Basic data

The product Xenoderm is a product for professional users, such as nurses, caregivers and other work groups trained in the medical care of burns or wound treatment. The product has been CE certified since 1996. No previous generations or variants of the product exist. It is a class III product, according to rules 7, 18 and 21. The collagen contained in the product is of animal origin, source of collagen is pig skin.

Xenoderm is offered in the sizes 5*5, 10*10, 10*20, 10*30 and 10*40 cm.

The manufacturer of the product is the company:

MBP-Medical Biomaterial Products GmbH, Lederstraße 7, D-19306 Neustadt-Glewe.

Contact:

E-mail: info@mbp-gmbh.de;

Tel: +49 38757-5090

The SRN (registration number of the company in the EUDAMED database) is: DE-MF-000004939.

Notified body, identification number: mdc medical device certification GmbH, CE 0483

The product is sold in sales units of 1, 5 or 10 pieces per box.

Product name	Size in cm	REF	Products/Box	UDI-DI
Xenoderm	5*5	0505X	10	426023090301
	10*10	1010X	5	426023090302
	10*20	1020X	5	426023090303
	10*30	1030X	5	426023090304
	10*40	1040X	5	426023090305
	5*5	Z0505X	1	426023090301
	10*10	Z1010X	1	426023090302
	10*20	Z1020X	1	426023090303
	10*30	Z1030X	1	426023090304
	10*40	Z1040X	1	426023090305

GMDN: 45023; EMDN: M04041001; UMDNS: 17-670.

Intended use of the product

Composition: sterile porcine collagen matrix made from pig skin.

Xenoderm is used as a temporary skin substitute within the function of the patient's own skin to reduce fluid and heat loss, promote epithelial cell and granulation tissue growth and protect granulating wounds. Xenoderm offers the following benefits:

- easy application after rehydration in sterile isotonic saline solution
- Adheres well to the wound surface
- Reduction of pain; exposed nerve endings are covered
- No vascularisation before seven days
- Does not have a clinical antigenic effect
- Protects underlying tissue against the penetration of bacteria
- protects against dehydration
- Dressing changes usually proceed without pain and blood loss.
- allows observation of the wound bed due to its transparency
- Xenoderm facilitates movement, early mobilisation and rehabilitation

Indications
Xenoderm is a temporary biological skin substitute indicated for

- the coverage of second and third degree skin loss due to burns or trauma
- Covering chronic non-healing wounds, such as venous, diabetic or pressure ulcers.
- the coverage of autologous grafts
- the coverage of dispensing points

Contraindications, contraindications

- Third degree burns before removal of the eschar
- Massively infected wounds before appropriate cleansing (debridement)
- Patients with sensitisation to materials of porcine origin
- Xenoderm should not be used in combination with antiseptics that release chlorine. Protein-damaging substances (tannic acid, silver nitrate) should also not be used.

Warnings, precautions

- Xenoderm is sterilised by gamma irradiation and must not be sterilised again,
- is individually packaged in sterile packaging,
- must, if the pack is damaged, be considered non-sterile and disposed of,
- has a shelf life of five (5) years when stored at room temperature (≤ 30°C),
- must not be used after the expiry date,
- must be protected from moisture,
- is a medical device and must not get into the hands of children.
- The Xenoderm surgical matrix must not be reused once it has been removed from the packaging and/or has come into contact with a patient, as there is then an increased risk of contamination with subsequent risk of infection.

Use Pregnancy and lactation

There are no studies available on the use of Xenoderm during pregnancy and breastfeeding or on the influence on human reproductive ability. Before using Xenoderm, the attending physician must therefore weigh up the benefits for the mother and the possible risks for the child on an individual basis.

Use in children and elderly patients

There are no findings that suggest the need for special precautions depending on the age of the patients to be treated.

Instructions for use

Xenoderm is intended for use by medically trained personnel.

(1) After sterile removal from the packaging, rehydration takes place at room temperature in sterile isotonic saline. The dressing should be soaked for at least 2 min or until the dressing becomes transparent.
(2) At the time of initial application or reapplication of Xenoderm, the wound area should be thoroughly debrided and gently cleansed, for example with an antiseptic; on second degree wounds Xenoderm may be left, once adherent, until it detaches at the onset of re-epithelialisation.
(3) Press Xenoderm firmly onto the wound and smooth it to avoid blistering; fit it to the wound borders.
(4) As a precaution, Xenoderm should not be applied to weight-bearing areas of the body (risk of maceration).
(5) Xenoderm can be fixed with gauze bandages or other suitable dressing materials.
(6) Renewal of the Xenoderm overlay should be done according to the usual ward routine for dressing changes.
(7) Xenoderm dressing changes are virtually painless. Always moisten the dressing with sterile isotonic saline solution before removal.

(8) The length of time Xenoderm remains on the wound is variable and is determined by the wound healing process.
(9) Infected, highly exuding wounds require more frequent dressing changes initially.
(10) Xenoderm dressing changes may be necessary daily for the above wounds.
(11) On all aseptic wounds - including granulating wounds - Xenoderm should be removed after 10 days at the latest to prevent excessive adhesion.

Durability

The expiry date (EXP) is printed on the folding box and the sterile inner packaging. Xenoderm must not be used after the stated date.

Disposal

After use, handle and dispose of all unused products and packaging materials in accordance with accepted medical practices and applicable national and regional environmental laws for the disposal of packaging materials and biological materials.

Product description, functional mechanism

Xenoderm is a biological temporary skin substitute for second and third degree burns and traumatic wounds. Xenoderm prevents the loss of fluid, electrolytes, heat and energy. In addition, Xenoderm ensures the physiological wound environment.

When collagen membranes are used as temporary biological skin substitutes (xenoderm) to cover acute, chronic and burn wounds, they support wound healing by maintaining a moist wound environment through granulation, angiogenesis and re-epithelialisation without being integrated into the granulation tissue by cellular and vascular infiltration. They either detach from the wound when re-epithelialisation has occurred or are replaced by an autograft graft after sufficient conditioning of the wound bed.

