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Chetosil® spray powder in the treatment of skin lesions

Contents

1. Skin wounds and ulcers

The skin is the body's main protective organ. Wounds are interruptions in the continuity of the skin and soft tissues, whereas **ulcers are interruptions in skin continuity with loss of tissue** that affect the **various layers of the skin extending down to the hypodermis and, in severe cases, to the underlying tissues,** as occurs in the diabetic foot.[1]

Chronic skin ulcers are lesions that affect the various layers of the skin and fail to undergo the physiological process of tissue repair within 3 months of onset.

Skin ulcers and wounds are classified into acute and chronic.[2] Acute wounds are predominantly of traumatic and postoperative origin and, if adequately treated, they usually progress through a series of events leading to final healing of the lesion with restoration of tissue integrity.[2]

Chronic ulcers or wounds are defined as those that **within 3 months of onset have not undergone a normal and rapid process of restoration to anatomical and functional integrity**, owing to intrinsic or extrinsic factors that have an impact on both the individual and the wound.[2,3]

Lower limb ulcers and **pressure ulcers** are considered chronic lesions.[2] Most lower limb ulcers are caused by venous insufficiency (around 45-60%), arterial insufficiency (10-20%), diabetes (15-25%), decubitus (18%) or a combination of these aetiological factors (10-15%) (*Table 1*).[4,5]

Lower limb ulcers, diabetic foot ulcers and pressure ulcers are all chronic lesions.

Table 1. Common causes of chronic ulceration of the lower limbs. Modified from[4,5]

Aetiology	Prevalence
Venous insufficiency (post-thrombotic syndrome)	45-60%
Peripheral arterial disease (arteriosclerosis)	10-20%
Diabetes (neuropathy and/or arterial occlusion)	15-25%
Decubitus (pressure ulcers)	18%
Combination of these aetiological factors	10-15%

Incidence and prevalence

The incidence of lower limb ulcers is thought to be rising as a result of both the ageing of the population and the increase in risk factors for arteriosclerosis, such as smoking, diabetes and obesity.[6]

According to the most recent guidelines of the European Dermatology Forum, lower limb ulcers affect 1.5% to 3% of the general population up to 4-5% of subjects ≥80 years of age.

The yearly incidence of diabetic ulcers is even higher, between 1.9% and 4.1%, and the prevalence of foot ulcers in diabetic patients reaches 7.7% (against 2.8% in the general population).[3]

Foot ulcers in diabetic patients have a prevalence of 7.7% (against 2.8% in the general population).

The Italian Study on Cutaneous Ulcers (*Studio Italiano Ulcere Cutanee*, SIUC), conducted between 2015 and 2016 by the Italian Cutaneous Ulcers Association (*Associazione Italiana Ulcere Cutanee,* AIUC) to collect as many data as possible on the presence of patients with skin ulcers in Italy, found that the majority of affected patients were women (60%), had a mean age of 77 years and presented with an average of 1.66 lesions per patient. The most frequent forms were venous, diabetic and arterial ulcers (*Figure 1*). The leg was the most commonly affected site (53% of cases), followed by the sacral region and the foot (14.9% and 14.7% of cases, respectively). Over 31% of the 3,975 patients entered in the database had skin ulcers for over 1 year and 16% of patients for over 2 years.[7]

