



# Secundum Artem

Current & Practical Compounding  
Information for the Pharmacist.

## COMPOUNDING FOR WOUND CARE

### GOALS AND OBJECTIVES

**Goal:** To provide information on wounds and their care and the drugs and dosage forms that can be compounded and used in wound treatment, especially pressure ulcers.

**Objectives:** Objectives: After reading and studying the article, the reader will be able to:

1. List five types of skin ulcers and describe their causes.
2. Describe the items important for documenting wound healing progression.
3. Discuss the role of the wound exudates and eschar in the healing process.
4. Discuss the role of debridement in wound treatment.
5. Describe at least 5 different formulations that can be compounded for wound care.

### INTRODUCTION

The skin is the body's largest organ (making up about 10% of the body's weight) and is our first line of defense in protecting us from the environment. Our skin provides us with protection, sensation, thermoregulation, metabolism, ability to discharge some waste from the blood, tissues and organs and directly impacts our appearance. Since the skin is the outer covering of the body, it is subject to injury sometimes resulting in wounds as in the case of cuts, scrapes, bruises, skin ulcers, etc. The skin generally has the ability to heal itself, but if the wound is serious or becomes infected, medical assistance is sometimes required. The wound healing process is a complex series of events lasting from the moment of injury to healing and may involve months to years.

There are many types of wounds, including acute, chronic, full-thickness, laceration and partial-thickness. A prominent problem today is skin ulcer wounds, which can be categorized as pressure, arterial, venous and diabetic ulcers. Also, burn wounds can involve superficial (first degree burns), partial-thickness (second degree burns) and full-thickness (third degree burns). While all these are wounds, this *Secundum Artem* issue will primarily address skin ulcer wounds.

Wound care has become increasingly important to geriatricians and long-term care providers. Pressure ulcers are in the spotlight today and are the subject of many news media reports. However, there are many other types of lesions commonly found in the nursing home environment, pressure ulcers among the most prevalent.

Pressure ulcers promise to become an even bigger problem as the US population ages. These ulcers can possibly lead to serious complica-

tions and place demands on an already-stressed healthcare system.

### PRESSURE ULCERS

Pressure ulcers are a common problem across all health care settings and can occur as a result of immobility, especially where the body's soft tissue is compressed between a bony part of the body and an external surface, such as a mattress or chair. Pressure ulcers can result from a number of factors that often involve ischemia at the cellular level, such as pressure that occludes blood vessels. The ischemia leads to necrosis; the necrosis may actually involve deep tissue that may be adjacent to a bony prominence, etc. This may be seen as skin discoloration or redness and may involve underlying adipose or muscular necrosis. It is possible that the necrosis may be the result of frictional or shearing forces, which should be reduced or eliminated. As the ulcer advances, tissue involvement spreads outward and upward until the skin surface is involved and a crater is apparent. Table 1 presents the four stages of pressure ulcer progression.

### ARTERIAL ULCERS

The blockage, partial or complete, of an artery may lead to tissue necrosis and/or ulceration. Extremity symptoms include lack of pulse in the extremity, painful ulceration, small, well-circumscribed punctate ulcers, cool or cold skin, delayed capillary return, skin appearance (shiny, thin, dry), and loss of hair on the fingers or toes. The primary goal of treatment is to increase the circulation to the involved area; this can be done surgically or medically depending

upon the cause of the ulcer and the patient's overall medical condition. Treatment goals also involve keeping the tissue moist, free of infection and free of necrotic debris.

## VENOUS ULCERATIONS

The most common type of ulcer affecting the lower extremities is the venous ulcer. When the valves preventing the backflow of blood in the veins become inoperative, venous congestion occurs. The hemoglobin begins escaping from the red blood cells and leaks into the extravascular space, resulting in a brownish discoloration. Venous ulcers may appear indurated and edematous on the legs; they are shallow, not too painful and may result in a weeping discharge from the leg.