Xenoderm consists of native collagen fibres. These collagen fibres are obtained from pig skin, where they are abundant and easily separable in the different skin layers. In the products, the collagen fibres obtained form an unaltered mesh with varying pore sizes between 35 and 100 µm, resulting from the gaps between the fibre bundles. The products have a hydroxyproline content of more than 10 % (collagen content in % dry matter factor: 7.46 - corresponding to at least 74.6 %). Collagen-containing wound dressings exhibit a haemostyptic effect by leading to adhesion, aggregation and activation of platelets and the subsequent release of clotting factors. Their degradation products as well as cytokines released by platelets initiate wound healing through chemotaxis of cells of the immune system and fibroblasts. This creates the conditions for orderly regeneration of the wound tissue.

Initially, the contact of platelets with the collagen fibres of the destroyed vessel walls and the ECM of the injured tissue leads to their aggregation and activation, which induces haemostasis via the cascade-like release of various extrinsic and intrinsic coagulation factors. The effect of haemostasis is supported by wound dressings containing native collagen fibres. Their tripelhelical structure is a prerequisite for platelet activation [46]. The result of haemostasis is a fibrin scaffold that forms an initial matrix for the immigration of cells (fibroblasts and leukocytes), which are directed into the wound area by chemotactically active cytokines produced by the platelets (e.g. platelet derived growth factor PDGF and transforming growth factor TGFβ). The transition to the inflammatory phase occurs. In addition to the cytokines produced by platelets, cell contents released by destruction or necrosis (e.g. ATP, DANN, heat-shift proteins), endotoxins (lipopolysaccharides of the bacterial cell wall of Gram-negative bacteria) and fragments of components of the ECM (e.g. collagen, hyaluronic acid) are also released.collagen, hyaluronic acid, elastin, fibronectin, laminin) as alarm factors for the immediate activation of the immune system (damage- or pathogen-associated molecular patterns - DAMPs or PAMPs). Neutrophil granulocytes are the first leukocytes to appear in the wound area and phagocytose foreign material, destroyed cellular material and invading bacteria, releasing catabolic enzymes (serine protease, elastase, collagenase, MMPs). Mast cells, by releasing the contents of their granules, cause changes in the blood vessel walls that facilitate the passage of monocytes, as well as the onset of the visible signs of inflammation (redness, warmth, swelling, pain). The aim of this phase is to cleanse the wound area of destroyed tissue structures and to eliminate invading germs. Monocytes and the macrophages they produce play an important role in this process. They digest the neutrophils and intensify the inflammatory reaction by producing a large number of proinflammatory mediators. The decrease in alarm factors and necrotic neutrophils through macrophyte phagocytosis, along with an altered cytokine profile, are

among the stimuli that cause a change in phenotype towards the anti-inflammatory profibrotic macrophage (M2a, IL-4 influenced) and initiate the transition to the proliferation phase. This increases the production of cytokines such as FGF, VEGF, EGF and TGFβ, which are growth factors that accelerate the proliferation of fibroblasts, vascular endothelial cells and epithelial cells, thus promoting the formation of granulation tissue, angiogenesis and re-epithelialisation. Collagen synthesis by fibroblasts builds up a collagen scaffold whose turnover by matrix metalloproteases - MMPs - and their inhibitors, tissue inhibitors of metalloproteinases-TIMPs, among others, controls the formed structure and thus the outcome of wound healing. The regeneration phase can lead either to fibrotic wound closure or to the regeneration of a functionally largely intact replacement tissue. The balance of corresponding formation mechanisms is controlled by the interaction of anti-inflammatory and anti-fibrotic macrophages (M2c, IL-10 influenced) and T cells (T2h, Treg), which trigger the tissue-typical differentiation of stem cells by releasing growth factors. The regeneration phase is completed with epithelialisation. This originates from keratinocytes of the basal membrane from the wound edge area and stem cells of the skin appendages, if corresponding dermis areas are still present, which spread over the granulation tissue formed.

Skin wounds close by re-epithelialisation and contraction, depending on wound location, depth, size, microbial contamination, patient health status, genetic and epigenetic factors. In uninfected, small-surface wounds involving only the epidermis and parts of the dermis, wound healing is primary and may result in rapid wound closure with minor scarring. Superficial skin wounds with a largely intact dermis can also heal primarily (e.g. split skin removal sites). Skin appendages such as hair, sebaceous and sweat glands remain intact.

Deep wounds involving the dermis and underlying layers, characterised by tissue loss, heal secondarily. Reconstruction of the damaged tissue is initiated by the formation of granulation tissue, followed by epithelialisation. Skin appendages such as hair, sebaceous and sweat glands are not preserved. The use of skin substitutes supports granulation and creates the prerequisite for the transplantation of an autograft for re-epithelialisation if the size of the wound makes it necessary. Tertiary wound healing includes complex cases where a wound is kept open until, for example, an infection has been successfully controlled. Subsequently, wound healing is supported by plastic surgical reconstruction or suture closure. In superficial, small and clean wounds, the phases of haemostasis and inflammation extend over a shorter period of time because only small amounts of exudate are required to cleanse the wound and the blood coagulum induces rapid wound closure. In larger wounds, these phases take a longer period of time.

