walking splints or other devices can help with off-loading.¹,⁴ If complete off-loading is impossible then try to relieve as much as is possible.¹ Off-loading should be continued for the rest of the patient’s life or the ulcer may reoccur.

It is important that the environment of the wound stay moist.⁸ This prevents further tissue damage.¹ Wounds that are exposed to the air will have an increase in tissue necrosis and death of cells.⁸ If eschar is formed and is not removed, epithelialization will be impaired. Wet-to-dry dressings may be more harmful than beneficial. The dressing may remove the margin where epithelial tissue is forming and therefore impair wound healing. A moist environment can be achieved by changing the dressing 2 times per day with a saline moistened gauze.¹

Platelet-derived Growth Factors (PDGF)

Growth factors were discovered in the late 1970’s.⁹ Platelet-derived growth factors (PDGF) were one of the first growth factors to be discovered and they play an important role in wound healing. The phases of wound healing are initiated and regulated by growth factors which include PDGF.¹ Platelet-derived growth factors are
synthesized and released at or near the wound site. A major source of PDGF are platelets. Macrophages are also a major source of PDGF. Platelet-derived growth factors are also produced by endothelial cells and under certain circumstances, fibroblasts.\(^{10}\)

All the primary healing components either synthesize and release or respond to PDGF indicating how they are an integral part of the wound healing process.\(^1\) Some of the activities that PDGF is involved in include cell mitogenesis and migration and synthesis of protein and extracellular matrix components.\(^{10}\) Cell chemotaxis and proliferation of inflammatory cells is stimulated by PDGF.\(^{1,10}\) Platelet-derived growth factors also stimulate macrophages to migrate to the wound site in later stages of wound healing. During the remodeling phase, PDGF plays an important role in synthesizing the extracellular matrix such as collagen and stimulating the lysis of collagen.

PDGF-BB is a homodimer [two identical proteins (B) are formed together] of PDGF held together by intermolecular disulfide bonds and is a dimeric protein.\(^{1,3,10}\) Becaplermin [rhPDGF-BB], a recombinant human form of PDGF, is produced by inserting the human gene for the B chain of PDGF into the yeast \textit{Saccharomyces cerevisiae}. It is purified and can than be applied to wounds.\(^1\)

Becaplermin (rhPDGF-BB) gel contains either 30 or 100\(\mu\)g of becaplermin per gram of vehicle gel, sodium carboxymethylcellulose aqueous-based gel or NaCMC.\(^{1,3}\) It is commercially known as REGRANEX (becaplermin) Gel 0.01%. REGRANEX (becaplermin) Gel 0.01%

REGRANEX is the first recombinant human growth factor to be developed and approved by the FDA for the treatment of lower extremity diabetic neuropathic ulcers.\(^{1,9}\) The active ingredient is becaplermin.\(^1\) REGRANEX is available in 2, 7.5 or 15 gram multi-use tubes. It is a clear, colorless to straw-colored topical gel.

The 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.¹ When it is used along with good wound care, REGRANEX has been shown to increase the incidence of complete healing. The efficacy in the treatment of other types of chronic, nondiabetic wounds is under investigation.

Contraindications for REGRANEX are few. Those patients with a known hypersensitivity to any component of the gel should not be using this treatment.¹ It is also not to be used with known neoplasms at the site of application. REGRANEX should not be used on wounds that close by primary intention (surgical incisions). The reason is that REGRANEX is a nonsterile, low bioburden, preserved product.

REGRANEX has an excellent safety profile.¹ Although safety and effectiveness have not been established in patients below 16 years of age. In a study in mice, toxicity was not observed at a significant level following a single IV dose of 3 mg/kg becaplermin.¹¹ In another study, systemic toxicity was not evident in rabbits or monkeys following multiple doses of becaplermin. The rabbits also did not show significant dermal irritation. No cardiographic abnormalities were seen in monkeys following high doses of becaplermin.

In a bacteria and mammalian cell mutation assay results indicated that becaplermin was not mutagenic.¹¹ Becaplermin did not induce unscheduled DNA synthesis and it is not considered a reproductive genotoxin or a systemic carcinogen. The study concluded that based on the results, the potential for becaplermin to cause adverse reactions after being applied to open wounds is insignificant.

Similar incidence of adverse reactions such as infection, cellulitis and osteomyelitis occurred in patients receiving REGRANEX, placebo gel and good wound care alone.¹ Erythematous rashes occurred in 2% of patients treated with REGRANEX gel or placebo gel and none in patients receiving good wound care alone. Patients who were treated with REGRANEX did not develop antibodies against becaplermin.
It is not known if REGRANEX can cause fetal harm or be excreted in milk so caution should be used when administering in these situations.\(^1\) It is also not known if REGRANEX interacts with other topical medications that have been applied to the ulcer site. This has not been studied.

**Preclinical Animal Studies**

Animal studies have shown that rhPDGF-BB accelerates the wound healing process by promoting the formation of granulation tissue.\(^1,9,10\) Within these studies epithelialization, contraction, granulation tissue formation, and wound strength were evaluated.\(^9\)

In a guinea pig partial-thickness model it was found that becaplermin had no consistent effect on epithelialization and contraction and these parameters were thrown out of later studies.\(^9\) However, becaplermin was found to be effective in increasing the granulation tissue thickness of the wound bed by at least 2- to 3-fold over vehicle control in this model. The efficacy of becaplermin was reduced in shallow wounds with many hair follicles that epithelialize quickly suggesting that the effects diminishes as the wounds remodel.

