Nutritional Management in Adults with Wound Healing Needs

Product Monograph

Abound®

Supports healing and recovery

Therapeutic Nutrition™ Drink Mix
A Medical Food That Supports Wound Healing and Helps Build Lean Body Mass

Use under medical supervision
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Executive summary

Wound healing depends on a combination of good nutrition and hygienic wound care. But sometimes good nutrition—based on a diet of varied foods and/or on a complete and balanced nutritional supplement—is not enough. Despite these usual strategies, some wounds persist. Abound® is a therapeutic nutrition product that can benefit people with hard-to-heal wounds.

Abound® is formulated to meet specific nutritional stresses of healing wounds such as pressure ulcers, diabetic foot ulcers, venous leg ulcers, surgical incisions with complications, and burns. Abound works because it is a unique blend of ingredients that support wound healing above and beyond the limits of basic nutrition; it contains amino acids arginine and glutamine, and beta-hydroxy-beta-methylbutyrate (HMB; a metabolite of the amino acid leucine). Because these ingredients are vital for the anabolic processes of wound healing, short supplies can limit healing.

Combined, the 3 key components of Abound® help support specific anabolic processes and immune functions that are vital to healing wounds. HMB has been shown to inhibit muscle proteolysis and modulate protein turnover, functions important to overcoming the metabolic toll of hard-to-heal wounds. Glutamine and arginine support synthesis of collagen, a protein essential to skin integrity and elasticity. Glutamine and arginine also serve as metabolic fuels for immune cells, thereby enhancing immune function to prevent or fight infections that can complicate wound healing. In addition, arginine is also recognized to play a key role in producing mediators that stimulate activity of immune cells and enhance formation of new blood vessels.

Proper wound care also requires a diet planned for wound healing. Appropriate nutrition for healing of acute or chronic wounds includes increased caloric energy, adequate protein, ample fluid supplies, and increased doses of certain vitamins and minerals (zinc, and vitamins A, C, and E).

Abound therapeutic nutrition, along with a diet planned for wound healing, must also be accompanied by all-around good care for wounds and total health. Wound healing requires a multi-disciplinary team of health care professionals who take care of nutrition, surgical procedures, wound hygiene, wound dressings, and the general health status of the patient.
Introduction to Abound® and wound care

When the latest principles of wound management are paired with the newest nutritional science, it is possible to design medical nutrition therapy that targets the needs of patients with hard-to-heal wounds. For such individuals, healing can be enhanced by ensuring an adequate supply of nutrients recognized to support tissue growth and repair, sustain immune responses, and compensate other special metabolic needs. Abound® is a therapeutic nutrition product intended to benefit people who need treatment for hard-to-heal wounds.

This monograph reviews the personal and economic impact of hard-to-heal wounds; discusses the pathology of hard-to-heal wounds; describes the role of nutrition in wound healing; explains how, when, and why to use Abound® to support healing; and summarizes the clinical evidence underlying the benefits delivered by Abound.
Hard-to-heal wounds

- Wounds may be acute or chronic. Surgical incisions, burns, and traumatic injuries are examples of acute injuries. If acute injuries are extensive or complicated by infection, they may become hard-to-heal. Other hard-to-heal wounds—venous leg ulcers, diabetic foot ulcers, and pressure ulcers—develop in people with chronic health conditions. Hard-to-heal wounds fail to progress through an orderly sequence of repair in a timely fashion. A wound is usually considered chronic if it takes more than 30 days to heal.

Figure 1. Hard-to-heal wounds fail to progress through an orderly sequence of repair in a timely fashion.

- Hard-to-heal wounds occur in the general population, but older individuals who are hospitalized or reside in long-term care facilities are at particular risk. Up to 3% of individuals over 60 years in the UK are reported to suffer from hard-to-heal skin wounds such as leg and pressure ulcers. Approximately 3.5% of the US population older than 65 years have venous leg ulcers. Of the 150 million people in the world with diabetes, at least 15% are expected to develop one or more foot ulcers in their lifetime, especially in older years. The prevalence of pressure ulcers among elderly people living in long-term care facilities exceeds 20% in the US and Canada.

- The prevalence of hard-to-heal wounds and the costs of management have continued to rise over time, despite increasing availability of advanced wound-care specialists and wound-healing centers.
The link between nutrition and wounds

- A key factor for wound healing is the patient's nutritional status. Hard-to-heal wounds will heal faster and with fewer complications when the patient is well nourished. But in many cases, even a diet planned for healing wounds is not enough.

- If adequate protein—including dietary supplies of essential and conditionally-essential amino acids—is not consumed in the diet, impaired wound healing will result from limits on protein synthesis. A conditionally-essential amino acid is one that is normally synthesized by the body, but an additional dietary supply is needed during times of rapid growth, as in infancy or wound healing.

- Conditionally-essential amino acids arginine and glutamine play multiple roles in wound healing. Glutamine and arginine support synthesis of collagen, a protein that determines skin integrity and elasticity. Glutamine and arginine also serve as metabolic fuels for immune cells, thereby enhancing immune function to prevent or fight infections that can complicate wound healing. In addition, arginine is recognized to play a key role in production of mediators that stimulate activity of immune cells and enhance formation of new blood vessels.

- Beta-hydroxy-beta-methylbutyrate (HMB; a metabolite of the amino acid leucine) increases collagen deposition, an action important to wound closure and healing. HMB has been shown to inhibit muscle proteolysis, a function important to overcoming the metabolic toll of hard-to-heal wounds. HMB also increases nitrogen retention, a general indicator of lowered protein catabolism, and it has anti-inflammatory properties as well.