The use of pure collagen wound dressings on contaminated wound areas and necrotic tissue remnants is contraindicated. Pure collagen wound dressings have no antimicrobial effect, contaminations could develop into infections under the covering. Microbial pathogens and endotoxins released during their immunological defence as well as necrotic tissue remnants represent PAMPs and DAMPs (pathogen or demage associated molecular patterns), which prevent the transition of the inflammatory phase into the regenerative wound healing phase. They are therefore most effective on wounds after surgical debridement, starting with the first phase of wound healing, haemostasis. The more temporary skin substitute Xenoderm is indicated for primary and secondary healing wounds. For grade IIa wounds (superficial partial thickness wounds), the materials remain on the wound until healing occurs and detach from the wound when re-epithelialisation is complete. For grade IIb (deep partial thickness wounds) and grade III (full thickness wounds), they remain on the wound until covered with an autologous split-thickness skin graft, but can be changed several times if exudate formation and necessary cleansing of the wound bed require it. Temporary skin substitutes also support the formation of granulation tissue, but are not integrated into it. They are also used to cover autografts and autograft removal sites.

Biological assessment

Results of biocompatibility tests confirm the high biocompatibility of the product according to DIN EN ISO 10993. Extensive biological studies with the help of animal testing have been conducted and prove the clinical safety of the product. The many years of experience of MBP Medical Biomaterial Products GmbH with the sale of Xenoderm as well as the continuous post-marketing monitoring show that the products are biocompatible within the scope of their intended use.

Alternative treatment methods

Skin substitutes are an established method in the treatment of wounds of various aetiologies. They partially take over the function of the skin, support the healing process and the closure of wounds and are used as temporary or permanent substitutes, depending on their nature. Restoring the protective function of the skin as quickly as possible is crucial for the successful treatment of burn victims[1] .

An ideal skin substitute would be characterised by the following properties [2][3] :

- Prevent infections
- Pain-relieving
- Non-immunogenic
- Cost-effective, unlimited availability, can be stored for longer periods under simple conditions
- prevents the loss of fluid and thus of electrolytes and proteins
- Applicable to all wounds, regardless of location, depth, topology, aetiology and risk of infection.

Among the multitude of existing skin substitutes with their various advantages and disadvantages, there is none that meets all these requirements.

Various combinations of collagen-based matrices with structural and functional elements of the extracellular matrix of the dermis and other tissue membranes (e.g. small intestine submucosa, amnion) as well as with living cells (fibroblasts, keratinocytes) have been developed with the aim of supporting different aspects of wound healing[4] [23], so that the range of properties is as follows:

- Support of haemostasis as the first phase of wound healing by activating platelets to trigger the coagulation cascade
- the binding of proteolytic activity - exogenous collagen as a competing substrate for MMPs, more pronounced in fleece-type wound dressings with gel formation than in membrane-type skin substitutes.
- Covering freshly debrided wound surfaces protects against loss of fluid, electrolytes, protein and heat and reduces pain by covering free nerve endings (2nd degree burns)
- At the same time, maintaining a moist wound environment that allows the mobility of cells involved in the processes of wound healing.
- Offer a three-dimensional structure of native, tripelhelical collagen fibrils that support the formation of granulation tissue through chemotactic action on fibroblasts - Matrices from native collagen fibrils of the ECM e.g. human, bovine, porcine source tissues such as dermis, SIS (small intestine submucosa), pericardium, amnion/chorion of the placenta [5][6]
- Support of wound tissue regeneration by actively influencing anabolic processes - collagen matrices containing e.g. proteoglucans, glycoproteins, hyaluronic acid or growth factors or living cells (fibroblasts, keratinocytes) producing these substances of the ECM.

- Eliminating the germ load/biofilms or preventing their reconstitution after debridement by antibacterial and/or fungicidal ingredients, which both counters the risk of systemic infection and removes a stimulus to maintain the chronic inflammatory state - e.g. additions of Ag, polyhexanide or Cu.

The following effects are already achieved through the collagen alone:

- Collagen accelerates and supports wound healing through its haemostatic effect and stimulates the release of various growth factors such as PDGF and TGFβ by activating platelets.
    - Schonauer and co-workers, for example, give an overview of different local preparations for haemostasis, such as bone wax, gelatine, collagen and oxidised cellulose. The inves-

1 Halim AS et al; (2010): Biologic and synthetic skin substitutes: An overview. Indian J Plast Surg. 2010 Sep; 43 (Suppl): p. 23-S.28
2 Nathoo R et al; (2014): Skin Substitutes An Overview of the Key Players in Wound Management. J Clin Aesthet Dermatol. 2014;7(10):44-48.
3 Varkey M et al; (2015): Advances in Skin Substitutes-Potential of Tissue Engineered Skin for Facilitating Anti-Fibrotic Healing. J. Funct. Biomater. 2015, 6, 547-563
4 Dreifke MB et al; (2015): Current wound healing procedures and potential care. Mater Sci Eng C Mater Biol Appl. 2015 March; 48: 651-662.
5 Frykberg RG et al; (2017): A prospective, multicentre, open-label, single-arm clinical trial for treatment of chronic complex diabetic foot wounds with exposed tendon and/or bone: p ositive clinical outcomes of viable cryopreserved human placental membrane. Int Wound J. 2017 Jun;14(3):569-577
6 Koob TJ et al; (2013): Properties of dehydrated human amnion/chorion composite grafts: implications for wound repair and soft tissue regeneration. J Biomed Mater Res Part B 2014:102B:1353-1362

tigators conclude that fibrillar collagen is the most effective and that this material is recommended because it is quickly absorbed and causes little local tissue reaction. All other comparative substances were inferior to collagen in both tolerability and efficacy[7] .

- The binding of platelets to collagen fibrils was studied in detail by Hovig. He was able to demonstrate that only fibrillar collagen, but not dissolved collagen, led to platelet aggregation and that platelets adhered to collagen fibrils themselves released ADP, which led to further aggregation. Calcium ions also enhance collagen- and ADP-induced aggregation with platelets.

