

HYAL^o4 Plus

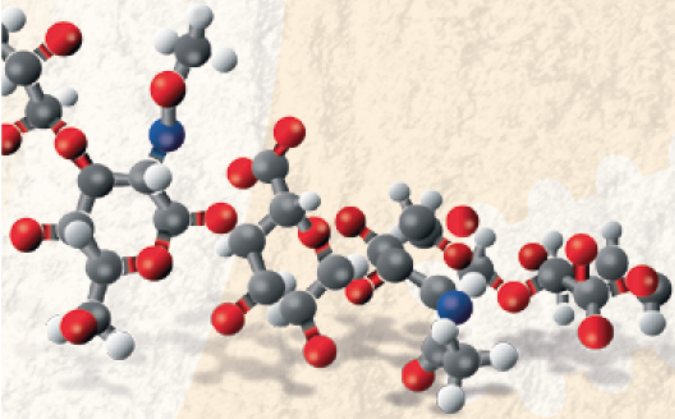
**A synergic combination
for promotion of healing
and prevention of infection¹**



CE 0459
Medical Device

Hyaluronic Acid and Silver Sulfadiazine

The right combination for promotion of healing and prevention of infection¹

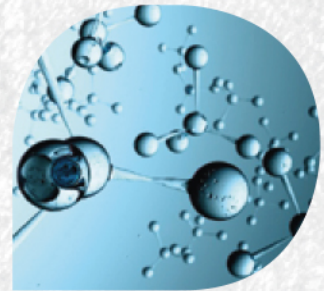


Hyaluronic acid

- 🔬 Creates a moist environment for optimal tissue repair²
- 🔬 Increases keratinocytes and fibroblasts proliferation and promotes angiogenesis²
- 🔬 Mediates production of the antimicrobial peptide beta-Defensin2 by wound keratinocytes³

Silver sulfadiazine

- 🔬 Wide spectrum antibacterial action⁴
- 🔬 Effective against many species of fungi^{4,5}
- 🔬 Included in the WHO Model List of Essential Medicines⁶
- 🔬 Gold standard for the topical treatment of burns⁷



Hyalo4[®] Plus:

Cream containing:

- 🔬 %0.2 hyaluronic acid
- 🔬 %1 silver sulfadiazine

INDICATIONS¹: local management of acute and chronic wounds at high risk of infection or to help prevention of recurrence of infection.

Hyalo4[®] Plus: effective in healing and reducing infection in pressure ulcers

Prospective, observational, cohort study in 127 patients with stage II-III pressure ulcers²:

- Improvement or complete healing in %67 and %87 of patients at days 10 and 35, respectively
- Improvement of exudation and pain
- Wound infection decreased from %12 as baseline to %2 after 30 days

	RESULTS			
	Baseline	10 days	20 days	30 days
Number of patients with infections	15	6	2	2
Number of patients with increased exudate	10	2	0	1
Number of patients with pain	8	0	0	0

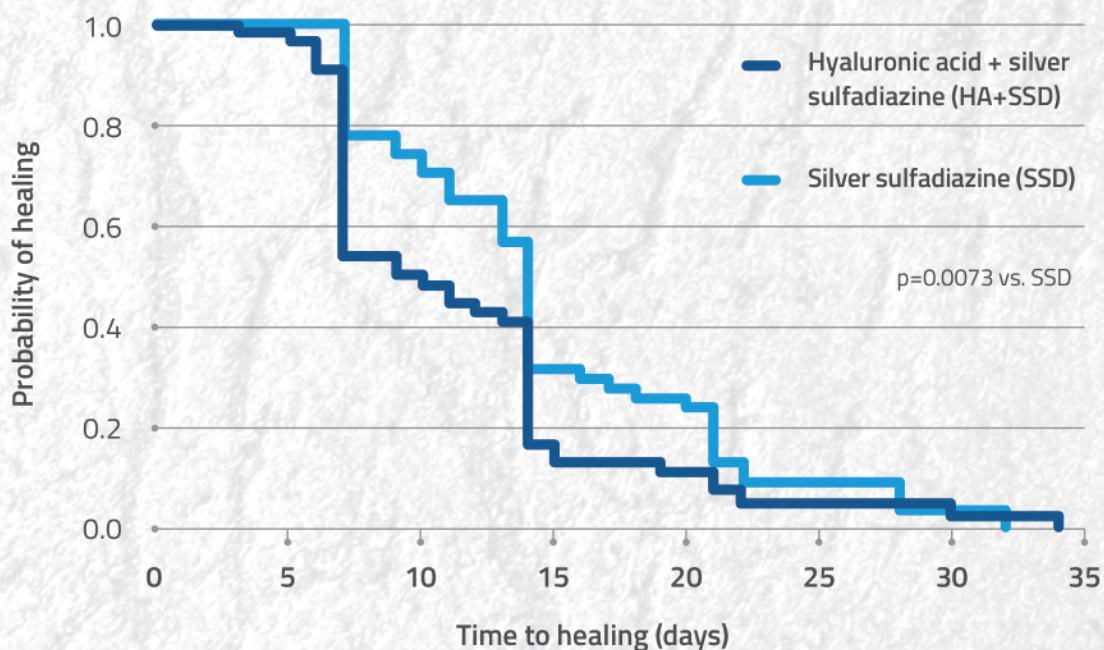
Patients aged ≥ 18 years with at least one stage II or III pressure ulcer (according to NPUAP '89 classification) and a lesion size < 25 cm². Hyaluronic acid + silver sulfadiazine was given for a minimum of 10 days to a maximum of 35 days in addition to standard therapy. Patients were assessed at baseline and at 20, 10, and 30 days following treatment initiation. Signs of infection were present in %12 of cases at the beginning of the observation period².