- Abound® is a therapeutic nutrition product that can help wound healing. Abound® has a unique blend of key ingredients—amino acids arginine and glutamine, and HMB. Combined, the 3 key components of Abound® help support specific anabolic processes and immune functions that are vital to healing wounds.

- In addition to rate-limiting nutrients, wound healing requires a diet planned for wound healing. Appropriate nutrition for treating hard-to-heal wounds includes increased caloric energy, adequate protein, ample fluid supplies, and increased doses of certain vitamins and minerals (zinc, and vitamins A, C, and E).
Abound® ingredients support processes involved in wound healing

<table>
<thead>
<tr>
<th>ARGinine</th>
<th>GLUTAMINE</th>
<th>HMB (LEucINE MEtabOLITE)</th>
</tr>
</thead>
</table>
| • Enhances wound healing¹², 20-22  
• Stimulates synthesis and deposition of collagen¹⁰, 12  
• Supports protein synthesis¹³  
• Supports immune function¹⁴ | • Enhances wound healing, especially by stimulating collagen synthesis⁷-¹⁰  
• Supports protein synthesis¹⁰, ¹³  
• Supports gut integrity and immune function¹³ | • Decreases breakdown of muscle proteins¹⁵-¹⁷  
• Increases nitrogen retention, a measure of protein anabolism¹⁸  
• Anti-inflammatory effects¹⁹ |
A Case Study From the US—a man with a diabetic foot ulcer

Mr. S is a 62-year-old man with a 20-year history of diabetes mellitus. During the cold winter season, he noticed that the skin on the sole of his foot was cracking, a condition he attributed to extremely dry indoor air. Over several weeks, he developed a severely inflamed and necrotic plantar sore on his right foot. His general physician referred him to a wound care center, where the lesion was debrided, and Mr. S. was given instruction to care for his wound.

Unfortunately, the ulcer worsened and was complicated by osteomyelitis, which required repeated antibiotic treatments. After 7 months, the wound care team recommended Mr. S for another surgical debridement, which resulted in a wound 6 cm long, 5 cm wide, and 2.5 cm deep. Mr. S was directed to clean the wound and change the dressings daily, take an oral antibiotic (levofloxacin), and follow his usual diabetic diet. Despite careful attention to wound care and nutrition, Mr. S could not control his blood glucose levels, the foot ulcer failed to heal, and osteomyelitis persisted.

On return to the clinic, the wound care team recommended that Mr. S have hyperbaric oxygen therapy, a consulting surgeon recommended a below-the-knee amputation, and a wound care nutritionist recommended a trial with Abound medical nutrition therapy. Mr. S opted to try Abound first. For the next 2 months, he added 2 packets of Abound to his daily diet. Typically he mixed one pack of Abound powder with 8 to 10 fl oz of cold water. He had one serving of Abound at 7:30 AM and another at 6:30 PM. Each Abound serving was counted as ½ starch or carbohydrate exchange.

On a follow-up visit to the wound care center, Mr. S reported that he felt stronger and more energetic. He noted that his foot ulcer appeared to be healing. On examination, the wound had closed, and the ulcer surface had diminished to 3.8 cm long and 1.2 cm wide. Because of this satisfactory ulcer healing, the wound care team decided that neither surgery nor hyperbaric therapy was needed.
Prevalence and impact of wounds by type

Wounds and wound care take high personal and financial tolls. The most common types of hard-to-heal chronic wounds are pressure ulcers, diabetic foot ulcers, and venous leg ulcers; hard-to-heal acute wounds are complicated incisions and serious burns. For people with wounds, non-healing decreases quality of life by causing social isolation, impaired physical mobility, pain, emotional stress, loss of self-image, and depression. In the UK, the annual cost of caring for hard-to-heal wounds was reported as 3% of the total health care budget, i.e. £3.1 billion out of £89.4 billion GBP per year. On a global scale, costs for hard-to-heal wounds could exceed $100 billion USD each year (when estimated at 3% of total costs for worldwide health care expenditures of $4.1 trillion USD). Indirect costs, such as days absent from work, loss of employment, or forced retirement, considerably increase the overall burden.
Pressure ulcers

Pressure ulcers are a common problem in all health care settings and can result in severe patient discomfort and treatment cost. Current standards of care in the US recognize that most pressure ulcers are preventable.26

• Pressure ulcer prevalence varies greatly by health care setting and provider.
  – In the US, prevalence ranges from 0 to 38% in hospitalized patients; 2 to 24% of those in long-term care, and 0 to 17% in home care.27
  – A recent study covering five European countries found a prevalence of 18% for all pressure ulcers. The study found that only 9.7% of patients in need of care received adequate treatment.28
  – In Canada, pressure ulcers were found in 25% of patients in acute care facilities and 30% of patients in non-acute care facilities.6

• Costs of pressure ulcer treatment are considerable and are likely to increase as the population ages.29
  – Pressure ulcer treatment costs are 4% of total health care expenditures in the UK (NHS)30 and 1% of the total Dutch health care budget.31
  – Most of the cost is absorbed by nurses’ time, and the severity of the sore increases the cost dramatically: a stage IV ulcer is over 10 times more costly to treat than a stage I ulcer.30
  – In the US, it is estimated that treatment cost per patient ranges from $500 to $40,000. 27

• Pressure ulcers are painful, slow to heal, and susceptible to infections that further impair healing.32
Diabetic foot ulcers

Diabetic foot ulcers are relatively common among persons with diabetes mellitus. Such ulcers often become painfully infected, reducing quality of life and resulting in considerable treatment expense. The most costly and feared consequence of these ulcers is limb amputation.

- 171 million people around the world were estimated to have diabetes in the year 2000.\(^{33}\)
  - Diabetes prevalence is predicted to double to 366 million by 2030.
  - The number of people over the age of 65 with diabetes will increase two and a half times in the same period.