– Collagen leads to chemotactic migration and proliferation of fibroblasts and other cells required for wound healing [8][9][10][11][12][13] thereby accelerating wound healing (granulation, angiogenesis and re-epithelialisation).
  - Smith et al. investigated histological and immunohistological responses of patients to a bovine collagen matrix used primarily for haemostasis. They filled the collagen matrix into 24 punch biopsies and took test material again after different time intervals to examine the histological and immunohistochemical changes. The samples with the collagen matrix showed migration of stromal and epithelial cells along the collagen surface after 2 days, which increased significantly up to the 4th day. Hyaluronic acid was detected in the matrix during the first 8 - 10 days. Stromal cells and reticulum fibres were also detectable on day 8 - 10. Biopsy defects that healed without matrix implantation showed a delayed and uneven increase of hyaluronic acid, furthermore inflammatory infiltrate was detectable for longer and scarring occurred. The authors conclude that bovine collagen, which is suitable for haemostasis, also provides a good basis for cell migration and epithelial cell migration along the implant surface, thus accelerating the organisation of wound healing[14] [80].

Collagen binds as a competing substrate the activity of proteases that prevent the build-up of an extracellular matrix as a prerequisite for the free movement of cells involved in this process and the build-up of a granulation tissue. The prerequisite is the free accessibility of the collagen fibres for proteases. This is more likely to be the case in a collagen fleece, which transforms into a gel with the wound exudate, than in collagen membranes, in which the collagen fibres are much more densely packed. In addition to the highly complex and very cost-intensive bioengineering products, much less expensive temporary skin replacement products made of pure collagen of xenogeneic origin, such as Xenoderm, have therefore also proven themselves on the market.

User group

Xenoderm must only be used by professional medical personnel.

[7] Schonauer C, Tessitore E, Barbagallo G, Albanese V, Moraci A: The use of local agents: bone wax, gelatin, collagen, oxidized cellulose; Eur Spine J 2004; 13 (Suppl. 1):89-96.
[8] Diegelmann RF et al; (2004): WOUND HEALING: AN OVERVIEW OF ACUTE, FIBROTIC AND DELAYED HEALING. Frontiers in Bioscience 9, 283-289, January 1, 2004
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[14] Smith KJ et al; (1996): Histologic and immunohistochemical features in biopsy sites in which bovine collagen matrix was used for hemostasis. J AM ACADDERMATOL1996;34:434-8.)

Summary of the clinical evaluation and post-marketing clinical follow-up (PMCF)

Published clinical outcome reports Xenoderm:

(1) Kiene S et al; (1976): Lyophilised porcine split skin as a biological wound dressing. Zentralbl Chirurgie 101: 1481-1494
(2) Hartmann B; (2007): Xenoderm - Application in burn wounds Evaluation of 10 treatment protocols from 2006. Unfallkrankenhaus Berlin, Zentrum für Schwerbrandverletzte mit Plastischer Chirurgie.
(3) Hosseini SN et al; (2007): Xenoderm dressing in the treatment of second degree burns. burns 33 (2007) 776 - 781
(4) Hosseini SN et al; (2008): Xenoderm Versus 'Conventional' Treatment in Pediatrics Burns. International Journal of Pharmacology 4(1):46- 50, 2008
(5) Hosseini SN et al; (2009): A biological dressing versus 'conventional' treatment in patients with massive burns: a clinical trial. Ulus Travma Acil Cerrahi Derg. 2009 Mar;15(2):135-40.
(6) Hosseini SN et al; (2009): Xenoderm Versus 1% Silver Sulfadiazine in Partial-thickness Burns. Asian J Surg 2009;32(4):234-9
(7) Kasaraneni S et al; (2016): Outcomes of Xenoderm Versus Conventional Dressing in Case of Second Degree Burns. International Journal of Contemporary Medical Research 2016;3(6):1811-1815

Study	Year	Number of patients	Disease pattern	Clinical outcome
1	1976	26	Burns grade IIa and IIb	In superficial partial-thickness dermal burns, the wound covering remained on the wound from early necrotomy until healing by new epithelial formation, in deep partial-thickness dermal burns until covering with an autograft. In total skin defect, fresh granulations form under the dressing material (xenoderm), on which autografts later adhere well.
			dermal full-layer combustion Grade III	Dressing changes with Xenoderm until the wound was suitable for autograft uptake.
			Covering mesh grafts and removal sites	Any accumulation of secretions under the dressing was easily visible and could be drained through small incisions. After soaking, dressing changes could be performed easily and painlessly.
			Extensive infected full-layer damage	Stabilisation of the wound bed (8 weeks), with no signs of intolerance reactions, pus secretion and fever decreased, wounds could be gradually closed by autografts.
			fresh traumatic skin defects after leathering injuries and accompanying muscle tears	Clean granulations were formed in ≤ 12 days, on which autogenous dermoplasty healed well.
			Covering chronic lower leg ulcers (Ulcus cruris)	The wound bed formed fresh red granulations and the defects, some of which were several years old, closed by epithelialisation from the sides. Only in 4 of 11 patients was the remaining defect healed with an autograft.
2	2007	10	temporary skin substitute for second and third degree burns, covering of skin grafts, protection of necrosectomised wound surfaces and for extensive traumatic wounds. (4 burn wounds of grade IIa, 8 of grade IIb and one wound of third degree).	In 6 patients, the wound areas healed under the Xenoderm (on average within 9.16 days). In 3 cases, the xenoderm served as a temporary cover until the split skin transplantation. In one case, xenoderm loss and deepening necrosis occurred. In the other 2 cases, the xenoderm could remain on the wound until split skin grafting. No clinically relevant infections beyond proven colonisation were observed. Adverse events or side effects did not occur. the use of Xenoderm for the described wound types after thorough and radical debridement is successfully possible and a reasonable alternative to allogeneic donor skin or polylactide membranes from an economic point of view.
3	2007	96	Non-infected and non-contaminated burn wounds caused by exposure to flame or scalding, (Grade: IIa, IIb and III).	From the low number of dressings, analgesics consumed and infections occurred, the authors conclude a positive impact on treatment costs. In addition, Xenoderm contributed to patient satisfaction by reducing scarring. Comparative clinical studies are recommended to validate the results.
4	2008	86 (children)	86 Children with burns (grade and grade II with III-	**Comparative study:** Xenoderm with conventional treatment of burns (daily washes followed by topical treatment with silver sulphadiazine dress-