In the pig full-thickness model effects of becaplermin on granulation tissue was evident and statistically significant at day 7, but diminishes by day 14, when epithelialization was nearly complete.\(^9\) The conclusion of this study was that PDGF has been repeatedly shown to enhance the formation of granulation tissue in animal studies but its effects on epithelialization and wound contraction has been variable. Becaplermin was developed on the assumption that by stimulating a rich vascular wound bed it would promote epithelial ingrowth. One must take into consideration that no animal study will completely mimic a chronic human wound.
Dosage and Administration

The amount of REGRANEX that should be applied to a wound depends on the size of the ulcer. The first step in deciding the dosage is measuring the greatest length and the greatest width. These two numbers are then multiplied. If they were measured in inches then that number is multiplied by 0.06 and if it is measured in centimeters, it is divided by 4. In other words, each square inch of ulcer surface requires approximately 2/3 inch length of REGRANEX gel from a 15 gram tube. Each square centimeter of ulcer requires 0.25 cm length of REGRANEX gel from a 15 gram tube.

Once the dose is determined REGRANEX gel should be squeezed from the tube onto a clean measuring surface i.e. wax paper. The gel can then be applied with a tongue blade or cotton swab over the ulcer in a thin, continuous layer approximately 1/16 inch thick. It is then covered with saline moistened gauze dressing and left for 12 hours. After that time it is rinsed with saline or water to remove excess gel. The ulcer is then covered with a saline moistened gauze without application of REGRANEX. REGRANEX is to be applied one time per day and excess application has not been proven to be beneficial. The amount of REGRANEX to be applied should be recalculated weekly or biweekly. Use of REGRANEX should be reassessed if the ulcer does not show a decrease in size by 30% after 10 weeks of application or complete healing after 20 weeks. REGRANEX must be stored in the refrigerator.

Clinical Efficacy

Four randomized controlled studies were completed on REGRANEX. There were 922 patients which participated in the studies. The first study was completed on 118 patients with diabetic neurotrophic foot ulcers. They were treated with either REGRANEX Gel 0.003% or a placebo gel. The criteria for the study included all patients free of infection, all ulcers were secondary to neuropathy, had adequate arterial blood supply and wounds were present for at least 8 weeks. Patients were excluded if
they had poor diabetes control, renal failure, abnormal liver function and no patients with exposed bone were included in this study. Patients were treated until the ulcer was completely healed or up to 20 weeks. Healing was defined as 100% closure.

All the patients had aggressive, sharp debridement of callus and necrotic tissue down to bleeding tissue initially and then as needed throughout the study. The mean percentage of office visits where debridement was performed was 46.8% for REGRANEX and 48.0% for the placebo gel. The results of this study included 48% of patients treated with REGRANEX healed and 25% of patients treated with the placebo gel healed during the 20 weeks. For the REGRANEX group, the site with the highest debridement rate had the highest healing rate and the site with the lowest debridement rate had the lowest healing rate. For the placebo group, the site with the lowest debridement rate had the lowest healing rate but at the sites with higher debridement there was no relationship between healing and frequency of debridement.

In a second study 382 patients were treated with either REGRANEX gel 0.01%, REGRANEX gel 0.003% or a placebo gel. The incidence of complete healing for the REGRANEX 0.01% group was 50%, REGRANEX 0.003% group was 36% and the placebo group was 35%. Treatment with REGRANEX 0.01% increased the incidence of complete healing by 43% when compared with the placebo group. The study found that there was no statistically significant difference in the incidence of complete healing between patients receiving REGRANEX 0.003% and the placebo group.

There were 3 groups with 172 patients in the third study. The groups were good wound care alone, good wound care plus NaCMC (Sodium Carboxymethylcellulose) gel and good wound care plus becaplermin gel 100 μg/g, NaCMC is the vehicle gel. It was found that the incidence of complete healing for the good wound care alone was 22%, NaCMC group was 36%, and becaplermin group was 44.
The fourth study included 250 patients. The 2 groups in this study were REGRANEX gel and good wound care alone. The incidence of complete healing for the REGRANEX group was 36% and for good wound care alone was 32%. These were not statistically different in this study.

There was a 3 month follow-up study completed for the incidence of ulcer recurrence. It was found that 30% of patients had an incidence of ulcer recurrence. This demonstrates that the ulcers were of comparable durability across all treatment groups.
CHAPTER III

METHODOLOGY

A review of medical charts was completed at Altru Wound Clinic to determine if REGRANEX is effective in speeding the closing of wounds and/or production of healthy granulation tissue. Altru Wound Clinic was contacted for permission to review charts on adult patients (18 years or older) who had been treated for lower extremity ulcers.

Subjects

Medical charts selected included patients who had received REGRANEX as a treatment for lower extremity ulcer(s) and patients who did not receive REGRANEX as a treatment but had a similar medical background. A description of demographic data on subjects included in this study is summarized in Table 1.

Subjects were assigned to 2 separate groups on the basis of treatment. The treatment group received REGRANEX application 1 time per day while the control group did not receive REGRANEX. Both groups received normal clean wound care. Information on the treatment they received was located in their medical charts.

Approval and Consent forms

Approval was obtained prior to any collection of data. This was accomplished by completing a University of North Dakota (UND) Human Subject Review Form (Appendix A) and submitting it to the UND Institutional Review Board. Approval was also obtained from Altru Health Systems Institutional Review Board.
Table 1. Demographic data of patients used in chart review.