- Among people with diabetes, estimates of lifetime risk for diabetic foot ulcers range from 15% to a high of 25%,\(^ {\text{34}}\) and prevalence from 3% to 13%\(^ {\text{35, 36}}\)
  - In a US study, prevalence was reported as 13%.\(^ {\text{36}}\)
  - In a German study, prevalence was approximately 3%.\(^ {\text{35}}\)

- Diabetic foot ulcers seriously impact quality of life and long-term health; diabetic foot ulcers result in significant medical treatment expense.
  - Foot ulcers can result in loss of mobility that affects everyday tasks and leisure activities.\(^ {\text{37}}\)
  - One third of diabetic individuals with their first foot ulcer suffered from clinical depression, which was in turn associated with increased mortality.\(^ {\text{38}}\)
  - A European study found 23% of diabetic patients with foot ulcers had not healed after a year;\(^ {\text{39}}\) the rate of recurrence was high, up to 50% after 3 years,\(^ {\text{40}}\) further impacting quality of life, costs, and amputation risks.

- Foot ulcers continue to be the most common underlying factor leading to lower-extremity amputation.\(^ {\text{41}}\)
  - Limb amputation occurs 10 to 30 times more often in diabetic persons than in the general population.\(^ {\text{34}}\)
  - A UK study found that 19% of diabetic patients newly reporting a foot ulcer had a lower extremity amputation within 5 years, and 44% died within that same period.\(^ {\text{42}}\)
• A Swedish study estimated the direct costs of treatment for a diabetic foot ulcer were $17,500 (1998 US$); costs rose to $33,500 when amputation was required.\textsuperscript{43} Cost estimates in a 2003 US study were $9,000 to $45,000 USD for annual treatment of a diabetic foot ulcer (depending on severity) and about $50,000 for leg amputation.\textsuperscript{44}

• Diabetic foot ulcers have a large negative impact on patients, both psychologically and socially. These ulcers are associated with a reduction in social activities, increased family tensions, limited employment and financial distress.\textsuperscript{45}

### Venous leg ulcers

Venous leg ulcers are wounds that result from underlying chronic venous insufficiency.\textsuperscript{46} These leg ulcers are common in adults, and are costly to treat due to prolonged healing time.

• Venous ulcers are common. Estimates of prevalence of venous leg ulcers vary considerably due to differing sampling methods, ulcer definition, and population ages. A rough estimate places prevalence at 0.3%, or about 1 in 350 adults.\textsuperscript{46}
  – Studies found a history of either unhealed or healed ulcers occurs in about 1 to 2% of the adult population.\textsuperscript{47, 48} Studies in Sweden and Australia found prevalence rates of 0.16% and 0.06%, respectively.\textsuperscript{49}
  – Prevalence of venous leg ulcers increases with age,\textsuperscript{47, 48} with no difference between men and women at any age.\textsuperscript{49}

• The significant cost associated with treatment of venous leg ulcers is attributed to prolonged healing time.
  – A US study found the average duration of follow-up care for venous ulcer patients was 119 days with an average of seven clinic visits.\textsuperscript{50}
  – At home treatment accounted for nearly half of medical costs incurred in the US study; the 18% of patients requiring hospitalization consumed 25% of all medical costs.\textsuperscript{50}
  – In France and Belgium, the cost of venous ulcer treatments was about 2.5% of the countries’ total health budgets in 1995.\textsuperscript{46}

• Patients report leg ulcers affect nearly every aspect of their daily lives, commonly experiencing pain, interrupted sleep and reduced mobility.\textsuperscript{51} Furthermore, patients’ social activities are often restricted due to fear of injury and negative body image.\textsuperscript{52}
Burns are a devastating trauma requiring immediate, specialized care. Burn survival rates have dramatically increased in the developed world. In the US, the burn-related death rate declined by more than half in the last 40 years. This improvement is a result of advances in the care of severely burned patients, such as fluid resuscitation, nutritional support, wound care and infection control.

- 500,000 people with burn injuries seek medical care annually in the US, and 40,000 require hospitalization.
- The proportion of hospital admissions for burn injury per 1000 people in the general population varies greatly around the world: Finland = .042/1000; Singapore = 0.07/1000; United States = 0.14/1000 (40,000 admissions for burn injuries annually); India = 0.75/1000 (with 700,000 to 800,000 hospital admissions for burn injuries annually).
- Men around the world are at risk for burn injuries in the workplace. Most burn injuries, particularly among women and children, occur at home. Scald burns account for most burn injuries in children around the world, and for 33% of all burns in the US.
- Expenses associated with hospitalized burn injuries in developed countries are enormous, with per patient expenses for the initial, specialized care of a person with a major burn injury estimated to be $200,000 in the US.
- In Israel, mean length of hospitalization was nearly 14 days; 15% of burn patients were in an intensive care unit for a mean duration of 12.1 days. In the US, length of hospital stay averaged just over 8 days in 2005, down from 13 days in 1995.
- Severe burns inflict devastating physical and psychological injuries to victims; pain and suffering continue long after the initial trauma.
Surgical incisions

WHO estimates that 230 million major operations are performed around the world each year, one for every 25 people, or nearly twice as many surgeries as childbirths. Current guidelines emphasize patient nutrition before and after surgery as a means of promoting recovery and helping prevent infections.