Study	Year	Number of patients	Disease pattern	Clinical outcome
			grade less than 5% TBSA) and non-infected wounds.	ings). the wounds were covered with Xenoderm membrane soaked in saline after thorough debridement, fixed with sutures or secondary dressing, the limbs were immobilised by splints. After 24 h, the secondary dressing was removed. After 2-6 weeks, the Xenoderm wound dressing lifted from the wound. In third-degree wounds, Xenoderm was removed after 2-4 weeks and the wounds were treated with a split-skin autograft. The authors found significant differences in mortality rates (conventional-14.3% / xenoderm-0%), median length of hospitalisation (20 / 7.5 days) and median number of dressing changes (10 / 3), which were particularly evident in the group with 20%-39% body surface area affected (TBSA). Conventional dressing changes are usually very painful. A reduction in the number and pain achieved by Xenoderm application is a welcome relief, especially in paediatric patients. Xenoderm can be used to cover grade II burns in children and results in reconstruction of the wound with reduced scarring by suppressing infection and preserving remnants of the epithelium. Wounds can be reconstructed step by step. Xenoderm increases survival in extreme cases, reduces hospitalisation time, dressing changes and treatment costs.
5	2009	78	Grade II burns and 10-60%TBSA due to scalding or flame exposure.	**Comparative study**: silver sulphadiazine (SSD) and Xenoderm, in a cohort of adult patients. Wounds in group 1 (38 patients) were managed by daily washing followed by topical treatment with silver sulphadiazine dressings. In group 2 (38 patients), Xenoderm rehydrated in saline was applied to the saline-flushed wound after thorough debridement by tangential excision or dermabrasion and fixed with sutures or secondary dressing. In less than one week, 38.4% of patients in the SSD group were discharged with an average of 14.7% TBSA, and 83.7% of patients in the Xenoderm group were discharged with an average of 17.2% TBSA. According to the authors, the reduction in the infection rate is due to the barrier effect of covering the wound with Xenoderm. This reduces the "necrotic space", haematoma and seroma formation with the risk of subsequent infections are avoided. Based on the authors' clinical experience, Xenoderm is superior to SSD application in terms of pain control, wound infection, number of dressing changes and length of hospital stay required, and is suitable for the treatment of second-degree burn wounds.
6	2009	118	Burns (grade II and III) from 30%-75% TBSA.	**Comparative study:** treatment of burns by Xenoderm (65 patients) and by conventional application of saline-soaked wound dressings (53 patients). The significant differences in mortality rate (35% / 10.8%), hospitalisation days (31.3 / 18.2 days) and number of dressing changes (22.1 / 9.9) underline the benefits of xenoderm use, but are offset by the theoretical risk of zoonotic disease transmission and ethical/religious barriers. It is evident that Xenoderm reduces the risk of mortality especially in the critical, severe burns (>40% TBSA). The mortality of both groups was in a ratio of 3:1. In 30-39%TBSA, hospital stay was significantly shorter with Xenoderm use. The lower intravenous serum administration shows that Xenoderm significantly reduces the loss of fluid, electrolytes and proteins. According to the authors, reduced dressing changes promote the preservation of intact epidermal remnants, allowing for wound closure with less scarring, which in turn leads to greater patient satisfaction.
7	2014-2015	60 (< 48 years)	Grade II burns (TBSA 10 - 50 %)	Retrospective control and comparative study of 2014-2015 comparing the efficacy of Xenoderm treatment of 2nd degree burns with conventional treatment using silver sulphadiazine, povidone-iodine and paraffin wax. Xenoderm was left on the wounds until healing, and any initial excess exudate was removed with a change of secondary dressings. This eliminated a significant pain-causing and healing-delaying factor, which contributed to the superiority of Xenoderm treatment over the conventional approach. Advantages of Xenoderm treatment are expressed in the significant differences in re-epithelialisation time, number of dressings needed, pain duration and infection rate, which is reflected in significantly lower hospitalisation time and treatment costs. Especially the lower pain burden results in greater patient compliance. Treatment costs with Xenoderm were half those of conventional treatment

The results of the 7 clinical trials with Xenoderm can be summarised as follows:
Xenoderm

- is suitable as a temporary wound dressing for the treatment of 2nd and 3rd degree burns or wounds of the same condition but with different aetiologies.

  - In burns/grade IIa wounds, wound healing takes place with re-epithelialisation under the xenoderm, which detaches from the wound edges as wound closure progresses.
  - In grade IIb and III burns/wounds, granulation tissue develops under the xenoderm, which enables the successful growth of a split-thickness skin autograft after removal of the xenoderm overlay.
- Adheres well to the wound bed
- has a beneficial effect on scarring
- Preserves vital dermis remnants, thereby shortening re-epithelialisation
- reduces the loss of fluid, electrolytes, proteins and corresponding intravenous administration of serum, albumin and plasma,
- Reduces pain and the consumption of analgesics
- Reduces the risk of infection through contact closure with the wound bed
- Increases the chance of survival in the case of extensive burns
- Enables early mobilisation
- Reduces hospitalisation time and treatment costs

Good results are achieved when Xenoderm is applied to freshly debrided wound areas after rehydration in physiological saline solution. Depending on the degree of exudation, Xenoderm can remain on the wound for up to 10 days; necessary dressing changes in deep partial and full thickness wounds (grade IIb and III) lead to cleansing of the wound bed and support granulation. Dressing changes are largely painless after soaking in physiological saline solution.

From the information in the current literature, the data from public reporting databases, completed studies, customer feedback and the complaints received, no conclusions could be drawn about additional, previously unknown risks for Xenoderm. It can therefore be assumed that no new risks are associated with the use of Xenoderm when used as intended.