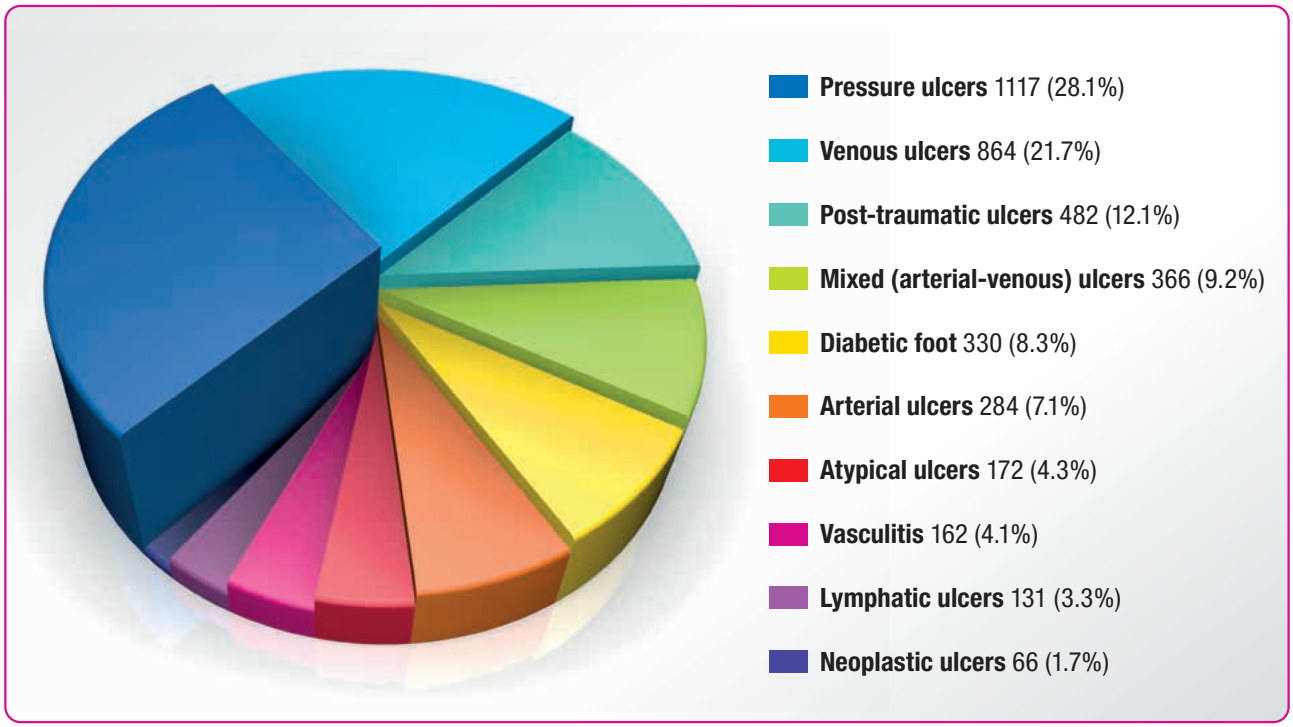

Figure 1. Ulcers: distribution and aetiology (modified from[7]).

Chronic skin ulcers represent an ongoing challenge for health professionals and a significant public health problem representing a major economic burden for the Italian National Health System.[3]

From the patient's point of view, chronic skin ulcers are debilitating and painful, and they limit independence and seriously impair quality of life, if not adequately treated.[8]

Pathophysiology of tissue repair in chronic lesions

Regardless of the type of lesion, whether acute or chronic, and the extent of tissue loss, healing of a skin lesion is a dynamic process consisting of a series of sequential events that initiate immediately after lesion onset and end with repair of the damaged tissue.[9] The physiological sequence of the repair process is made up of 3 phases:

- inflammatory or exudative phase (first 3-7 days);
- proliferative or granulation phase (5 to 14 days);
- remodelling phase (from around day 10 onwards).

Healing of a skin lesion is a complex and dynamic process, schematically divided into three phases.

The sequence is a continuum and is often termed the "healing cascade" (*Figure 2*). Skin lesions in which this sequence is altered, often because of comorbidities, tend to become chronic.[3]

Inflammatory phase. During the first week after lesion onset, platelets and mast cells are activated and a temporary thrombus is formed. A clotting process is triggered and cytokines are produced with activation of neutrophils which cleanse the wound of cellular debris and bacteria. In addition, granulocytes secrete proteolytic enzymes that eliminate the damaged and unviable components of the extracellular matrix; the neutrophils are then replaced by macrophages that finish cleansing the wound and produce growth factors and other mediators such as prostaglandins and complement factors, which stimulate the formation of new tissue.[9,10]

In the ***proliferative phase***, the fibroblasts recruited from the surrounding dermis to replace the macrophages produce collagen, fibronectin and proteoglycans, such as hyaluronic acid, to form granulation tissue. The fibroblasts present on the border of the wound in part turn into fibrocytes and in part into myofibroblasts, and are responsible for contraction of the wound.