- Surgical site infections (SSIs) are a major source of illness in post-operative patients and a significant source of increased costs. Though rates vary from procedure-to-procedure and from physician-to-physician, on average these infections make up about one quarter of all hospital-acquired infections in the US.
  - In the US (1994), about 1.8% of surgeries resulted in a severe (non-superficial) SSI. More recently, a study conducted in the southeastern US (1994) found site infections occurred in 1.4% of surgical procedures.
  - In the UK, one study found 4.2% of surgical procedures resulted in a surgical site infection, though about half of these were superficial incisional infections, which other measures noted here exclude.
  - A Canadian study identified 2.5 site infections per 100 surgical procedures; similar measures in Thailand and Indonesia found 1.4 SSIs and 1.7 SSIs per 100 surgical procedures, respectively.

- Surgical site infections have serious health consequences for patients and are very costly to manage.
  - In a US study of 255 matched patients, patients with SSIs were twice as likely to die, 60% more likely to spend time in intensive care, and five times more likely to be readmitted to the hospital. On average, patients with an infection stayed 6.5 days longer in the hospital than patients without a surgical site infection.
  - A study in the UK found a wide range of increased length of stay, depending on the type of surgery. The extra post-operative days attributable to the infection ranged from 3 days to 21 days depending on the type of surgery.
  - Worldwide, at least 7 million disabling complications and 1 million deaths result from surgical procedures; at least half of these could be avoided, both in the developed and developing worlds, if certain basic standards of care are followed.
Wounds and healing

Normal wound healing

Wound healing is a complex interaction between epidermal and dermal cells, the extracellular matrix, and plasma-derived proteins; all of these activities are coordinated by an array of signaling molecules, including cytokines and growth factors. The dynamic process of healing normal wounds is characterized by three overlapping phases—inflammation, proliferation, and remodeling. Understanding the healing process is critical to successful management of wound patients.

Inflammation. Wound healing begins with clotting, also called hemostasis. Platelets, endothelial cells, and coagulation factors interact to stop bleeding and form a clot. Cells trapped within the fibrin clot, mainly platelets, release vasodilators and chemoattractants, including tissue growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF). These signaling molecules trigger an inflammatory response.

The inflammatory phase of wound healing. Figure with permission from the New England Journal of Medicine. As discussed in this monograph, successful wound healing requires adequate supplies of energy, protein (including essential and conditionally-essential amino acids), vitamins A, C, and E, and the mineral zinc.
In the early inflammatory phase, neutrophils are the most prominent cell type in the wound. Neutrophils release enzymes and perform phagocytosis, thus beginning processes for breakdown and removal of bacteria and debris. Circulating monocytes are attracted to the wound site, ultimately maturing into macrophages responsible for finishing the cleanup process.

Macrophages secrete proteases and clear dead cells, bacteria, and expended neutrophils by phagocytosis. Macrophages also secrete substances that trigger production of cells that are important in the subsequent proliferative phase. As the wound site is cleared of damaged tissues and bacteria, the numbers of neutrophils and macrophages decline, thus ending the inflammatory phase and beginning the proliferative phase.

**Proliferation.** The proliferation phase is characterized by buildup of connective tissue, starting with granulation tissue. Granulation tissue is made up of macrophages, fibroblasts, immature collagen, blood vessels, and ground substance.\(^4\)

Fibroblasts enter and proliferate in the wound site. Fibroblasts secrete collagen molecules, which are assembled into fibers and cross-linked into bundles, thus affording tensile strength and structure. This newly-formed matrix is host to angiogenesis, so that new vascular structures can deliver nutrients as well as plasminogen activator and collagenase to the fibroblasts. Some fibroblasts differentiate into myofibroblasts, which bind to and draw the wound edges closer together, thereby reducing the size of the wound.\(^7\) While new matrix is built, existing matrix around the wound margins is degraded by enzymes, i.e. metalloproteinases and plasminogen activators.\(^72\) Activity of these enzymes is regulated, so excessive matrix degradation will not occur. In the final step of the proliferation phase, some keratinocytes migrate from the wound margins and divide until they form a contiguous epidermis, or surface layer of the skin. Other keratinocytes phagocytose debris. Keratinocyte-mediated changes, coupled with wound contraction, result in re-epithelialization and wound closure.\(^4,72\) A scar forms when epithelialization is complete. Fibroblasts produce collagen molecules, which are assembled into fibers that rebuild the matrix of tissue so that blood vessels can be restored (angiogenesis). Keratinocytes help close the wound and remove dead cells and other debris.
The proliferative phase of wound healing. Figure with permission from the New England Journal of Medicine. Anabolic processes of the proliferative phase involve structural proteins (mainly collagen) as well as functional proteins (regulatory enzymes). Protein synthesis, supported by ample supplies of constituent amino acids, is therefore critical to supporting this phase of wound healing.
Remodeling. Once the wound has closed, remodeling of the wound commences, a phase that can continue for months or years. Early, randomly-placed collagen is remodeled into a better-organized structure, providing greater tensile strength. Over time, cell content and blood flow in the scar tissue decreases.

Conditions that impair wound healing

Hard-to-heal wounds lack anatomic and functional integrity, so they heal slowly or do not heal at all. These wounds remain in the inflammatory or proliferative phase, allowing the excessive accumulation of extracellular matrix components, which in turn may lead to the premature degradation of collagen and growth factors. Various factors, both local and systemic, are known to impede wound healing; wound infection and nutritional deficiencies are common contributors (Table 1). Less common factors include local or distant cancers, use of certain anti-cancer drugs, and genetic healing abnormalities.