In the present clinical evaluation, it had to be demonstrated that the product Xenoderm as a wound dressing for the temporary covering of burn and traumatic/chronic wounds meets the basic requirements. For this purpose, extensive clinical studies, such as Kiene et al [52], on the basis of which the product was first approved in 1981, 4 studies by Hosseini [42-45] from the years 2007-2009 and a study by Kasaraneni et al [97], published in 2016, could be consulted.

Summary of post-market surveillance results according to PMCF plan.

From the information in the current literature, the data from public databases (MAUDE of the FDA and corrective measures of the BfArM) and the complaints received by MBP GmbH, no conclusions could be drawn regarding additional, previously unknown risks for the above-mentioned products.

It can therefore be assumed that, in accordance with the information in the instructions for use, there are no additional risks associated with the use of MBP GmbH's collagen fleece wound dressing MB-Collagen. Based on the available information on product safety and efficacy, no corrective measures, e.g. updating of risk management or amendment/supplementation of the IFU, are required.

There was a very low complaint rate, i.e. the ratio of complaints to products sold is below 0.00%.

During the time the product was on the market, no recalls, field safety corrective actions, serious adverse events or adverse events were reported for Xenoderm.

MBP GmbH's PMS system is up to date and actively and systematically collects and analyses information and data on the quality, performance and safety of products throughout their entire life cycle. As part of this clinical evaluation, relevant safety-related databases were searched for events related to the product. In addition, all PMCF studies reported neutral or positive outcomes following treatment with Xenoderm. Therefore, no preventive or corrective measures are required. For these reasons, no additional post-marketing clinical follow-up measure is recommended. There is no evidence of an increased rate of complications associated with the use of the product.

Residual risks associated with the use of the product

The following residual risks were identified:

- Allergic reactions to the collagen membrane cannot be ruled out in rare cases.
- In very rare individual cases, incompatibility with collagen may occur.

Any residual risks associated with clinical use are inherent in the nature of the product or determined by its indication. The risk of using animal material is justified by the medical benefit. The risk-benefit balance of the devices under assessment is therefore in compliance with the essential safety and performance requirements. The clinical benefit has been demonstrated. In addition, products of porcine origin, such as Xenoderm, have the advantage over bovine collagen products of eliminating the very small residual risk of BSE/TSE.
The risk monitoring of the production of the downstream phases is carried out by the evaluation of the market surveillance (PMS and PMCF), the handling of complaints (after evaluation of the system for corrective and preventive actions) by the PRRC of MBP GmbH. Market surveillance is carried out. As a result, no risks from market monitoring are known: There were no reportable incidents with medical devices of MBP GmbH. Research on comparative products on the market was carried out and evaluated as part of the PMS process. The complaint data did not lead to any negative results. The clinical evaluations do not indicate any risks that were not taken into account as part of the risk management process.

Patient group, users, training courses

Persons or patient group: no restrictions. The products are used by medically trained personnel. Training can be provided by the medical product consultants of MBP GmbH on request. Contact: info@mbp-gmbh.de, + 49 38757 5090.

Applied norms, laws and standards

The requirements of the following standards are applied within the scope of the manufacture, placing on the market and monitoring of the MB collagen product (13.02.2024). The standards are checked at regular intervals for the need of updating. The following standards are applied by MBP Medical Biomaterial Products GmbH as of today. An update will take place within the scope of the update of this SSCP.