Treatment involves maintaining freedom from infection, absorption of any excess discharge, maintaining a moist wound environment, using compression as indicated, and promoting activity using the involved extremity. Controlling the edema is also important.

## DIABETIC FOOT ULCERS

Common diabetic foot infections include cellulites, ulcers, abscesses, osteomyelitis and gangrene. Patients with diabetes develop foot ulcers often due to neurologic and vascular complications. Sensation of the foot and/or leg can be altered or lost due to peripheral neuropathy. Since diabetics with advanced neuropathy lose all sharp-dull sensation, any cuts or trauma to the foot or lower extremities can go unnoticed for days or weeks. Strict glucose control may slow the progression of the diabetic neuropathy.

Another cause of ulcerations in diabetics is microvascular disease. A narrowing of the small arteries may occur so it is critical that diabetics maintain close control of their glucose levels, maintain good nutrition and body weight and avoid smoking.

Treatment involves enhancing blood flow/perfusion to heal the ulcer. Also, proper fitting shoes and modified shoes that can distribute the weight away from the ulcer area should be worn. Any excess ulcer discharge should be absorbed but the wound should be maintained moist. Observations should be regularly made for infections and necrotic debris should be debrided.

## TRAUMATIC ULCERS

Compromised arterial, venous or lymphatic systems can result in a traumatic ulcer which may result in changes to the skeleton, loss of tissue layers, damage to body parts or organs and trauma to the body that may result in loss of body parts or organs.

## CHARACTERISTICS OF WOUNDS/SKIN ULCERS

When describing wounds and their characteristics for documentation purposes, it is important to list the following:

1. Location-Where is the wound located on the body (be exact)?
2. Size-Measure the length, width and depth of the wound to document the progress of wound closure/healing. Generally, the perpendicular measurements of length and width, in centimeters, are multiplied to provide a "square centimeter" surface area for wound size.
3. Drainage-Is there drainage? If so, is it serous, purulent, bloody, green, yellow, clear, thick, etc.?
4. Odor-Is there any odor emanating from the wound? If so, is it fruity (possibly indicative of staphylococcus infection) or foul (possibly indicative of gram negative infection).
5. Necrotic tissue-Approximately what percentage of the wound appears necrotic, i.e., does not appear reddish and granular? Draw a diagram if necessary.

6. Infection-Is the wound red, hot and swollen? Is it tender and sensitive?

7. Presence of scar tissue after wound healing. This should be evaluated carefully as scar tissue is only about 80% as strong as normal tissue and the health of the underlying tissue also needs to be evaluated.

## WOUND EXUDATES

Wounds generally will produce an exudate. An exudate consists of fluids, cells or other substances that have been slowly exuded, or discharged from cells or blood vessels through small pores or breaks in cell membranes.

Dry wounds tend to have higher infection rates than moist wounds. Moist wound healing is based on the concept that the presence of exudates in the wound provides an environment that stimulates healing. This results from the composition of the exudates consisting of lysosomal enzymes, white blood cells, lymphokines and growth factors. Commercially available products are designed to maintain a moist wound bed.

## WOUND TREATMENT

The desired successful outcome is that which produces wound closure in the shortest amount of time and with the fewest number of office visits. If the wound is recurring, it helps to know the previous treatment and the obtained results. Wound treatment modalities include electrical current, ultrasound, whirlpool baths/hydrotherapy, hyperbaric oxygen therapy, negative pressure therapy, and pharmacotherapeutics. Of these, the compounding pharmacist can be involved in preparing various gels for ultrasound and in pharmacotherapeutics.

Current treatment using drugs may involve the use of irrigating solutions, compounded drug preparations and dressings. It is important to understand the role of the wound eschar and the factors impacting wound healing in therapeutic strategies to enhance wound healing. The wound eschar debrides itself as a part of the wound healing process. The wound color will change from black to yellow to red to granular red during healing. Generally a red/yellow/black color designation is used to describe the wound at each visit. Observations should be made daily for any change in the wound eschar.