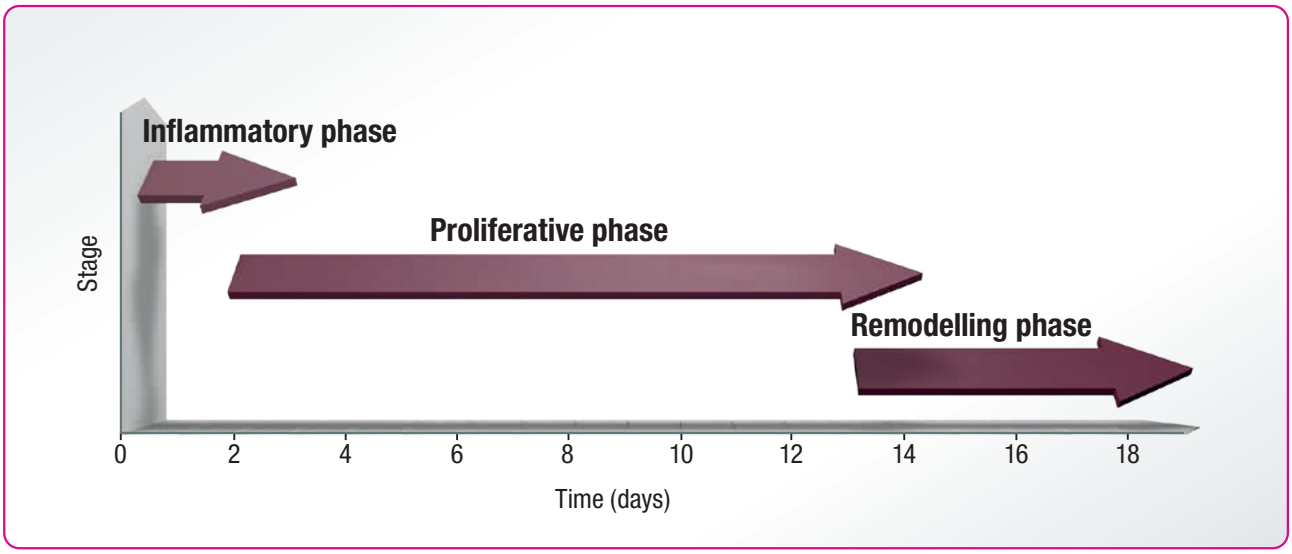

Figure 2. Graphic representation of the physiological tissue repair process (modified from[9]).

Both of these processes are crucial for the ulcer to heal. While new matrix is being synthesised, metalloproteinases, a family of 14 proteolytic enzymes, degrade the cellular matrix on the borders of the ulcer. This phase is characterised by angiogenesis and re-epithelialisation.[9,10]

During the ***remodelling phase***, which may last up to 1 or 2 years after lesion onset, the damaged tissue evolves until a mature or hypertrophic scar is formed through collagen synthesis by the fibroblasts and the reduction of inflammatory cells and blood vessels.[9,10]

In a chronic wound, the microenvironment is characterised by reduced levels of growth factors and transformation factors which, under physiological conditions, aid the transition from the inflammatory or exudative phase to the proliferative phase. The repair process stops during the inflammatory or proliferative phases; the presence of exudate is constant, there is accumulation of metalloproteinases, collagenases and elastase that degrade the collagen and growth factors prematurely, thereby hindering the healing process.[2] For this reason, one of the therapeutic goals of the treatment of chronic ulcers is to reduce tissue inflammation and the related production of exudate.