Table 1. Factors commonly involved in hard-to-heal wounds

<table>
<thead>
<tr>
<th>LOCAL FACTORS</th>
<th>SYSTEMIC FACTORS</th>
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<tbody>
<tr>
<td>Wound Infection</td>
<td>Nutritional deficiencies (i.e., deficiencies of proteins, vitamins, minerals)</td>
</tr>
<tr>
<td>Ischemia</td>
<td>Chronic diseases (i.e., diabetes mellitus, renal disease)</td>
</tr>
<tr>
<td>Venous insufficiency</td>
<td>Advanced age and general immobility</td>
</tr>
<tr>
<td>Mechanical trauma (i.e., pressure sores)</td>
<td>Smoking</td>
</tr>
<tr>
<td>Tissue maceration</td>
<td></td>
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<tr>
<td>Presence of a foreign body</td>
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Care of hard-to-heal wounds

The wound care team

Taking a team approach is essential to treating hard-to-heal wounds—with effective interactions between the patient, his or her family members, and the health caregivers. Successful wound management particularly requires communication among members of the wound care team, including nurses, physicians, and other health professionals in:

- Specialty areas
  - Wound care specialists
  - Dermatology
  - Surgery

- Nutrition
  - Dietitians
  - Medical nutrition specialists, including Certified Diabetes Educators

- Primary care
  - Geriatrics
  - Family medicine
  - Social worker

The patient and his or her personal/professional support team members will be involved in cleaning and dressing the wound as it heals, as well as in maintaining a nutritional status that can facilitate wound healing.
Cleaning and dressing a wound

Normal wound healing requires proper vascular circulation, infection prevention, and avoidance of negative mechanical forces; these principles are the basis for cleaning and dressing a wound.75

Debridement. Debridement is the process of removing dead, damaged, or infected tissues to improve the potential for healing the remaining healthy tissue in a wound site. A variety of techniques accomplish debridement—sharps (scalpel, forceps, scissors), enzymes (collagenase or papain-containing ointments), or autolysis (self-digestion in the context of a wound dressing that afford moisture at the wound site).75

Moisture control. Moisture is essential for proper healing. Acute wounds with occlusive or semi-occlusive dressings that retain moisture have been shown to heal twice as fast as wounds exposed to air. Since highly exudative wounds may cause excessive wetness and tissue maceration, the ideal dressing is one that absorbs exudates without excessive drying.75

Wound dressings. Many wound dressings are available around the world, so it is challenging to select the dressing best suited for each wound. The ideal dressing is one that removes excess exudates, maintains a moist healing environment, protects against contamination, is easily removable when appropriate, leaves no debris in the wound, provides thermal insulation, and does not induce allergic reactions.75 Wound dressings include barrier creams to protect skin around the wound, semi-occlusive films, hydrogels to moisturize the wound site, hydrocolloids or alginates to absorb excessive exudates fluids, and collagen-containing products to provide a matrix for deposition of new tissue.75

Prevention and treatment of infections. Topical antimicrobial agents help prevent excessive colonization of the wound site by bacteria, while systemic antibiotics are usually reserved for clinically infected wound sites.75
Nutritional care: rationale to implementation

- **Rationale.** Nutrition is a key component of the health care team’s approach to wound treatment. Hard-to-heal wounds will heal faster and with fewer complications when the host is well nourished.

- **Action plan.** Nutrition-based prevention and treatment of wounds uses a multi-step strategy: 1) assess nutritional status, 2) estimate nutritional needs, and 3) implement appropriate and comprehensive nutritional interventions.

- **Basic nutrition.** Adequate basic nutrition for healing wounds includes caloric energy, protein, fluid supplies, and certain vitamins and minerals. Caloric energy from carbohydrates and fats is essential to meet basic energy needs, thus sparing breakdown of proteins for energy. Dietary protein supplies, including essential and conditionally-amino acids, are needed for synthesis of proteins that are involved in wound healing and immune function. Fluid intake is critical to compensate for loss from wound injury and wound exudates. Despite efforts to maintain normal nutritional status through basic nutrition strategies, wound healing may be suboptimal because of specific nutritional deficiencies.

- **Targeted nutrition.** For wound healing, “targeted nutrition” products may be necessary to meet conditionally-essential needs. Under normal conditions, such nutrients are derived from regular foods or oral nutrition supplements. However, to meet the high demands of wound healing, additional sources are often needed. If these special needs are unmet, wounds will fail to heal.

- There is evidence for the use of Abound® (HMB + arginine + glutamine) to support wound healing, increase protein synthesis and lessen protein breakdown, and immune function [see section below on Abound® Clinical Trial Results].

Nutrition is a key component of the health care team’s approach to wound treatment.

Nutrition for healing of wounds includes:
- Caloric energy
- Protein (including ample supplies of conditionally-essential amino acids such as arginine and glutamine)
- Fluid supplies
- Certain vitamins and minerals, such as vitamins A, C, and E, and zinc

Abound® is a “targeted nutrition” product formulated to meet condition-essential needs that are associated with wound healing.
Overall nutrition for wound healing

If adequate dietary nutrition is not consumed, malnutrition can lead to impaired wound healing and immune function. Immune compromise correlates clinically with increased wound complication and infection rates. Malnutrition may pre-date wounding or may be secondary to the catabolism resulting from the wound itself. Wounding increases metabolic rates, catecholamine levels, loss of total body water, and turnover of protein in cells, thus resulting in an overall catabolic state.