v Medical Devices Act - MPG:2002-08, last amended on 26/05/2021
v Act on the Adaptation of Medical Devices Law to Regulation (EU) 2017/745 and Regulation (EU) 2017/746 (Medical Devices EU Adaptation Act - MPEUAnpG), 19 May 2020, (MPDG), last amended 28 June 2022.
v REGULATION (EU) 2023/607 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL 15 March 2023
v REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, 5 April 2017 (MDR)
v Medical Devices Operator Ordinance (Ordinance on the Installation, Operation and Use of Medical Devices) - MPBetreibV:1998-06, last amended on 26 May 2021
v Ordinance on the Adaptation of Medical Device Law to Regulation (EU) 2017/745 and Regulation (EU) 2017/746 (Medical Devices EU Adaptation Ordinance - MPEUAnpV), last amended on 21 April 2021
v Ordinance on the Reporting of Suspected Serious Incidents involving Medical Devices and on the Exchange of Information between Competent Authorities (Medical Device User Notification and Information Ordinance - MPAMIV), last amended on 21 April 2021
v European Medical Device Nomenclature (EMDN), https://webgate.ec.europa.eu/dyna2/emdn/?utm_source=CleverReach&utm_medium=email&utm_campaign=19-11-2021+Institutes-Journal+39%2F21%3A+Regulations+-+of+Understanding+to+Implementation&utm_content=Mailing_13164833
v Therapeutic Products Advertising Act - HWG:1965-07, last amended on 19 July 2023
v EMDN V1.1 European Medical Device Nomenclature (EMDN), https://webgate.ec.europa.eu/dyna2/emdn/?utm_source=CleverReach&utm_medium=email&utm_campaign=19-11-2021+Institutes-Journal+39%2F21%3A+Regulations+-+of+Understanding%C3%A4ndnis+to+Implementation&utm_content=Mailing_13164833
v MEDDEV 2.1/1:1994-04 Guidelines for manufacturers and Notified Bodies concerning the Medical Device Directives - concerning Definitions of 'medical devices', 'accessory' and 'manufacturer'
v MEDDEV 2.7.1, Rev. 4: 2016-06 - concerning clinical investigation/ clinical evaluation (Guidelines for clinical evaluation)
v Informative: Structure documentation for clinical evaluation (medical devices), MDC document: 'Structure documentation for clinical evaluation (medical devices)' 001/11.2023, ID: 11959. link: https://www.mdc-ce.de/news/detailansicht/news/detail/News/struktur-dokumentation-zur-klinischen-bewertung-medizinprodukte.html
v MEDDEV 2.12/1 Rev. 8: 2013-01 - concerning market surveillance (requirements for vigilance systems)
v MDCG 2022-21 - Guidance on Periodic Safety Update Report (PSUR) according to Regulation (EU) 2017/745 - December 2022
v MDCG 2022-4 rev.1 - Guidance on appropriate surveillance regarding MDR Art.120 transitional provisions - devices covered by MDD or AIMDD certificates - December 2022
v MDCG 2022-18 - Position Paper - application of Art.97 MDR to legacy devices for which an MDD/AIMDD certificate expires before the issuance of an MDR certificate, December 2022
v MDCG 2021-22 rev.1 - Clarification on 'first certification for that type of device' and corresponding procedures to be followed by notified bodies, September 2022
v MDCG 2022-11, Rev. 1 - MDCG Position Paper: Notice to manufacturers to ensure timely compliance with MDR requirements, November 2023
v MDCG 2022-7 - Questions and Answers on the Unique Device Identification system under Regulation (EU) 2017/745 and Regulation (EU) 2017/746, May 2022
v MDCG 2019-9 - Rev.1 - Summary of safety and clinical performance, update March 2022.
v MDCG 2021-27 - Questions and Answers on Articles 13 & 14 of Regulation (EU) 2017/745 and Regulation (EU) 2017/746, December 2021
v MDCG 2021-24 - Guidance on classification of medical devices, October 2021
v MDCG 2021-19 - Guidance note integration of the UDI within an organisation's quality management system, July 2021
v MDCG 2021-11 - Guidance on Implant Card - Device types, June 2021
v Guidance - Clinical evaluation assessment report template, July 2020
v MDCG 2020-5 - Clinical Evaluation - Equivalence, A guide for manufacturers and notified bodies, April 2020
v MDCG 2020-6 - Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC, April 2020
v MDCG 2020-1 - Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software, March 2020
v MDCG 2023-7 - Guidance on exemptions from the requirements to perform clinical investigations pursuant to Article 61(4)-(6) MDR and on 'sufficient levels of access' to data needed to justify claims of equivalence, December 2023
v MDCG 2021-6 - Rev.1 - Regulation (EU) 2017/745 - Questions & Answers regarding clinical investigation, December 2023
v MDCG 2024-2 - Procedures for the updates of the EMDN, February 2024
v MDCG 2021-27 - Rev.1 - Questions and Answers on Articles 13 & 14 of Regulation (EU) 2017/745 and Regulation (EU) 2017/746, December 2023
v MDCG 2024-3, Guidance on content of the Clinical Investigation Plan for clinical investigations of medical devices; Appendix A: Clinical Investigation Plan Synopsis Template, April 2024
v MDCG 2021-28, Substantial modification of clinical investigation under Medical Device Regulation, December 2021
v MDCG 2020-13, Clinical evaluation assessment report template, July 2020
v MDCG 2020-8, Guidance on PMCF Evaluation Report Template, April 2020
v MDCG 2020-7, Guidance on PMCF Plan Template, July 2020
v MDCG 2020-6, Guidance on Sufficient Clinical Evidence for Legacy Devices Background note on the relationship between MDCG 2020-6 and MEDDEV 2.7/1 rev.4 on clinical evaluation, June 2020
v MDCG 2021-13 Rev. 1, Questions and answers on obligations and related rules for the registration in EUDAMED of actors other than manufacturers, authorised representatives and importers subject to the obligations of Article 31 MDR and Article 28 IVDR, July 2021
v MDCG 2021-1 Rev. 1, Guidance on harmonised administrative practices and alternative technical solutions until EUDAMED is fully functional, May 2021
v MDCG 2020-15, MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States, August 2020
v MDCG 2019-5, Registration of legacy devices in EUDAMED, April 2019