> ***Chronic ulcers are skin lesions that, owing to intrinsic or extrinsic factors, do not follow the physiological "healing cascade".***

The presence of a hypoxic microenvironment contributes to the proliferation of fibroblasts and, as a consequence, to increased tissue fibrosis. In addition, altered oxygen diffusion from the capillaries reduces leukocyte phagocytosis, increasing the risk of wound infection with a bacterial or fungal contamination that inhibits the tissue repair process.[2]

Infections are indeed an unpleasant complication that need to be effectively prevented.[9]

Systemic conditions such as diabetes, venous stasis and immunosuppression as well as steroid use or smoking may hinder wound healing.[9]

2. Focus on diabetic foot disease

Foot ulcerations are among the most common complications of both type 1 and type 2 diabetes. They potentially affect up to 25% of diabetic patients during their lifetime, in particular men aged 60 years and over, and represent the most frequent cause of hospital admissions among diabetic patients in Western countries.[1]

Diabetic ulcer is a common complication of both neuropathy, which increases the perception threshold for minor injuries, and of peripheral vasculopathy, in which the reduced blood flow facilitates ulcer development as well as hindering healing.[1] Indeed, not only is the blood supply needed to heal an ulcer greater than that needed to maintain intact skin, but the reduced blood flow impedes the distribution of antibiotics at the site of the wound.[11] Infection is not the primary cause, but a phenomenon that sets in after ulceration of the skin.[1] The frequency

and severity of wound infection are increased in the diabetic patient and are related to both elevated blood glucose levels and altered granulocyte function and chemotaxis. Moreover, the diabetic patient seems to present prolonged inflammation, impaired neovascularisation, reduced collagen synthesis and fibroblast proliferation, and impaired synthesis of extracellular matrix proteins.[4]

3. Treatment goals

The treatment of chronic ulcers requires an overall assessment of the patient followed by selection of appropriate therapy aimed at treating both the wound and its causes.[2]

Chronic ulcers represent a major public health problem. They impair the patient's quality of life and require appropriate treatment.

The main goals of wound treatment are:[12]

- **prevent or control any infection** with topical treatments and, if necessary, with systemic treatments to prevent the infection from spreading;
- **remove excess exudate**, which alters the protein composition and growth factors of the extracellular matrix, prolongs the inflammation and inhibits cellular proliferation thereby delaying healing;
- **reduce the inflammation**;
- **achieve scar formation**.

4. Chetosil® spray powder

Chetosil® spray powder is a class 2a medical device (Non-invasive devices in contact with injured skin), **to be used on injured skin** on which it creates an **effective barrier film that supports the natural healing processes**. In particular, this protective barrier:[13]

Chetosil® spray powder acts by coating the injured skin with an effective film barrier that supports the physiological healing process.

- **isolates the application area**, creating a wound microenvironment conducive to rapid scar tissue formation;
- **resists microbial aggression**, limiting contamination of the application area.

This way, **Chetosil® spray powder** promotes **restoration of the normal physiological conditions necessary for scar tissue formation**.

Composition and mechanism of action

Chetosil® spray powder is composed of: kaolin, starch, MicroSilver, sodium hyaluronate, as well as butane, disiloxane, isobutane and propane. These ingredients create a **protective barrier that has the ability to absorb exudate, thereby preventing wound maceration and the onset of possible infections**.[13]

Each component of Chetosil® spray powder serves a specific function, the final outcome of which is scar tissue formation (*Figure 3*).[13]

Figure 3. Mechanism of action of Chetosil® spray powder (modified from[13]).

- **Kaolin (or white clay)**: is a neutral layered aluminium silicate, which presents as an absorbent powder owing both to the presence of electrical charges and to the extensive specific surface area. Thanks to its hydrophilic property it acts as an absorbent material in the case of exudative wounds. The absorbent properties of these materials are well known and used in the pharmaceutical industry for different purposes, e.g., in the treatment of diarrhoea or to absorb toxic substances.[13]

- **Starch**: a form of starch that has been hydrophobically modified to give it greater microbiological stability and ability to absorb even fat-soluble molecules when used on exudative wounds; in addition, this form of starch has improved sensory properties in terms of softness and silkiness. In the pharmaceutical industry, starch has been used for several years to absorb wound exudates.[13]
- **Hyaluronic acid**: with a molecular weight of 1,000,000 Daltons and a particle size of 20 microns, hyaluronic acid promotes wound healing thanks to its strong film-forming and moisturising properties. It creates an effective barrier that protects against external contaminations.[13]

The kaolin, starch, silver and sodium hyaluronate contained in Chetosil® spray powder create a protective barrier that absorbs the exudate and prevents wound maceration and the possible onset of infections.