Hyaluronic acid combined with silver sulfadiazine is effective in the treatment of infected stage II and III pressure ulcers²


Hyalo4[®] Plus: reduces healing time in patients with burns⁸

TIME TO COMPLETE HEALING

Kaplan-Meier cumulative survival curve



Randomized study conducted in 111 adult patients with superficial and deep dermal second-degree burns. Patients received treatment with either hyaluronic acid + silver sulfadiazine or silver sulfadiazine alone once daily for up to 4 weeks⁸.

 **Significantly shorter time to healing with HA+SSD than SSD alone: 9.5 days vs. 14 days ($p=0.0073$)⁸**

Clinically demonstrated

Promotion of healing and prevention of infection

Female patient, -79years-old, with atrial fibrillation and senile dementia.
The patient has a multiple venous ulcer in the internal malleolar area.
The wounds are slightly exuding, with a fibrous bed and oedematous margins.

RESULTS



Baseline

After disinfection with %0.05 chlorhexidine, Hyalo4® Plus was applied and covered with a medium stretch compression bandage to treat oedema.
Dressing was changed daily.



After 25 days

The size of the two major wounds decreased, with less oedematous wound margins and development of granulation tissue.
The small wound in the lower area is completely healed.
Dressing was changed daily to prevent infection.



Final visit (55 days)

All lesions are completely healed with formation of repair tissue.
For prevention of recurrence, class 1 compression stockings are prescribed.

Key points

Hyalo4® Plus

- Indicated for local management of acute and chronic wounds at high risk of infection or to help prevention of recurrence of infection¹
- Concerted efficacy of hyaluronic acid and silver sulfadiazine¹
- Effective in management of pressure ulcers²
- Faster wound healing than with silver sulfadiazine alone⁹

Hyalo4® Plus

Product description¹

Hyalo4® Plus is a topical preparation constituted by hyaluronic acid sodium salt as its principal component. Hyaluronic acid is a biological polysaccharide (glycosaminoglycan) distributed in the extracellular matrix of most tissues. Several studies have documented that it may participate in many and diverse tissue repair processes facilitating healing and re-epithelialization. Due to its hydrophilic properties it provides a moist wound environment necessary to the natural healing process. Silver sulfadiazine is a well known anti microbial agent inhibiting the growth in vitro of nearly all pathogenic bacteria and fungi. The presence of silver sulfadiazine in the product composition plays a role in preventing the microbial contamination, thus improving the hyaluronic acid ability to support wound healing. These characteristics allow to change the dressing even only once a day : this causes the minimum discomfort to the patient and the minimum exposure of the lesion to the air, thus reducing the possibility of wound contamination.

Indications

Hyalo4® Plus is indicated for the management of skin lesions, especially those at high risk of infection. In particular, it is intended to cover acute and chronic wounds (first and second degree burns, vascular and metabolic ulcers and pressure sores) and to provide a moist microbe-free wound environment. Hyalo4® Plus can be used on non-infected wounds to help in preventing infection and, following successful treatment of infected wounds, to help prevent the reoccurrence of infection.

Advantages

- Hyaluronic acid: creates the ideal conditions for improved healing processes.
- Silver sulfadiazine has a wide spectrum antibacterial action and is effective against many species of fungi. Effective against *P. aeruginosa* and *E. pyogenes*, the most frequently found microorganisms in wounds and infected burns.

Mechanism of action

Hyaluronic acid aids the migration of the fibroblasts and endothelial cells. Hyaluronic acid moderates the inflammatory phase, by acting as scavenger of the free radicals and activating a negative feedback. During the remodelling phase, it reduces fibrosis by controlling the collagen secretion. Silver sulfadiazine bonds to the bacterial walls or the DNA of gram positive and gram negative germs. On contact with organic tissue, the medication reacts with sodium chloride (NaCl) and proteins, releasing sulfadiazine, which reduces the risk of infection.

Composition

- Hyaluronic acid, sodium salt %0.2
- Silver sulfadiazine %1

Product description	Format	Articles per pack
Hyalo4® Plus	Cream 25 g tube	1
Hyalo4® Plus	Cream 100 g tube	1



REFERENCES: 1. Hyalo4® Plus. Instructions for use. Rev. 6. 2. Peghetti A, et al. Efficacy of topical administration of hyaluronic acid associated with silver sulfadiazine (Connettivina® Plus) in the treatment of pressure ulcers: a prospective, observational, cohort study. Professioni Infermieristiche 77-62:67;2009. 3. Gariboldi S. et al. Low molecular weight hyaluronic acid increases the self-defence of skin epitelium by induction of beta-Defensin2 via TLR2 and TLR4. J Immunol, 2110-181:2103, 2008. 4. Farris A, et al. Association of hyaluronic acid and silver sulfadiazine for topical use: rational basis and recent clinical evidence in wound healing. Farmaci 7-9:61;2010. 5. Wright JB, et al. Efficacy of topical silver against fungal burn wound pathogens. Am J Infect Control 50-27:344;1999. 6. World Health Organization. Available at: http://www.who.int/medicines/publications/essentialmedicines/EML-8_2015May15-.pdf. 7. Silva MN, et al. Comparative study of the efficacy of nanocrystalline silver dressing and silver sulfadiazine applied on burns in hospitalized patients. IOSR 7-63;(4)13 2014. 8. Costagliola M, Agrosi M. Second-degree burns: a comparative, multicenter, randomized trial of hyaluronic acid plus silver sulfadiazine vs. silver sulfadiazine alone. Curr Med Res Opin 40-21:1235;2005.