v MDCG 2019-4, Timelines for registration of device data elements in EUDAMED, April 2019
v MDCG 2020-3 Rev. 1, Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD, May 2023
v MDCG 2022-4 Rev.2, Guidance on appropriate surveillance regarding the transitional provisions under Article 120 of the MDR with regard to devices covered by certificates according to the MDD or the AIMDD, May 2024
v MDCG 2019-07, Rev. 1 Guidance on Article 15 of the medical device regulation (MDR) and in vitro diagnostic device regulation (IVDR) on a 'person responsible for regulatory compliance' (PRRC), December 2023
v MDCG 2023-3, Questions and Answers on vigilance terms and concepts as outlined in the Regulation (EU) 2017/745 on medical devices, February 2023
v MDCG 2018-1 Rev. 4 Guidance on BASIC UDI-DI and changes to UDI-DI, April 2021
v GENERAL PUBLICATIONS EUROPEAN COMMISSION, MDR - language requirements for manufacturers Rev. 1, March 2024
v VDI 2519:2001-12 - Procedure for the preparation of specifications (guideline)
v ASTM F 2212:2020 - Standard Guide for Characterisation of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)
v ASTM F 1929:2023- Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration
v DIN EN ISO 13485:2021-12 (EN ISO 13485:2016 + AC:2018 + A11:2021) Medical devices - Quality management systems - Requirements for regulatory purposes
v DIN EN ISO 14971:2022-04 Medical devices - Application of risk management to medical devices
v DIN EN 62366-1:2021-08, Medical devices - Part 1: Application of fitness for use to medical devices
v DIN EN ISO 10012:2004-03, Measurement management systems - Requirements for measurement processes and measuring equipment
v DIN EN ISO 10993-1:2021-05, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management system
v DIN EN ISO 10993-3:2015-02, Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
v DIN EN ISO 10993-4:2017-12, Biological evaluation of medical devices - Part 4: Selection of tests for interaction with blood
v DIN EN ISO 10993-5:2009-10, Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity
v DIN EN ISO 10993-6:2017-09, Biological evaluation of medical devices - Part 6: Tests for local effects after implantation
v DIN EN ISO 10993-9:2022-03, Biological evaluation of medical devices - Part 9: Framework for the identification and quantification of potential degradation products
v DIN EN ISO 10993-10:2023-04, Biological evaluation of medical devices - Part 10: Tests for skin sensitisation
v DIN EN ISO 10993-11:2018-09, Biological evaluation of medical devices - Part 11: Tests for systemic toxicity
v DIN EN ISO 10993-12:2021-08, Biological evaluation of medical devices - Part 12: Sample preparation and reference materials
v DIN EN ISO 10993-18:2023-11 Biological evaluation of medical devices - Part 18: Chemical characterisation of materials for medical devices within a risk management system
v ISO/TS 10993-19:2020-03, Biological evaluation of medical devices - Part 19: Physical/chemical, morphological and topographical characterisation
v DIN EN 556-1:2002-03, Sterilisation of medical devices - Requirements for medical devices labelled as 'STERILE' - Part 1: Requirements for medical devices sterilised in the final packaging
v DIN EN 556-1 Corrigendum 1:2006-12
v DIN EN ISO 11137-1:2020-04 Sterilisation of health care products - Radiation - Part 1: Requirements for the development, validation and control of the use of a sterilisation process for medical devices (ISO 11137-1:2006, including Amd.1:2013 + Amd.2:2018); German version EN ISO 11137-1:2015 + A2:2019
v DIN EN ISO 11137-2:2023-08, Sterilisation of health care products - Radiation - Part 2: Determination of sterilisation dose
v DIN EN ISO 11137-3:2017-11, Sterilisation of health care products - Radiation - Part 3: Guidance on dosimetric aspects
v DIN EN ISO 11737-1:2021-10 (EN ISO 11737-1:2018 + A1:2021), Sterilisation of health care products - Microbiological methods - Part 1: Determination of the population of microorganisms on products
v DIN EN ISO 11737-2:2020-07 Sterilisation of health care products - Microbiological methods - Part 2: Sterility testing in the definition, validation and maintenance of a sterilisation process
v DIN EN 868-2:2017-05, Packaging for medical devices to be sterilised in the final packaging - Part 2: Sterilisation packaging - Requirements and test methods
v DIN EN 868-5:2019-03, Packaging for medical devices to be sterilised in the final packaging - Part 5: Sealable transparent pouches and tubes made of porous materials and laminated plastic film - Requirements and test methods
v DIN EN ISO 11607-1:2024-02, Packaging for medical devices to be sterilised in the final packaging - Part 1: Requirements for materials, sterile barrier systems and packaging systems
v DIN EN ISO 11607-2:2024-02 Packaging for medical devices to be sterilised in the final packaging - Part 2: Validation requirements for forming, sealing and assembling processes
v DIN EN ISO 14644-1:2016-06, Cleanrooms and associated cleanroom areas - Part 1: Classification of air cleanliness by particle concentration
v DIN EN ISO 14644-2:2016-05, Cleanrooms and associated cleanroom areas - Part 2: Specification for testing and monitoring for verification of monitoring for verification of cleanroom performance in terms of air cleanliness based on particle concentration
v DIN EN ISO 14644-3:2020-08, Cleanrooms and associated cleanroom areas - Part 3: Test methods
v DIN EN ISO 14644-4:2023-04, Cleanrooms and associated cleanroom areas - Part 4: Planning, execution and initial commissioning
v DIN EN ISO 14644-5:2005-03, Cleanrooms and associated cleanroom areas - Part 5: Operation
v DIN EN ISO 14644-7:2005-01, Cleanrooms and associated cleanroom areas - Part 7: SD modules
v DIN EN ISO 14644-8:2022-10, Cleanrooms and associated cleanroom areas - Part 8: Assessment of chemical air cleanliness (ACC)
v DIN EN 17141:2021-02, Cleanrooms and associated cleanroom areas - Biocontamination control
v DIN EN ISO 22442-1:2021-08, Animal tissues and their derivatives used in the manufacture of medical devices - Part 1: Application of risk management
v DIN EN ISO 22442-2:2021-04, Animal tissues and their derivatives used in the manufacture of medical devices - Part 2: Controls on procurement, sourcing and handling
v DIN EN ISO 22442-3:2008-03, Animal tissues and their derivatives used in the manufacture of medical devices - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy agents
v DIN EN 13726:2023-12 Test methods for dressings (wound dressings) - Aspects of absorbency, moisture penetration, water tightness and conformability
v DIN EN ISO 15223-1:2022-02 Medical devices - Symbols for use in the context of information to be provided by the manufacturer - Part 1: General requirements

Result of risk management, residual risks associated with the use of the product

The risk analysis has been completed. All listed risks including the use of material of animal origin (pig skin) are reduced as far as possible and according to the state of the art. All residual risks associated with clinical use or animal material are inherent in the nature of the product or determined by its indication. Treatment alternatives of synthetic origin were included in the evaluation and do not result in a better risk-benefit ratio in comparison, so that the benefit of using animal material outweighs the risk posed by animal material. The products are used by professionals, so the residual clinical risks are acceptable. Therefore, the overall risk of the products is acceptable according to the risk management plan, the products fulfil their intended purpose and can be used safely for the benefit of the patient when used as intended. No uncontrolled risks have been identified in the practical use of the products. The possible residual risks and undesirable effects, warnings and precautions are fully described in the instructions for use.

Languages, queries

The SSCP is produced by MBP Medical Biomaterial Products GmbH in German and English.
Translations into other languages can be requested from the manufacturer.

Should the user or patient have any questions about our Xenoderm product or its application, please do not hesitate to contact us.

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Revision history

Version	Change	Date
C	Correction, List of appli. Stand.	22.07.2024
B	Review 2024	17.06.2024
A	Initial production	22.02.2023