- **MicroSilver**: Chetosil® spray powder contains a novel form of pure metallic silver derived from a unique and complex production process that guarantees the release of silver in its ionic form over a longer period of time (depot effect). The silver incorporated in the scaffolding created by the kaolin, starch and hyaluronic acid ensures stability of the product's film-forming properties. The broad spectrum antimicrobial properties of silver have been known since the early 1800s. The soluble silver ions inactivate several enzymes, damage the membranes of bacterial pathogens and exert an anti-inflammatory action (*Figure 4*).[13]

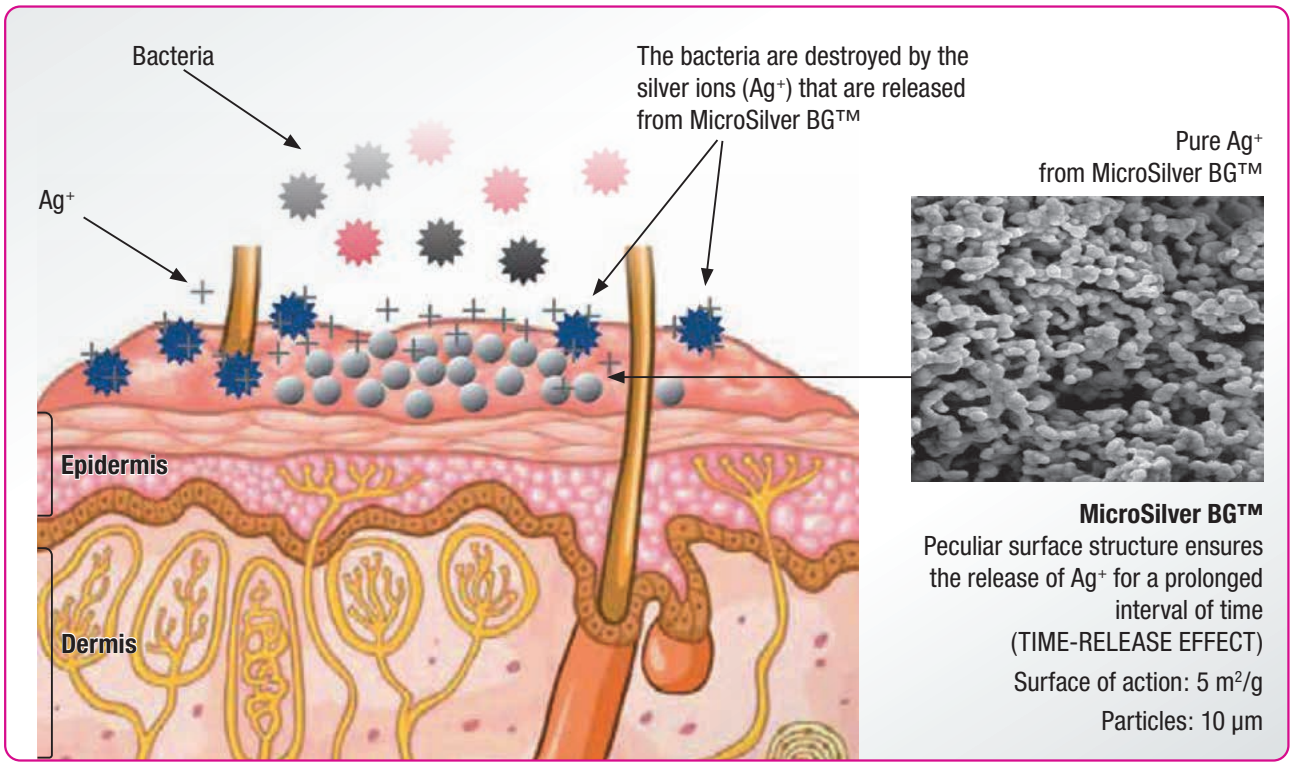

Figure 4. Silver MicroSilver BG™.