<table>
<thead>
<tr>
<th>ID#</th>
<th>SEX</th>
<th>DATE OF BIRTH</th>
<th>REGRANEX / NO REGRANEX</th>
<th>PAST MEDICAL HISTORY</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>06/05/11</td>
<td>REGRANEX</td>
<td>Cellulitis</td>
<td>Venous stasis ulcer, dermatitis, venous insufficiency</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>12/28/26</td>
<td>No REGRANEX</td>
<td>Carotid occlusive disease, AAA, gout, renal insufficiency, heart bypass</td>
<td>Diabetes, severe neuropathy, PVD, coronary disease, COPD, obesity</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>08/09/42</td>
<td>No REGRANEX</td>
<td>CHF, renal insufficiency, (B) carotid artery stenosis</td>
<td>Diabetes, chronic calcaneal osteomyelitis, HTN, obesity, asthma, good circulation</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>11/14/60</td>
<td>No REGRANEX</td>
<td>Good arterial circulation</td>
<td>Ulcer left foot, Diabetes, peripheral neuropathy, HTN, asthma</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>07/07/24</td>
<td>No REGRANEX</td>
<td>Head and neck cancer, normal circulation, claudication</td>
<td>Diabetes, Neuropathy</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>06/21/38</td>
<td>REGRANEX</td>
<td>Ovarian cancer, cellulitis</td>
<td>Diabetes, severe neuropathy, Charcot foot</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>04/24/37</td>
<td>REGRANEX</td>
<td>HTN, orthotic, normal arteriole circulation</td>
<td>Neuropathic, chronic and recurrent left heel ulcer</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>08/03/27</td>
<td>REGRANEX</td>
<td>Smoker, HTN</td>
<td>Diabetes, neuropathy, pressure ulcer left heel, arteriole insufficiency</td>
</tr>
</tbody>
</table>
Instrumentation

A data collection tool (Appendix B) was used to gather demographic data, location of wound, treatment procedure, length, width, depth and percent granulation and other information about the patient and their wounds.

Procedure

Upon completion of the approval process, a list of names was compiled by the Altru Wound Clinic. This list included subjects who had received REGRANEX and subjects who did not receive REGRANEX as a treatment but had similar medical backgrounds. Altru Medical Records department was then contacted and given the list of names. The chart review took place at the medical records department.

Data was gathered from the Altru Initial Wound Documentation Record and the Altru Wound Care Flowsheet (Appendix C) in the chart using the data collection tool (Appendix B) previously described under instrumentation.

Data Analysis

The independent variables used in this study included treatment, REGRANEX or no REGRANEX, and time (Start, Month 1, Month 2, Month 3). The dependent variable used was size of wound (area) and the percentage of eschar. Data collected will be analyzed with the Statistical Package for Social Sciences (SPSS) version 8.0 software to demonstrate if there is significant improvement in size of ulcer when compared with the nominal data of treatment, time and measure. An alpha level of .05 will be used during analysis.
CHAPTER IV

RESULTS

Eight charts were reviewed at Altru Health Systems, one was eliminated due to the type of ulcer and the patient’s medical history. A total of 12 wounds were evaluated from which data collected included the percentage of eschar and wound size (area = length x width). This information was utilized to evaluate the effectiveness of REGRANEX (becaplermin) gel 0.01% to speed the closing of wounds and/or production of healthy granulation tissue. The length and width of the ulcers were measured in centimeters and are recorded in Tables 2 and 4 for patients who were treated with REGRANEX. Information for those individuals who did not receive REGRANEX can be found in Tables 3 and 5. Percentage of eschar can be found in Tables 6 and 7. Data was analyzed on SPSS using a two-way analysis of variance.¹³

The statistical analysis for percent eschar is as follows:

- An interaction occurred between treatment and time. F(3,31) = 3.417; p < 0.05; p = 0.03
- Treatment has a significant effect on percent eschar. F(1,31) = 11.371; p < 0.05; p = 0.002
- Time has a significant effect on percent eschar. F(3,31) = 5.810; p < 0.05; p = 0.003

When looking at time as a simple main effect for percent eschar:

- There was a significant difference between times for percent eschar with no REGRANEX. F(3,31) = 4.829; p < 0.05; p = 0.015. The significant difference was between initial evaluation and month 2.
Table 2. Length of ulcers at each time interval measured in centimeters in patients treated with REGRANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1&lt;sup&gt;ST&lt;/sup&gt; MONTH</th>
<th>2&lt;sup&gt;ND&lt;/sup&gt; MONTH</th>
<th>3&lt;sup&gt;RD&lt;/sup&gt; MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right medial ankle</td>
<td>3.3</td>
<td>3</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td>1</td>
<td>Right lateral ankle</td>
<td>1.5</td>
<td>1.5</td>
<td>1.4</td>
<td>1.3</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-lateral</td>
<td>0.7</td>
<td>0.6</td>
<td>0.2</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-middle</td>
<td>0.3</td>
<td>0.2</td>
<td>Healed</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-medial</td>
<td>3.5</td>
<td>2.7</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>8</td>
<td>Left heel</td>
<td>2.4</td>
<td>2.7</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>9</td>
<td>Left heel</td>
<td>1.2</td>
<td>0.13</td>
<td>0.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Table 3. Length of ulcers at each time interval measured in centimeters in patients not treated with REGANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1&lt;sup&gt;ST&lt;/sup&gt; MONTH</th>
<th>2&lt;sup&gt;ND&lt;/sup&gt; MONTH</th>
<th>3&lt;sup&gt;RD&lt;/sup&gt; MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Right great toe</td>
<td>1</td>
<td>0.6</td>
<td>0.2</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>Left great toe</td>
<td>2.1</td>
<td>1.0</td>
<td>0.8</td>
<td>*</td>
</tr>
<tr>
<td>3</td>
<td>Right heel plantar</td>
<td>3.4</td>
<td>Not measured</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-base</td>
<td>0.3</td>
<td>Not measured</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-lateral</td>
<td>0.3</td>
<td>0.2</td>
<td>Healed</td>
<td>Healed</td>
</tr>
<tr>
<td>5</td>
<td>Right heel-medial</td>
<td>2</td>
<td>2</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>5</td>
<td>Right great toe</td>
<td>0.2</td>
<td>0.1</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* These patients did not return to the physician.
Table 4. Width of ulcers at each time interval measured in centimeters in patients treated with REGRANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1&lt;sup&gt;ST&lt;/sup&gt; MONTH</th>
<th>2&lt;sup&gt;ND&lt;/sup&gt; MONTH</th>
<th>3&lt;sup&gt;RD&lt;/sup&gt; MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right medial ankle</td>
<td>1.3</td>
<td>1.1</td>
<td>1.1</td>
<td>1.2</td>
</tr>
<tr>
<td>1</td>
<td>Right lateral ankle</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-lateral</td>
<td>1.2</td>
<td>0.7</td>
<td>0.5</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-middle</td>
<td>0.3</td>
<td>0.2</td>
<td>Healed</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-medial</td>
<td>3.4</td>
<td>2.9</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>8</td>
<td>Left heel</td>
<td>2.1</td>
<td>2.4</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>9</td>
<td>Left heel</td>
<td>0.4</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table 5. Width of ulcers at each time interval measured in centimeters in patients not treated with REGRANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1&lt;sup&gt;ST&lt;/sup&gt; MONTH</th>
<th>2&lt;sup&gt;ND&lt;/sup&gt; MONTH</th>
<th>3&lt;sup&gt;RD&lt;/sup&gt; MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Right great toe</td>
<td>0.7</td>
<td>0.4</td>
<td>0.3</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>Left great toe</td>
<td>1.5</td>
<td>1.4</td>
<td>1.1</td>
<td>*</td>
</tr>
<tr>
<td>3</td>
<td>Right heel plantar</td>
<td>3.4</td>
<td>Not measured</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-base</td>
<td>4.7</td>
<td>Not measured</td>
<td>2.5</td>
<td>0.7</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-lateral</td>
<td>2.7</td>
<td>0.2</td>
<td>Healed</td>
<td>Healed</td>
</tr>
<tr>
<td>5</td>
<td>Right heel-medial</td>
<td>1.0</td>
<td>1.3</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>5</td>
<td>Right great toe</td>
<td>0.2</td>
<td>0.1</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* These patients did not return to the physician.
Table 6. Measurement of percent (%) eschar and necrotic tissue at each time interval in patients treated with REGRANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1ST MONTH</th>
<th>2ND MONTH</th>
<th>3RD MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right medial ankle</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>1</td>
<td>Right lateral ankle</td>
<td>50</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-lateral</td>
<td>20</td>
<td>0</td>
<td>10</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-middle</td>
<td>Not measured</td>
<td>Not measured</td>
<td>Healed</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Right foot plantar-medial</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Left heel</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>Left heel</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 7. Measurement of percent (%) eschar and necrotic tissue at each time interval in patients not treated with REGRANEX.