Complications and factors impacting wound healing include dryness, swelling, infection, incontinence, dead tissue, age, body type (i.e. obesity since fatty tissue has less blood supply), nutrition, vascular insufficiencies, suppressed immune system and chronic diseases. These factors will determine the therapeutic approach or changes during therapy.

Debridement of wounds can be accomplished by autolysis, by using enzymes, or by mechanical and surgical means, and by the use of maggots. Autolysis involves the use of the body's own enzymes and moisture (exudates). Enzymatic debridement uses chemical enzymes that are relatively fast acting and induce necrotic tissue sloughing. Mechanical debridement can involve hydrotherapy. Surgical debridement involves surgical instruments and/or lasers. Maggot therapy involves the excretory/secretory products of *Lucilia sericata* (greenbottle fly) larvae. These products provide beneficial effects upon a chronic nonhealing wound including removal of necrotic tissue, disinfection of the wound and active promotion of granulation tissue formation.<sup>1</sup>

## DRESSINGS

The general consensus is that "wet" dressings should be used. Gauze dressings should not be used as they do little to impede fluid evaporation and allow a loss of tissue temperature and can also result in some healthy tissue being removed, upon gauze removal, causing reinjury and pain. A wet dressing tends to cut healing time by about half as compared to dry dressings.<sup>2,4</sup>

Gauze dressings can now be replaced by polymeric materials, including polyurethane films, foams, hydrogels and hydrocolloids, along with calcium alginates, collagens and other materials that are moisture-retentive or semi-occlusive.

Even a wet dressing may become dry. For example, if normal saline is used to impart moisture to a dressing, it is initially isotonic with no fluid movement between the dressing and the wound. However, as the water evaporates, the dressing becomes hypertonic, resulting in a movement of fluid from the wound into the dressing to try to maintain an isotonic state. Since the movement of fluid cannot keep pace with evaporation, the dressing soon becomes dry. When the dry dressing is removed, damage to the wound can occur. Gels tend to slow down the rate of evaporation and will keep the wound area moist for a longer period of time, thus enhancing the healing process.

The general categories of dressings, in addition to gauze, include transparent film dressings, hydrogels, polyurethane foam dressings, hydrocolloids and alginates.

The transparent film dressings are usually self-adhesive, help maintain moisture in the wound, are semipermeable, semioclusive, allow for autolytic debridement, protect from external contaminants and allow for easy wound visualization.

Hydrogels are water or glycerin-based gels that may be formed into sheet dressings or impregnated into gauze. Since they are water-based, they cannot absorb large amounts of drainage exudates but will assist in maintaining a moist wound-healing environment and promoting the natural wound-healing process. They also tend to reduce pain and produce a soothing effect in patients. The hydrogels maintain moisture, are semipermeable and semioclusive, allow for autolytic debridement, act as a polymer dressing to absorb fluid, are non-irritating when removed and decrease the wound temperature.

The polyurethane foam dressings maintain moisture, are semipermeable, semioclusive, allow for autolytic debridement, are highly absorbent, protect the wound bed, are waterproof and serve to insulate the wound bed.

Hydrocolloids are occlusive and vary in their ability to absorb and may or may not leave a residue in the wound. Hydrocolloids will assist in the healing process and are generally self-adhesive and easy to shape. They will absorb light to moderate drainage. The hydrocolloids are self-adhesive, maintain moisture are semi- to totally impermeable, semioclusive to occlusive, allow for autolytic debridement, are absorbent, provide minimal irritation when removed and insulate the wound bed.

Alginate dressings consist of soft fibers made from brown seaweed that can hold up to twenty times their weight and easily fill in open spaces. When applied to a wound, they mix with the wound fluids and form a gel, maintaining a moist wound-healing environment within the wound. They are easily applied and removed. The alginates maintain moisture, are permeable, nonocclusive, allow for autolytic debridement, are highly absorbent, contribute to hemostasis, convert to a hydrophilic gel after calcium/sodium ion exchange, conform to the wound bed and are nonirritating upon removal.