Indications for use

The composition and characteristics of the ingredients of Chetosil® spray powder make the product particularly indicated for subjects with:[13]

- **diabetic foot**
- **athlete's foot**
- **small decubitus ulcers**
- **small cuts**
- **burns.**

Instructions for use

Before using **Chetosil® spray powder** the skin should be carefully cleaned and dried. A thin layer of powder should then be applied to the affected area. This operation should be repeated twice daily. After application, the area should not be touched or massaged as the powder has to form a continuous protective film. Application of the product does not require specialised personnel. Thanks to its formulation, there is **no contact** between the wound and the hands, so that possible infections are prevented.[13]

5. Conclusions

Chronic ulcers are wounds which, because of intrinsic or extrinsic factors, fail to proceed through the physiological "healing cascade", that is, they do not undergo a rapid and physiological process of tissue repair within 3 months of onset. Lower limb ulcers, diabetic foot and pressure sores are all chronic ulcers.

These wounds have a high incidence and prevalence, which tend to increase as a result of ageing of the population; they therefore constitute a major public health problem and reduce the patient's autonomy and quality of life, if not adequately treated. **The management of chronic ulcers therefore requires appropriate therapy aiming at healing the wound and treating its causes**.

Chetosil® spray powder is a medical device formulated as a powder to be used on damaged skin. Thanks to its components (kaolin, starch, hyaluronic acid, MicroSilver) it forms a barrier film that promotes the physiological process of tissue repair. With its fast healing action and suitability even for exudative wounds, **Chetosil® spray powder is indicated for diabetic foot, athlete's foot, small decubitus ulcers, small cuts and burns**.

The product is **simple** and **convenient** to apply and its **formulation is specially designed to avoid contact between the affected area and the hands**.

6. References

1. Boulton AJM. The diabetic foot. Medicine 2014;38(12):644-8.
2. Colenci R, Abbade LPF. Fundamental aspects of the local approach to cutaneous ulcers. An Bras Dermatol 2018;93(6):859-70.
3. Aliquò MS, Monge L, Romagnoli F, Tasinato R. Trattamento delle ulcere croniche difficili: il ruolo centrale della preparazione del letto della ferita. AboutOpen 2017;3 (1):43-62.
4. Mekkes JR, Loots MA, Van Der Wal AC, Bos JD. Causes, investigation and treatment of leg ulceration. Br J Dermatol 2003;148:388-401.
5. Vanderwee K, Clark M, Dealey C, et al. Pressure ulcer prevalence in Europe: a pilot study. J Eval Clin Pract 2007;13(2):227-35.
6. Agale SV. Chronic leg ulcers: epidemiology, aetiopathogenesis, and management. Ulcers. 2013;2013:1–9.
7. Petrella F, Abbritti F, Bachetti F, et al. Progetto S.I.U.C. (Studio Italiano Ulcere Cutanee) (1 gennaio 2015-31 dicembre 2016). Dati conclusivi. Ital Wound Care 2017;1(1):1-8.
8. Di Giulio P. Le ulcere cutanee croniche. BIF 2001;6:227-31.
9. Gonzalez AC, Costa TF, Andrade ZA, Medrado AR. Wound healing - A literature review. An Bras Dermatol. 2016;91(5):614-20.
10. Harding KG, Morris HL, Patel GK. Science, medicine and the future: healing chronic wounds. BMJ 2002;324:160-3.
11. Gallo F, Salani C, Mazzucchelli C, et al. Fisiopatologia clinica del piede diabetico. G It Diabetol Metab 2014;34:22-31.
12. Dowsett C, von Hallern B. The triangle of wound assessment: a holistic framework from wound assessment to management goals and treatments. Wounds International 2017;8:1-39.
13. Chetosil. Fascicolo tecnico. Data ultima revisione Maggio 2019.