<table>
<thead>
<tr>
<th>ID#</th>
<th>LOCATION OF ULCER</th>
<th>INITIAL</th>
<th>1ST MONTH</th>
<th>2ND MONTH</th>
<th>3RD MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Right great toe</td>
<td>50</td>
<td>60</td>
<td>10</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>Left great toe</td>
<td>90</td>
<td>85</td>
<td>30</td>
<td>*</td>
</tr>
<tr>
<td>3</td>
<td>Right heel plantar</td>
<td>60</td>
<td>90</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-base</td>
<td>20</td>
<td>20</td>
<td>Pale pink callous</td>
<td>Not measured</td>
</tr>
<tr>
<td>4</td>
<td>Left great toe-lateral</td>
<td>Not measured</td>
<td>10</td>
<td>Callous</td>
<td>Healed</td>
</tr>
<tr>
<td>5</td>
<td>Right heel-medial</td>
<td>80</td>
<td>70</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>5</td>
<td>Right great toe</td>
<td>100</td>
<td>10</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* These patients did not return to the physician.
• There was no significant difference between times for percent eschar with
  REGRANEX. \( F(3,31) = 2.554; p < 0.05; p = 0.097 \)

When looking at treatment as a simple main effect for percent eschar:

• There was a significant difference in percent eschar at initial evaluation between
treatment groups. \( F(1,31) = 12.224; p < 0.05; p = 0.008 \)

• There was a significant difference in percent eschar at month 1 between treatment
groups. \( F(1,31) = 5.136; p < 0.05; p = 0.050 \)

• There was no significant difference in percent eschar at month 2 between treatment
groups. \( F(1,31) = 1.464; p < 0.05; p = 0.266 \)

• There was no significant difference in percent eschar at month 3 between treatment
groups. \( F(1,31) = 0.357; p < 0.05; p = 0.576 \)

The statistical analysis for size (area in centimeters) is as follows:

• No interaction occurred between treatment and time. \( F(3,30) = 0.068; p < 0.05; p = 0.976 \)

• Treatment had no significant effect on size. \( F(1,30) = 1.952; p < 0.05; p = 0.173 \)

• Time had no significant effect on size. \( F(3,30) = 0.813; p < 0.05; p = 0.497 \)

When looking at main effects only without a two way interaction:

• There was no significant difference in size (area in centimeter) between treatments.
  \( F(1,30) = 2.126; p < 0.05; p = 0.154 \)

• There was no significant difference in size (area in centimeter) between time.
  \( F(3,30) = 0.942; p < 0.05; p = 0.431 \)

When looking at time as a simple main effect:

• There was no significant difference for size (area in centimeter) with no
  REGRANEX. \( F(3,30) = 1.014; p < 0.05; p = 0.416 \)
• There was no significant difference for size (area in centimeter) with REGRANEX.
  