Specific nutritional guidelines by wound type

Pressure ulcers. The US Agency for Healthcare Research and Quality provides specific nutritional guidelines for a person who has a pressure ulcer and is malnourished:

- 30 to 35 cal/kg body weight per day
- 1.25 g – 1.5g of protein/kg of body weight per day
- Water intake from beverages + foods = 2.7 L/day (adult female) and 3.7 L/day (adult male)

The European Pressure Ulcer Advisory Panel provides similar, specific nutritional guidelines. Guidelines begin by recommending that patients at risk should be screened and assessed for possible malnutrition, and offered nutritional support, as needed. The presence of established pressure ulcers may demand greater supplementation (normal feeding, then oral supplements and finally tube-feeding). The amount of supplementation required by each individual varies, but guidelines suggest:

- a minimum of 30–35 kcal per kg body weight per day
- 1.25 to 1.5 g/kg/day protein, and
- 1ml of fluid intake per kcal per day.
Adequate nutrition and fluid intake have long been recognized as important to maintaining tissue integrity and promoting healing of pressure ulcers, while weight loss, low weight status, low albumin levels, and low body mass index are associated with pressure ulcer development and poor healing. Results of a meta-analysis of outcomes for elderly hospitalized patients showed that enteral nutritional support, particularly high-protein oral nutrition supplement, can significantly reduce the risk of developing pressure ulcers by 25%; there was a trend toward improved healing of pre-existing pressure ulcers.

**Diabetic foot ulcers.** There is considerable evidence to support the practice of maintaining glycemic status as close to normal as possible in order to prevent and delay complications of diabetes. Optimal glycemic control is thus recognized as a key strategy for preventing development of diabetic foot ulcers. The American Diabetes Association recommends:

- monitoring nutritional status indicators (e.g. change in body weight) and glycemia to ensure that needs are met and hyperglycemia is prevented
- protein needs of 1.25-1.5 g/kg body weight, with the higher end for more stressed patients; protein intake will not decrease catabolism, but it will enhance protein synthesis

Nutritional recommendations for people with diabetes are targeted to prevention of microvascular and neuropathic complications by maintaining blood glucose as close to normal as possible with a goal of maintaining hemoglobin A1c below 7%. Singh and colleagues summarized compelling evidence to support the importance of glycemic control as a means of preventing development of foot ulcers.
Burns. Patients with burns have the highest metabolic rate of all critically ill or injured patients, and survival among these patients has been shown to be inversely correlated with loss of lean mass. A guideline for burned patients aged 16-60 yrs is 25kcal/kg/day plus an additional 40kcal/%burn/day.88 Burn injuries can lead to extensive nitrogen loss, increased metabolic rates, malnutrition, and immunologic deficiencies. These changes predispose burn patients to frequent infections, poor wound healing, increased length of hospitalization, and increased mortality.89 Early and adequate nutritional support is vital to restoring protein synthesis and normal immune function.54 A number of studies have shown beneficial effects of increased dietary components such as glutamine, arginine, and (n-3) fatty acids and related compounds in burn victims.88 Providing adequate nutrition to burn patients promotes wound healing while reducing the loss of lean body mass.88

Macronutrient recommendations

Calories. Although caloric needs vary for each person based on activity level and health conditions, guidelines consistently recommend intake of 30-35 cal/kg body weight per day.26,79 Lower intake may be appropriate for certain people with diabetes in order to maintain glycemia within the normal range.87 Higher intake may be needed for people with severe wounds, e.g. burns can increase energy requirements as much as 100%.90

Protein. Although normal adults need just 0.8 g protein/kg body weight, people with wounds, e.g. pressure ulcers, need more protein to support healing—in the range of 1.25 to 1.5 g protein/kg of body weight.80

Fluid. Fluid is essential to normal functioning of cells. Wound drainage can be a major source of fluid loss and can lead to dehydration and electrolyte imbalance. Dehydration is a risk factor for pressure ulcer development because it can reduce blood volume, thereby interfering with peripheral circulation and decreasing nutrient and oxygen supply to tissues.91, 92 The average adult needs between 2000 to 3000 mL of fluid per day to replace losses from urine, stool, exhalation, and the skin.90
Roles of specific nutrients

Vitamins and minerals. Vitamins A, C, and E, and the mineral zinc have recognized roles in healing wounds. Nutritional deficiencies allow development of pressure ulcers and impair healing of wounds. Vitamin A seems to enhance the inflammatory response and contribute to wound healing by increasing monocyte influx and macrophage activation and by stimulating the synthesis of collagen and wound closure. Vitamin C facilitates wound healing by enhancing collagen synthesis and increasing angiogenesis; vitamin C also supports immune function to help prevent infection and promote recovery. Vitamin E is thought to maintain and stabilize cellular membrane integrity by its anti-oxidant capacity.

Zinc is a cofactor for both DNA and RNA polymerases and is therefore a key micronutrient to support DNA synthesis, protein synthesis, and cellular proliferation.

<table>
<thead>
<tr>
<th>NUTRIENT</th>
<th>PROVIDES SUPPORT FOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>Increased requirements due to inflammation and metabolic stress</td>
</tr>
<tr>
<td>Protein</td>
<td>Collagen synthesis, wound contraction, scar formation, immune response</td>
</tr>
<tr>
<td>Zinc</td>
<td>Protein synthesis, cellular growth</td>
</tr>
<tr>
<td></td>
<td>Note: deficiency impairs healing</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Collagen synthesis, immune response, wound closure</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Collagen synthesis, immune response, wound strength, angiogenesis</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Wound strength, antioxidant</td>
</tr>
</tbody>
</table>

Vitamins A, C, and E, and the mineral zinc have recognized roles in healing wounds.
Use of Abound® as part of optimal wound care

Abound® is a therapeutic nutrition product intended for people who have non-healing wounds. Abound® is intended for use in concert with a complete and balanced diet (oral food intake, oral nutrition supplements, enteral tube feedings, or some combination) along with optimal management of the wound (debridement, moisture control, wound dressings, and infection control).

Abound® and its ingredients

Abound® is a therapeutic nutrition product that combines 3 key active ingredients—arginine, glutamine, and HMB—with other ingredients affording flavor and stability of the blend.