## OTHER TREATMENT MODALITIES

The application of negative pressure to wounds may speed the formation of granulation tissue, decrease edema, increase localized blood flow and promote healing.<sup>5,7</sup>

Vitamin A (8,000 units twice daily) has been shown to resolve anorectal symptoms and anal ulcer sores resulting from radiation treatment within seven weeks.<sup>8</sup> Alternative agents used to heal chronic anal fissures include botulinum toxin, glyceryl trinitrate ointment and pentoxifylline.<sup>9-10</sup>

## DRUGS USED TO TREAT WOUNDS

Agents generally used to treat wounds include anti-infectives (hydrogen peroxide, sodium hypochlorite), antibiotics (aminoglycosides, penicillins, cephalosporins, metronidazole), granulation stimulants (phenytoin), enzymes for debridement, anesthetics (lidocaine), and moisture enhancers (dressings, humectants).

In addition to preventing and treating infection, anti-infectives can also be used to minimize odor emanating from some wounds. Many of these ingredients are illustrated in the formulations presented.

## WOUND HEALING PROCESS

### CLASSIFICATION

A widely accepted method of describing the stages of wound healing involves the inflammatory phase, proliferative phase and the maturation or remodeling phases.

The inflammatory phase is almost immediate and lasts approximately two to six days. During this time, bleeding is controlled and homeostasis is achieved through vasoconstriction, platelet aggregation and clot formation. A cleansing process is started within the wound and chemicals are released to enhance the healing process. These processes are accompanied by vasodilation and phagocytosis.

The second phase, the proliferative phase lasts from about four days to three weeks post-injury. During this phase, granulation occurs where fibroblasts lay down a bed of collagen, the defect begins filling and new capillaries are produced. Contraction begins where the wound edges pull together to reduce the defect. Also during this phase, epithelialization begins where new cells crossing the moist surface traveling about 3 cm from the point of origin in all directions.

The final phase, the maturation or remodeling phase, lasts from three weeks to two years. During this phase, new collagen forms which increases the tensile strength of the wounds. It should be noted that scar tissue formed is only about 80% as strong as the original tissue.

## DOSAGE FORMS USED TO TREAT WOUNDS

Topical dosage forms used in conjunction with various dressings to treat wounds generally include gels, creams and solutions.

Gels for wound therapy are semisolid systems consisting of dispersions made up of large organic molecules enclosing and interpenetrated by a liquid. The high degree of physical or chemical cross-linking may be involved. The increased viscosity caused by the interlacing and consequential internal friction is responsible for the semisolid state. Gels are water-soluble and are easily removed from the wound using a gentle stream of warm water or saline. Gels tend to keep the area moist, especially if the wound is covered with proper backing material. Almost any active ingredient can be formulated into a gel.

Creams are semisolid preparations containing one or more medicinal agents dissolved or dispersed in either an oil-in-water emulsion or in another type of water-washable base. One disadvantage of creams is the oil phase, which may not be completely removed from the wound cavity and the presence of the oil may affect the granulation process. Creams may also tend to support microbiological growth. A great variety of active ingredients can be prepared in cream dosage forms.

Solutions are liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents. Solutions can be used as irrigating solutions, baths, soaks and sprays. An advantage to sprays is that the wound area does not need to be mechanically touched and sprays can be perceived as imparting a cooling effect upon application. A wide variety of anti-infectives and anesthetics can be incorporated.