  \( F(3,30) = 0.211; p < 0.05; p = 0.887 \)

**Table 8.** The mean and standard deviation of percent eschar of each treatment group.

<table>
<thead>
<tr>
<th>Group</th>
<th>INITIAL</th>
<th>MONTH 1</th>
<th>MONTH 2</th>
<th>MONTH 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>REGRANEX</td>
<td>12.5 ± 9.6</td>
<td>0 ± 0</td>
<td>2 ± 4.5</td>
<td>4 ± 8.9</td>
</tr>
<tr>
<td>Non-REGRANEX</td>
<td>66.7 ± 29.4</td>
<td>37.9 ± 32.6</td>
<td>10 ± 14.1</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

**Table 9.** The mean and standard deviation of size (area in centimeters) for each treatment group.

<table>
<thead>
<tr>
<th>Group</th>
<th>INITIAL</th>
<th>MONTH 1</th>
<th>MONTH 2</th>
<th>MONTH 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>REGRANEX</td>
<td>3.7 ± 5.0</td>
<td>3.0 ± 3.9</td>
<td>2.1 ± 3.1</td>
<td>2.0 ± 3.1</td>
</tr>
<tr>
<td>Non-REGRANEX</td>
<td>2.8 ± 4.0</td>
<td>0.9 ± 1.1</td>
<td>0.4 ± 0.5</td>
<td>0.2 ± 0.3</td>
</tr>
</tbody>
</table>

When looking at Table 10, the number of wounds having 0% eschar increased for the REGRANEX group.

**Table 10.** Total number of wounds with 0% eschar at each time interval.

<table>
<thead>
<tr>
<th>Group</th>
<th>INITIAL</th>
<th>MONTH 1</th>
<th>MONTH 2</th>
<th>MONTH 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>REGRANEX</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Non-REGRANEX</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>
When looking at Table 11, the total number of healed wounds based on the area at Month 3 was 2 with REGRANEX and 1 with No REGRANEX.

**Table 11.** Total number of healed wounds based on size (area in centimeters) at each time interval.

<table>
<thead>
<tr>
<th>Group</th>
<th>INITIAL</th>
<th>MONTH 1</th>
<th>MONTH 2</th>
<th>MONTH 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>REGRANEX</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Non-REGRANEX</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
CHAPTER V
DISCUSSION

Depth measurements were not included in this study due to the fact that some of the measurements were either not taken or not recorded in the charts. It was felt that the missing information would not give accurate statistical data so therefore it was not include in this study.

It was also felt that the subject with the ID number of 1 should not be included in the statistical analysis. This subject's ulcer was diagnosed as a venous stasis ulcer. Since REGRANEX is approved for lower extremity diabetic neuropathic ulcers, it was decided that only subjects who carried this diagnosis would be included in the study.

The treatment groups were very different from the start. This makes it difficult to compare them. The mean of percent of eschar changed from 66.667% to 0% for the non-REGRANEX group and 12.5% to 4% for the REGRANEX group. The mean size (area in centimeters) changed from 2.81 to 0.21 for the non-REGRANEX group and 3.67 to 2.004 for the REGRANEX group. This indicates that the non-REGRANEX group had more eschar and the area was smaller than the REGRANEX group. It also shows that size of the wound changed more with the non-REGRANEX group then with the REGRANEX group.

The statistical analysis appears to demonstrate that REGRANEX was not effective in this retrospective clinical trial. An interaction did occurred between treatment and time for percent eschar. However it was for the non-REGRANEX group
and it occurred between initial evaluation and Month 2. There was also a significant difference for percent eschar at initial evaluation and Month 1 between treatment groups but again these groups were very different from the start.

Even though it was not shown to be very effective, the REGRANEX group has an overall decrease in eschar tissue and increase in granulation tissue when compared to the non-REGRANEX group when looking at Table 12 in Chapter IV. At initial evaluation the REGRANEX group had 1 patient with 0% eschar and at Month 1 there were 4 patients with 0% eschar. This indicates that REGRANEX does increase granulation tissue. This is consistent with the literature. REGRANEX has been proven in previous studies to increase the formation of granulation tissue.(A,I,N)

When looking at size (area in centimeters), there was no interaction that occurred between the time and treatment groups. No significant differences were found when looking at the main effects and simple main effects for either treatment group or time.

Limitations

There were several limiting factors to this study. Since this study was done in a small community, one limitation of this study was the insufficient number of subjects who received REGRANEX. Statistical analysis was done on 7 subjects with a total of 12 ulcers. A larger group would have given more accurate statistical outcomes. A minimum of 25 to 30 randomly selected charts should be used for increased accuracy.

There were some limiting factors because this was a chart review. They included interrater reliability and validity, patient compliance and the treatment of non-REGRANEX patients. Interrater reliability and validity was impossible to achieve due to the varied number of people who did the measuring and treating of the ulcers. Patient compliance was also a factor. There is no access to patients when doing a chart review so I was unable to check to see if patients were following their prescribed treatment. The treatment regimen for non-REGRANEX varied and this can affect healing. Another
limiting factor was that some data was missing from the charts. This limited the amount of statistical analysis that could be completed on this study.

Possible Future Studies

Since there is a difference in literature as to the effectiveness of REGRANEX, it should be investigated further. Future studies could also focus on venous stasis ulcers and pressure ulcers to see how effective REGRANEX is in these cases. Currently there is no literature available on how effective REGRANEX may be in these areas.

Conclusion

Since Physical Therapists are involved in wound care, I feel it is important for them to have information on the products they may be using in the clinic. This way they can make their own personal decision about the product. This study gives them a background on what REGRANEX is and investigates how and if it works. This study demonstrated REGRANEX is associated with less eschar and therefore more granulation tissue when viewed by the clinician. However, this was found to be not significant with statistical analysis. REGRANEX does not increase the incidence of healing when compared with patients who have not received REGRANEX as a treatment. Improvement in the formation of granulation tissue is a plus for patients with diabetes because it may prevent them from enduring the pain or other side effects that go along with debridement. The use of growth factors is good in theory but further investigation is warranted further, with a larger group, as to whether or not it works in the clinic.
APPENDIX A
APPLICATION TO CONDUCT RESEARCH AT ALTRU HEALTH SYSTEM FACILITIES

Any researcher proposing to conduct research using patients, staff, or records of Altru Health System must obtain organizational approval as well as IRB approval. Complete this application form and submit it along with a brief summary of the study, including consent and instruments to: Virginia Esslinger, MS, RN, Altru Health Research Center, P.O. Box 6002, Grand Forks, ND 58206-6002