• Abound® supports wound healing.22
• Abound® supports immune function to help prevent or recover from complicating infections.93
• The ingredients of Abound—arginine, glutamine, and HMB—play multiple roles: 1) slow protein breakdown, 2) facilitate synthesis of collagen and other proteins involved in wound healing, and 3) promote function of numerous cells involved in immune responses.

Arginine. Arginine is a conditionally-essential amino acid; it is made by the body in sufficient quantities under usual conditions, but a dietary source becomes necessary during periods of healing.94 Recognized to play a wide range of roles in wound-healing processes, arginine: (1) induces secretion of the anabolic hormones insulin and growth hormone, (2) stimulates T-lymphocyte responses for wound healing (3) serves as a metabolic precursor for nitric oxide, which in turn mediates bacterial killing by macrophages, and (4) is catabolized to ornithine and converted to proline, which is used for collagen synthesis.22, 23, 76
Glutamine. Glutamine is the most abundant amino acid in the body, and it has numerous metabolic roles. Glutamine is conditionally-essential during times rapid tissue growth, especially during wound healing. Glutamine is a nitrogen donor for synthesis of amino acids and amino sugars, and it is a precursor for synthesis of nucleotides in cells such as fibroblasts and macrophages, thereby supporting cell proliferation and function. Glutamine serves as a source of metabolic energy for lymphocytes and macrophages (immune cells), and it is also converted in the liver to glucose, which ultimately serves as an energy source for wound healing in the periphery. In addition, glutamine is a metabolic fuel for cells of the intestinal mucosa, thereby playing an important role to maintain gut integrity and function, including gut immune function.
In conditions such as trauma, infection, wound healing, and burns, the inflammatory processes involved in recovery increase needs for energy and for specific nutrients, particularly the conditionally-essential amino acid glutamine. If adequate glutamine is not available, muscle proteins will be broken down to meet the body’s energy needs. Supplemental glutamine has been shown to:

- Help maintain muscle protein during stress
- Support and regulate synthesis of proteins, including collagen, as needed for wound healing
- Helps maintain function of gut cells, including gut-associated lymphoid tissues (immune cells)

HMB, a leucine metabolite. Leucine is a member of the branched-chain amino acid family, along with valine and isoleucine. The branched-chain amino acids play a role in maintaining nitrogen balance in adults, especially in conditions such as sepsis, trauma, and burns; they support protein synthesis after injury and decrease muscle proteolysis.22 Beta-hydroxy-beta-methylbutyrate (HMB) occurs naturally in the body as a leucine metabolite; HMB has been shown to inhibit muscle proteolysis and modulate protein turnover.15-17, 96, 97

Muscle converts approximately 5% of available leucine to HMB.16 A 70 kg person would thus produce 0.2 to 0.4 g of HMB each day, a quantity that is insufficient to support metabolic needs during times of rapid growth and healing.16
### Ingredients of Abound®

<table>
<thead>
<tr>
<th>ACTIVE INGREDIENTS</th>
<th>OTHER INGREDIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• L-arginine</td>
<td>• Citric acid</td>
</tr>
<tr>
<td>• L-glutamine</td>
<td>• Orange juice powder</td>
</tr>
<tr>
<td>• Calcium beta-hydroxy-beta-methylbutyrate (HMB)</td>
<td>• Sugar (sucrose)</td>
</tr>
<tr>
<td></td>
<td>• Natural flavors</td>
</tr>
<tr>
<td></td>
<td>• Aspartame</td>
</tr>
<tr>
<td></td>
<td>• Medium-chain triglycerides (MCT oil)</td>
</tr>
<tr>
<td></td>
<td>• Acesulfame potassium</td>
</tr>
<tr>
<td></td>
<td>• FD&amp;C Yellow #6</td>
</tr>
</tbody>
</table>

### Abound® Label Information

**SERVING SIZE** 1 PACKET ORANGE FLAVOR (24 g)

**SERVINGS PER CONTAINER** 1

- **Energy**
  - 79.0kcal = carbohydrates 23kcal, amino acids 56kcal
- **HMB 1.2g, provided as 1.5g of calcium HMB**
- **Amino acids**
  - L-arginine 7 g
  - L-glutamine 7 g
- **Carbohydrate**
  - Sugars 2 g
- **Minerals per serving**
  - Calcium 200 mg
A Case Study From the US—an elderly woman with pressure ulcers

Mrs. B is an 84 year-old woman with diabetes and Alzheimer’s disease; she resided in a facility for skilled nursing care. During the summer, she developed multiple pressure ulcers, including a severe Stage IV wound, on her right gluteal fold.

Due to the severity of her condition, Mrs. B was limited to bed, and a Foley catheter was placed. Mrs. B’s initial treatment course involved routine wound care, a specialty mattress, protein powder supplement, and vitamin C, zinc, and multi-vitamins. She received oral food but only finished 50 to 75% of the meals, so she was also given high-calorie liquid medical nutrition supplements.

Mrs. B’s routine was maintained for 6 months. During that time, she made several trips to a wound care center for debridement and medication adjustments. Despite these efforts, the Stage IV wound did not heal, and Mrs. B experienced an overall decline in her health status.

In January, Mrs. B was transferred to hospice care with comfort measures only. After another 7 months, her health status was sufficiently stable for her return to the skilled nursing care facility. In October, 14 months after her pressure ulcer was first documented, twice-daily treatments with Abound® medical nutrition was initiated. She was continued on the specialty mattress, protein powder supplement, and vitamin C, zinc, and multi-vitamins. Her Foley catheter remained in place.

Just 10 weeks after Abound® was added to Mrs. B’s treatment regimen, her Stage IV wound was completely closed. The catheter was removed, and the specialty mattress was no longer needed. Mrs. B was able to get out of bed and walk.