## COMPOUNDED FORMULATIONS FOR WOUND CARE

### Rx TOPICAL WOUND HYDROGEL

Benzyl alcohol	1 mL
Glycerin	10 mL
Carbopol 934P	1 g
Trolamine	qs
Purified water	qs 100 mL

Add the benzyl alcohol and glycerin to about 80 mL of purified water. Slowly, sprinkle and disperse the Carbopol into this mixture. Add sufficient purified water to 100 mL and mix well. Slowly and dropwise add the trolamine until the gel is formed. Package and label.

**Rx SCARLET RED OINTMENT**

Scarlet red	5 g
White wax	5 g
White petrolatum	90 g

Levigate the scarlet red with about 10 g of white petrolatum. Melt the white wax in a suitable container, remove from heat and add the white petrolatum. Incorporate the scarlet red-petrolatum mixture and mix well. Package and label.

**Rx PHENYTOIN 5% GEL**

Phenytoin	5 g
Propylene glycol	10 mL
Methylparaben	50 mg
Propylparaben	20 mg
Hydroxyethylcellulose	2 g
Purified water	qs 100 mL

Mix the phenytoin, methylparaben and propylparaben with the propylene glycol. Add about 80 mL of purified water and place on a magnetic stirrer. Slowly sprinkle the hydroxyethylcellulose onto the water and allow to hydrate. Add sufficient purified water to volume and mix well. Package and label.

**Rx MISOPROSTOL 0.0024% GEL**

Misoprostol	2.4 mg
Propylene glycol	10 mL
Methylparaben	50 mg
Propylparaben	20 mg
Hydroxyethylcellulose	2 g
Purified water	qs 100 mL

Pulverize 12 of the 200 microgram misoprostol tablets. To this powder add the methylparaben and propylparaben and mix with the propylene glycol. Add about 80 mL of purified water and place on a magnetic stirrer. Slowly sprinkle the hydroxyethylcellulose onto the water and allow to hydrate. Add sufficient purified water to volume and mix well. Package and label.

**Rx GENTAMICIN 0.2%, MISOPROSTOL 0.0024% AND PHENYTOIN 5% GEL**

Gentamicin sulfate	200 mg
Misoprostol	2.4 mg
Phenytoin	5 g
Propylene glycol	15 mL
Methylparaben	50 mg
Propylparaben	20 mg
Hydroxyethylcellulose	2 g
Purified water	qs 100 mL

Based on the labeled activity of the gentamicin sulfate powder, calculate the quantity required to provide 200 mg of gentamicin activity. Pulverize 12 of the 200 microgram misoprostol tablets. Blend the gentamicin sulfate, misoprostol, phenytoin, methylparaben and propylparaben powders and mix with the propylene glycol. Add about 80 mL of purified water and place on a magnetic stirrer. Slowly sprinkle the hydroxyethylcellulose onto the water and allow to hydrate. Add sufficient purified water to volume and mix well. Package and label.

**Rx METRONIDAZOLE 2%, MISOPROSTOL 0.0024% AND PHENYTOIN 5% GEL**

Metronidazole	2 g
Misoprostol	2.4 mg
Phenytoin	5 g
Propylene glycol	15 mL
Methylparaben	50 mg
Propylparaben	20 mg
Hydroxyethylcellulose	2 g
Purified water	qs 100 mL

Pulverize 12 of the 200 microgram misoprostol tablets. Blend the metronidazole, misoprostol, phenytoin, methylparaben and propylparaben powders and mix with the propylene glycol. Add about 80 mL of purified water and place on a magnetic stirrer. Slowly sprinkle the hydroxyethylcellulose onto the water and allow to hydrate. Add sufficient purified water to volume and mix well. Package and label.

**Rx METRONIDAZOLE TOPICAL SPRAY FOR ODOR-PRODUCING SKIN ULCERS**

Metronidazole	1 g
Purified water	qs 100 mL

Dissolve the metronidazole powder in sufficient purified water to volume. Package and label.