Name: Melissa Wood
Address: 750 N. 43rd St. #478, Grand Forks, ND 58207
Telephones numbers: Work, Home
Department/College: UND School of Medicine/Physical Therapy
Project Title: Evaluation of the effectiveness of Regamycin (trepocol) on the treatment of wounds

Status of applicant (check all that apply):

- [ ] Altru physician/staff member
- [x] Student
  - Department: UND School of Medicine/Physical Therapy
  - Advisor: Dave Belling, MS, PT
  - Relationship to Altru, if any:
    - Coursework
    - Thesis
    - Dissertation
    - Other Independent Study
- [ ] Faculty
  - College/Department
  - Relationship to Altru, if any
- [ ] Other
  - Organization
  - Position
  - Relationship to Altru, if any

Please answer the following questions:

1. Describe the nature and extent of involvement expected of Altru staff with your project (include specific staff members by name and/or title, specific activities requested of them and an estimate of the amount of their time that would be required).

   See attached sheets

2. Describe the nature of patient contact required by your project, if applicable (i.e. access to medical records, patient interviews, etc.) (over)
1. I have already spoken with Pat Guthmiller, RN about this project. Once this project is approved I will need to get the chart numbers of the patients from her. Medical records will then be involved to retrieve the charts for me. The remaining part of the study will involve getting information from patient's charts by myself.

2. The extent of patient contact will be done through the access of their medical charts.

3. All patient's charts will be given an anonymous code. These along with all the information from this study will be kept in a locked cabinet in Room 1531 of the University of North Dakota Physical Therapy Department for 3 years and will be destroyed after this time.

4. I will require access to patient's medical records and the information will be taken from these charts.

5. The only space required will be space to review charts.

   Completion at Altru: 10/1/99
   Completion of project: 12/99

7. None
EXPEDITED REVIEW REQUESTED UNDER ITEM ___ (NUMBER[S]) OF HHS REGULATIONS
X EXEMPT REVIEW REQUESTED UNDER ITEM ___ (NUMBER[S]) OF HHS REGULATIONS

UNIVERSITY OF NORTH DAKOTA HUMAN SUBJECTS REVIEW FORM
FOR NEW PROJECTS OR PROCEDURAL REVISIONS TO APPROVED
PROJECTS INVOLVING HUMAN SUBJECTS

PRINCIPAL INVESTIGATOR: Melissa Wood/ Dave Reiling
ADDRESS TO WHICH NOTICE OF APPROVAL SHOULD BE SENT: UND, Physical Therapy, Box 9037, G.F., ND 58202-9037
TELEPHONE: 795-9285
DATE: 5/10/99
PROJECT TITLE: Evaluation of the effectiveness of Regranex (becaplermin) on treatment of wounds

FUNDING AGENCIES (IF APPLICABLE): __________________________________________________________________________

TYPE OF PROJECT (Check ALL that apply):

X NEW PROJECT ____ CONTINUATION ___ RENEWAL ___ THESIS RESEARCH ___ STUDENT RESEARCH PROJECT

PROPOSED PROJECT: ___ INVOLVES NEW DRUGS (IND) __ INVOLVES NON-APPROVED USE OF DRUG

X INVOLVES A COOPERATING INSTITUTION

IF ANY OF YOUR SUBJECTS FALL IN ANY OF THE FOLLOWING CLASSIFICATIONS, PLEASE INDICATE THE CLASSIFI-
CA-TION(S):

____ MINORS (<18 YEARS) ___ PREGNANT WOMEN ___ MENTALLY DISABLED ___ FETUSES ___ MENTALLY RETARDED

____ PRISONERS ___ Abortuses ___ UND STUDENTS (>18 YEARS)

IF YOUR PROJECT INVOLVES ANY HUMAN TISSUE, BODY FLUIDS, PATHOLOGICAL SPECIMENS, DONATED ORGANS,
FETAL MATERIAL, OR PLACENTAL MATERIALS, CHECK HERE ______

IF YOUR PROJECT HAS BEEN WILL BE SUBMITTED TO ANOTHER INSTITUTIONAL REVIEW BOARD(S), PLEASE LIST NAME OF
BOARD(S):

Status: ___ Submitted; Date ___________________ ___ Approved; Date ___________________ ___ Pending

1. ABSTRACT: (LIMIT TO 200 WORDS OR LESS AND INCLUDE JUSTIFICATION OR NECESSITY FOR USING HUMAN SUBJECTS.

The purpose of this case study is to review the effects of Regranex (becaplermin). Regranex Gel has been used on lower extremity diabetic neuropathic ulcers which extend into the subcutaneous tissue or beyond and the blood supply has not been compromised. Regranex contains a human platelet-derived growth factor which promotes the proliferation of cells for healing. From previous studies, Regranex has shown to increase healing. I am going to use patient medical records from Altru to analyze how effective Regranex has been in clinical use when compared with patients who have not received Regranex. Subjects: 50 Medical Charts will be reviewed from Altru Hospital Systems. Methods: The charts reviewed will include 25 subjects who have been treated with Regranex (becaplermin) and 25 subjects who have not received Regranex (becaplermin) for the treatment of wounds.
PLEASE NOTE: Only information pertinent to your request to utilize human subjects in your project or activity should be included on this form. Where appropriate attach sections from your proposal (if seeking outside funding).

2. PROTOCOL: (Describe procedures to which humans will be subjected. Use additional pages if necessary.)

SUBJECTS: 50 charts will be used from Atru. 25 charts will include subjects who have received Regranex (becaplermin) and 25 charts will include subjects who have not received Regranex (becaplermin) and have similar medical backgrounds such as diabetes, peripheral neuropathy and any other conditions which would effect healing time of wounds.