Clinical trial results

The safety and efficacy of Abound®, a proprietary blend of HMB, arginine, and glutamine, have been tested in seven clinical trials, including tests in healthy adult volunteers, critically injured trauma patients, men in resistance-training, cancer patients, and people with HIV/AIDS. These studies provided evidence for safety of Abound® as well as support for efficacy in attenuating loss of lean tissue and increasing body mass.

Abound® and wound healing

The principal evidence for enhancement of processes involved in wound healing comes from studies by Williams and colleagues. In addition, a study by Clark et al. provides evidence that Abound® helps enhance immune function, an important way to lower risk for wound complications.
Abound® testing in healthy elderly volunteers. Collagen deposition, a means of enhancing wound strength and integrity, was tested in a study of 35 healthy volunteers aged 70 years or older; subjects were randomized to receive twice-daily treatment with the HMB/glutamine/arginine mixture (Abound®) or an isonitrogenous, isocaloric supplement of nonessential amino acids.7 Prior to amino acid treatment, sterile catheter tubes were implanted into deltoid muscles of subjects to evaluate ingrowth of fibroblasts and deposition of collagen matrix (measured as hydroxyproline content). Results showed a significant 67% increase in hydroxyproline content after 14 days of treatment with Abound® compared to control. The authors concluded that oral administration of Abound® mixture significantly enhanced collagen synthesis in healthy elderly adults, thus providing a safe nutritional means for supporting wound repair in patients.7

Williams et al. study of Abound® and collagen synthesis7
Abound® in clinical practice

Abound® is a brand-new approach for patients with hard-to-heal wounds. Abound® fills an important gap in wound care practice.

People who can benefit from Abound®

Individuals who may benefit from Abound® include those with hard-to-heal wounds:

- Pressure ulcers
- Venous leg ulcers
- Diabetic foot ulcers
- Burn injury
- Complicated surgical incisions

How to incorporate Abound® into the therapeutic regimen

Patients with hard-to-heal wounds can benefit from Abound® in combination with an overall nutrition plan that be combined effectively with regular food or with other Abbott nutritional products to meet nutritional guidelines for wound healing. For individuals who can consume oral foods, Abound® can be given in combination with regular food or with regular food as well as a medical nutrition supplement such as Ensure (for malnourished individuals) or Glucerna® (for malnourished people with diabetes). For those who cannot consume oral food, Abound® can be combined with a complete and balanced tube-fed nutritional supplement such as a product in the Jevity® family.
Patients with hard-to-heal wounds

<table>
<thead>
<tr>
<th>Normal nutrition status</th>
<th>Malnourished nutrition status</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI 18-21</td>
<td>BMI &lt; 18</td>
</tr>
<tr>
<td>No weight loss</td>
<td>Weight loss &gt; 5% over 2 months</td>
</tr>
</tbody>
</table>

Able to consume oral foods?

Yes

- Regular food + Abound

No

- Jevity to meet kcal and protein needs + Abound
- Combination feeding
  - Regular food + Ensure or Glucerna + Abound
- Jevity to meet kcal and protein needs + Abound

Guidelines: 30-40 kcal/kg; 1.25-1.5 g protein/kg
Forms and Flavors

Because free glutamine has limited stability in liquid, Abound® is a powder that must be mixed with liquid. It is available in convenient single-serving packets of orange-flavored and neutral powders. Abound® neutral is for patients who prefer to mix it with their choice of juice, smoothie, or food.

Directions for use

Each packet of Abound® is dissolved with liquid to make one serving; the recommended dose is 2 servings (packets) a day. The 2 daily servings of product are best consumed with a morning meal and an evening meal. Each serving of Abound® provides 7 g of arginine, 7 g of glutamine, and 1.2 g of HMB (from 1.5 g CaHMB).

Preparation for oral consumption

1. Mix one packet of Abound® with 237 mL to 296 mL of cold water (use juice/other liquid for neutral product), and stir with a spoon until all powder is dissolved.
2. Note: Do not mix Abound® with hot or boiling water/juice.
3. Only use Abound® under medical supervision.

Administering as Tube Feeding

1. Abound® should not be mixed with formula in a tube-feeding bag.
2. For mixing, place one packet of Abound® in a small, clean container (about 177 mL to 237 mL volume).
3. Add 120 mL of water at room temperature.
4. Mix well with a spoon until all particles are dissolved.
5. Verify correct tube placement.
6. Flush feeding tube with 30 mL of water.
7. Administer Abound® through feeding tube using a 60 cc or larger syringe.
8. Flush with an additional 30 mL of water. A smaller amount of water can be used to flush the tube if the patient is on fluid-restriction.
9. Only use Abound® under medical supervision.
Conclusions

Abound® is a therapeutic nutrition product with a unique blend of key ingredients—amino acids arginine and glutamine, and beta-hydroxy-beta-methylbutyrate (HMB; a metabolite of the amino acid leucine). Combined, these Abound® components help maintain body proteins, which are vital for resolving hard-to-heal wounds. Glutamine and arginine also serve as metabolic fuels for immune cells, thereby enhancing immune function to prevent or fight infections that may otherwise complicate wound healing.

Individuals who may benefit from Abound® include those with:

- Pressure ulcers
- Venous leg ulcers
- Diabetic foot ulcers
- Burn injury
- Non-healing surgical incisions

Abound® is part of total care for wound healing. Abound is used along with a diet designed for wound healing and appropriate wound care. Overall nutrition can be provided as a food diet, food in combination with an oral nutritional supplement, or complete and balanced tube-fed nutrition. Proper wound care includes wound debridement, moisture maintenance by appropriate dressings, and prevention and treatment of infection.
References


78. ASPEN. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. J Parenter Enteral Nutr. 2002;26:1SA-138SA.