**Rx MISOPROSTOL 0.0024%, NIFEDIPINE 0.2% AND PHENYTOIN 5% GEL**

Misoprostol	2.4 mg
Nifedipine	200 mg
Phenytoin	5 g
Propylene glycol	15 mL
Methylparaben	50 mg
Propylparaben	20 mg
Hydroxyethylcellulose	2 g
Purified water	qs 100 mL

Based on the labeled activity of the gentamicin sulfate powder, calculate the quantity required to provide 200 mg of gentamicin activity. Pulverize 12 of the 200 microgram misoprostol tablets. Blend the misoprostol, phenytoin, methylparaben and propylparaben powders and mix with 13 mL of the propylene glycol. Add about 80 mL of purified water and place on a magnetic stirrer. Slowly sprinkle the hydroxyethylcellulose onto the water and allow to hydrate. Mix the nifedipine with 2 mL of the propylene glycol then incorporate into the mixture. Add sufficient water to volume and mix well. Work quickly as the nifedipine is light sensitive. Package and label.

**Rx NIFEDIPINE 0.2% GEL**

Nifedipine	200 mg
Propylene glycol	5 mL
Methylparaben	50 mg
Propylparaben	20 mg
Methylcellulose 1500 cps	2 g
Purified water	qs 100 mL

Prepare the gel by heating approximately 95 mL of purified water and adding the parabens. Slowly, sprinkle the methylcellulose powder onto the solution with continuous stirring. Remove from heat and continue stirring. Mix the nifedipine with the propylene glycol and incorporate into the gel. Work quickly as the nifedipine is light sensitive. Add sufficient purified water to volume and mix well. Package and label.

**RX ODOR STICK**

Eucalyptol	5 g
Polyethylene glycol 300	60 g
Polyethylene glycol 3350	35 g

Heat the polyethylene glycols to about 55 to 60° C and mix well. Cool slightly, then add the eucalyptol and mix well. Just prior to congealing, pour into medication stick molds, cool and package. Note: Other aromatic substances can be used in place of eucalyptol, if desired.

**RX PHENYTOIN TOPICAL POWDER**

Phenytoin	9-10 g
Polyox (optional)	0-1 g

Mix the powders thoroughly using a noncompacting technique, such as the bottle method, plastic bag method, or sieving.

**RX DECUBITUS ULCER OINTMENT**

Sucralfate	10 g
Bacitracin zinc and Polymyxin B sulfate powder	10 g
Aluminum hydroxide gel	30 mL
Aquabase	qs 120 g

Place 10 sucralfate tablets in a mortar with 30 mL of aluminum hydroxide gel and allow to soften. Triturate into a smooth, slurry-like mixture. Incorporate the bacitracin zinc and polymyxin B sulfate powder (Polysporin Powder) into the mixture. Incorporate this into the Aquabase to form a smooth, consistent ointment. Package and label.

**RX SODIUM HYPOCHLORITE 0.025% TOPICAL SOLUTION (MILLENNIUM MODIFIED DAKIN'S SOLUTION)**

Sodium hypochlorite solution	0.5 mL
Monobasic sodium phosphate monohydrate	102 mg
Dibasic sodium phosphate anhydrous	1.76 g
Purified water	qs 100 mL

Dissolve the dibasic sodium phosphate anhydrous and the monobasic sodium phosphate monohydrate in about 50 mL of purified water. Add the sodium hypochlorite solution and mix well. Add sufficient purified water to volume and mix well. Package and label.

**TABLE 1. STAGES OF PRESSURE ULCER DEVELOPMENT**

I	There is an observable pressure-related change in the skin related to skin temperature, consistency (firm/soft) and sensation (pain or itching).
II	There has been a partial thickness skin loss involving the epidermis, dermis or both. The ulcer is superficial and may appear as an abrasion, blister or shallow crater.
III	There is full thickness skin loss involving damage to subcutaneous tissue and possibly necrosis. It may extend down to, but not through, the fascia. The ulcer appears as a deep crater with or without undermining adjacent tissue.
IV	There has been full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures.

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