PROCEDURE:
These charts will be randomly selected from Medical Records at Atru. Information being recorded will be from evaluations and treatments which have already been completed by a health professional. Information will be taken from the initial evaluation, at 1 month, at 2 months and 3 months. It will include Pain Level, Length, Width and Depth of wound and treatment procedure. I will be using the attached form. See appendix A page 6.
3. **BENEFITS:** (Describe the benefits to the individual or society.)

This study will help inform healthcare professionals about Regranex (becaplermin). The results will show how effective it has been in clinical use so that healthcare professionals can make educated decisions as to when to use this product.

4. **RISKS:** (Describe the risks to the subject and precautions that will be taken to minimize them. The concept of risk goes beyond physical risk and includes risks to the subject's dignity and self-respect, as well as psycho-logical, emotional or behavioral risk. If data are collected which could prove harmful or embarrassing to the subject if associated with him or her, then describe the methods to be used to insure the confidentiality of data obtained, including plans for final disposition or destruction, debriefing procedures, etc.)

   This is a chart review and since treatments have already been completed, there are no physical risks to the patients. To ensure confidentiality, information will be anonymously coded and individuals will not be personally identified in any publication. The information collected will be kept for 3 years in a locked cabinet in room 1531 of the University of North Dakota Physical Therapy Department and then it will be destroyed.
5. **CONSENT FORM**: A copy of the CONSENT FORM to be signed by the subject (if applicable) and/or any statement to be read to the subject should be attached to this form. If no CONSENT FORM is to be used, document the procedures to be used to assure that infringement upon the subject's rights will not occur.

Describe where signed consent forms will be kept and for what period of time.

This is a retrospective chart review and all patients may not be available for signed consent. All information will be kept confidential. Patients will be given a code to ensure this and names will not be used during the publication of this information.

6. For **FULL IRB REVIEW** forward a signed original and thirteen (13) copies of this completed form, and where applicable, thirteen (13) copies of the proposed consent form, questionnaires, etc. and any supporting documentation to:

   Office of Research & Program Development
   University of North Dakota
   Grand Forks, North Dakota 58202-7134

   On campus, mail to: Office of Research & Program Development, Box 7134, or drop it off at Room 105 Twamley Hall.

   For **EXEMPT** or **EXPEDITED REVIEW** forward a signed original and a copy of the consent form, questionnaires, etc. and any supporting documentation to one of the addresses above.

   The policies and procedures on Use of Human Subjects of the University of North Dakota apply to all activities involving use of Human Subjects performed by personnel conducting such activities under the auspices of the University. No activities are to be initiated without prior review and approval as prescribed by the University's policies and procedures governing the use of human subjects.

   **SIGNATURES:**

   
   [Signature]
   Principal Investigator
   Date

   [Signature]
   Project Director or Student Advisor
   Date

   [Signature]
   Training or Center Grant Director
   Date
STUDENT RESEARCHERS: As of June 4, 1997 (based on the recommendation of UND Legal Counsel) the University of North Dakota IRB is unable to approve your project unless the following "Student Consent to Release of Educational Record" is signed and included with your "Human Subjects Review Form."

STUDENT CONSENT TO RELEASE OF EDUCATIONAL RECORD

Pursuant to the Family Educational Rights and Privacy Act of 1974, I hereby consent to the Institutional Review Board’s access to those portions of my educational record which involve research that I wish to conduct under the Board’s auspices. I understand that the Board may need to review my study data based on a question from a participant or under a random audit. The study to which this release pertains is Evaluation of the effectiveness of Regranex (becaplermin) on the treatment of wounds.

I understand that such information concerning my educational record will not be released except on the condition that the Institutional Review Board will not permit any other party to have access to such information without my written consent. I also understand that this policy will be explained to those persons requesting any educational information and that this release will be kept with the study documentation.

5/21/99 Melissa Wood
Date Signature of Student Researcher

1Consent required by 20 U.S.C. 1232g.
MEMORANDUM

To: Melissa Wood/Dave Relling  
University of North Dakota  
Physical Therapy Department  
Grand Forks, ND 58202

From: Kevin J. Tveter, MD  
Chair  
Altru Health System IRB

Date: June 11, 1999

Re: Evaluation of the Effectiveness of Regranex (beacaplermin) on Treatment of Wounds

The above project was approved by me on June 10, 1999, and enclosed is a copy of the Research Project Action Report. Please complete the enclosed Research Project Completion/Termination Report when you have completed your project and return to:

Eleanor Tveter  
Administration  
Altru Clinic  
P. O. Box 6003  
Grand Forks, ND 58206-6003

Thank you.

KJTv/ert  
Enc.
ALTRU HEALTH SYSTEM
APPROVAL TO CONDUCT RESEARCH STUDY
AT ALTRU HEALTH SYSTEM

Name: Melissa Wood Date: June 7, 1999
Address: 750 N. 43rd Street, #47B, Grand Forks, ND 58203
Telephone Numbers: Work ________ Home 701-795-9285
Department/College: Physical Therapy Dept, School of Medicine and Health Sciences, UND
Project Title: Evaluation of the Effectiveness of Regranex (Beclaplermin) on the Treatment of Wounds

Your request to conduct the above named study at an Altru Health System facility involving employees or patients as participants, and/or requiring facility resources has been reviewed. The following action has been taken:

✔ Permission to conduct the study is granted

___ Permission to conduct the study will be granted upon completion of the following:

___ Permission to conduct the study is denied for the following reason(s):

RECOMMENDATIONS/REMARKS:
Contact Linda Dennis in Medical Records Dept to arrange for chart review.

Signature

Title

Date
Institutional Review Board
Research Project Action Report

Date: June 10, 1999

Principal Investigator: Melissa Wood/Dave Relling
Department: Physical Therapy
Phone #: 795-6285

Address to which notice of approval should be sent: UND, Physical Therapy, Box 9037, Grand Forks ND 58202-9037

Research Coordinator: _________________________
Phone #: _________________________

Project Title: Evaluation of the Effectiveness of Regranex (becaplermin) on Treatment of Wounds

The above referenced project protocol and informed consent was reviewed by the Altru Health System Institutional Review Board on ________ and the following action was taken:

☐ Project approved. Next Scheduled review is on ________
If no date is given, then review will be required in 12 months. (See REMARKS SECTION for any special condition.)

☐ Project approved. EXPEDITED REVIEW NO. _________________________
Next scheduled review is on ________

☐ Project approved. EXEMPT CATEGORY NO. 4
No periodic review scheduled unless so stated in REMARKS SECTION.

☐ Project approval deferred. (See REMARKS SECTION for further information.)

☐ Project denied. (See REMARKS SECTION for further information.)

☐ Amendment approved
☐ Administrative change approved
☐ Protocol revision approved
☐ Revised consent form approved
☐ Adverse event reviewed - Date of event _________________________

☐ Other _________________________

REMARKS:
Any changes in protocol, adverse occurrences or deaths in the course of the research project must be reported immediatel
to the IRB chairperson or the IRB office (780-6161).

Signature of Chairperson or Designated IRB Member
Altru Health System Institutional Review Board

Date 6/10/99

If the proposed project is to be part of a research activity funded by a federal agency, a special assurance statement or a
completed 596 Form may be required. Contact IRB office to obtain the required documents.
DATA COLLECTION TOOL

"Evaluation of the Effectiveness of REGRANEX (becaplermin) Gel 0.01% on the Treatment of Wounds"

ID # __________________
Age _________________
Sex ________________

Medical Diagnosis: ____________________________________________

Past Medical History: __________________________________________

Location of wound(s) on body from Altru eval. form: ____________________

Stage of wound (circle): I   II   III   IV

Objective Information:

<table>
<thead>
<tr>
<th>Pain Level</th>
<th>Initial Evaluation</th>
<th>1 month</th>
<th>2 month</th>
<th>3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length (head to toe)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Width (side to side)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depth (deepest)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Granulation &quot;beefy&quot; red</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other % like Slough, Eschar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment Procedure (Including cleansing and home program):

1. Circle: Regranex No Regranex
2. Dressing: _______________________________________________________
3. Cleansing: _____________________________________________________
4. Other: (ie: ROM, Elevation, Other Medications) ____________________

44
Indicate location of skin breakdown/wound by letter. If more than 1 area, letter each area.

STAGES FOR PRESSURE ULCERS ONLY: (If ulcer is covered with eschar, do not stage until eschar is removed.)

Stage 1: Nonblanchable erythema of intact skin, the heralding lesion of skin ulceration. In individuals with darker skin, discoloration of the skin, warmth, edema, induration or hardness may also be indicators.

Stage II: Partial thickness skin loss involving epidermis, dermis or both. The ulcer is superficial and presents clinically as an abrasion, blister or shallow crater.

Stage III: Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia. The ulcer presents clinically as a deep crater with or without undermining of adjacent tissue.

Stage IV: Full thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone or supporting structures (e.g., tendon, joint capsule). Undermining and sinus tracts also may be associated with Stage IV pressure ulcers.

Wound Etiology: Pressure Ulcer (Stage - see above); Leg Ulcer (Etiology: IF KNOWN);
Surgical Wound (Surgical Procedure); Skin tear; other

<table>
<thead>
<tr>
<th>A.</th>
<th>B.</th>
<th>C.</th>
<th>D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size: ____ cm (L)</td>
<td>Size: ____ cm (L)</td>
<td>Size: ____ cm (L)</td>
<td>Size: ____ cm (L)</td>
</tr>
<tr>
<td>____ cm (W)</td>
<td>____ cm (W)</td>
<td>____ cm (W)</td>
<td>____ cm (W)</td>
</tr>
<tr>
<td>____ cm (D)</td>
<td>____ cm (D)</td>
<td>____ cm (D)</td>
<td>____ cm (D)</td>
</tr>
</tbody>
</table>

Date: __________________ Signature: __________________

Medical Park & Associates
Initial Wound Documentation Record
<table>
<thead>
<tr>
<th>Date/Initials</th>
<th>Location of Wound/Key Letter</th>
</tr>
</thead>
</table>

**Skin (Weekly)** | Measurements in cm. |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Length (head to toe)</td>
<td></td>
</tr>
<tr>
<td>Width (side to side)</td>
<td></td>
</tr>
<tr>
<td>Depth (deepest portion)</td>
<td></td>
</tr>
<tr>
<td>Undermining/Tunnel - location (measure with applicator)</td>
<td></td>
</tr>
<tr>
<td>Exposed Tendon: Y or N</td>
<td></td>
</tr>
<tr>
<td>Exposed Bone: Y or N</td>
<td></td>
</tr>
</tbody>
</table>

**COLOR**
- % of Granulation "beefy" red
- % of Epithelial "pearly" pink
- % of Slough (yellow, gray or white)
- % of Eschar (thick, black)

**DRAINAGE**
- Sanguinous
- Serous
- Sero-Sang
- Purulent - COLOR

Describe type and amount of dressing saturated

**ODOR**
- None, Mild, Foul (present after cleansing)

**Peri-Wound Skin Condition**
- Intact
- Red (Erythema)
- White
- Abrased
- Purple
- Gray
- Dry
- Macerated
- Edematous

Widest Point of Induration
Location of Induration (12, 3, 6, 9 o'clock)

**Cleansing Routine:**

**Treatment** (Describe type of dressing in detail)

**Patient’s Perception of Pain**
(Scale of 0 to 10) 0 = None 10 = Greatest

Initials: Signature:
Initials: Signature:
Initials: Signature:
Initials: Signature:

Wound Care Flowsheet

Altru Health System
REFERENCES

1. Product Monograph -REGRANEX (becaplermin) gel 0.01%. 1998 Ortho-McNeil Pharmaceutical, Inc.


