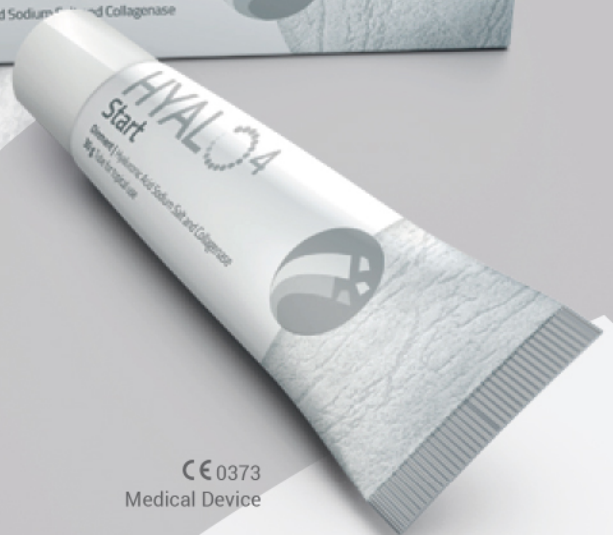


HYAL○4

Start

**Prepares the wound bed
to allow natural healing**



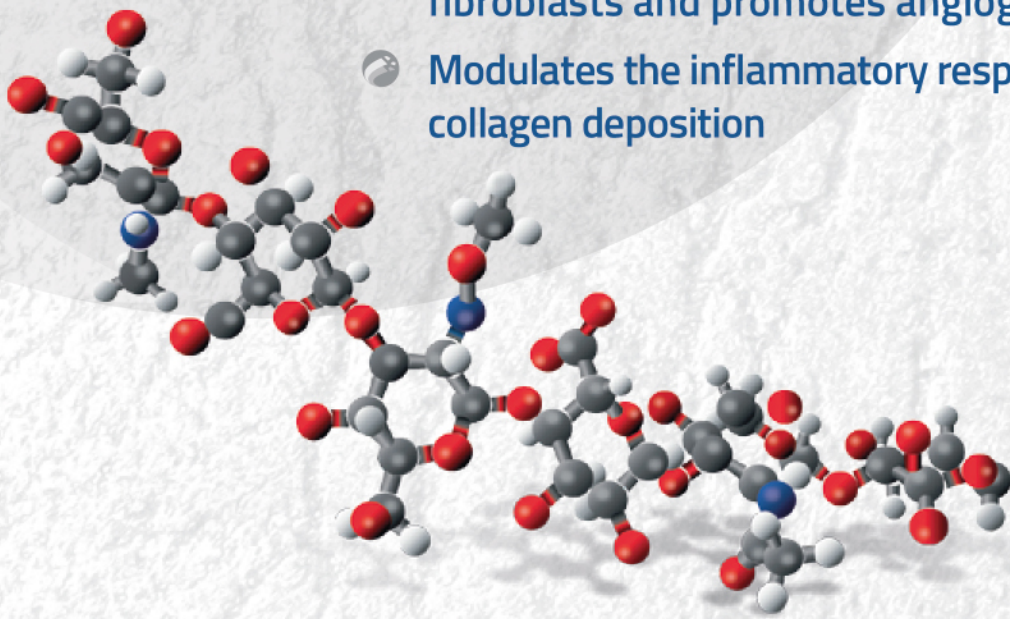
CE 0373
Medical Device

Hyaluronic Acid and Collagenase

Hyaluronic acid and collagenase promote healing of chronic wounds and prepare the wound bed¹

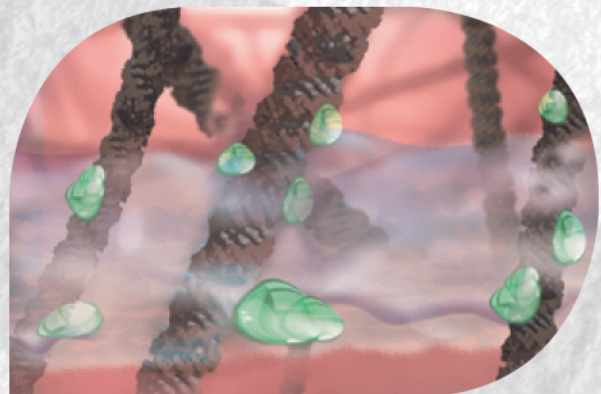
Hyaluronic acid^{1,2}

- Creates a moist environment for optimal tissue repair
- Increases proliferation of keratinocytes and fibroblasts and promotes angiogenesis
- Modulates the inflammatory response and improves collagen deposition



Collagenase from *Vibrio alginolyticus*^{1,2}

- Highly purified enzymatic preparation from *Vibrio alginolyticus*
- Degrades fibrinous and necrotic tissue contributing to wound bed preparation
- Preserves peri-lesional skin and healthy tissue



Hyalo4 Start: prepares wounds to allow natural healing

Hyalo4 Start is an ointment for topical application that contains **sodium hyaluronate %0.2** from bacterial fermentation and bacterial collagenase derived from non-pathogenic *Vibrio alginolyticus*¹

INDICATIONS¹: local management of chronic wounds such as pressure sores, vascular leg ulcers, and diabetic ulcers

Advantages

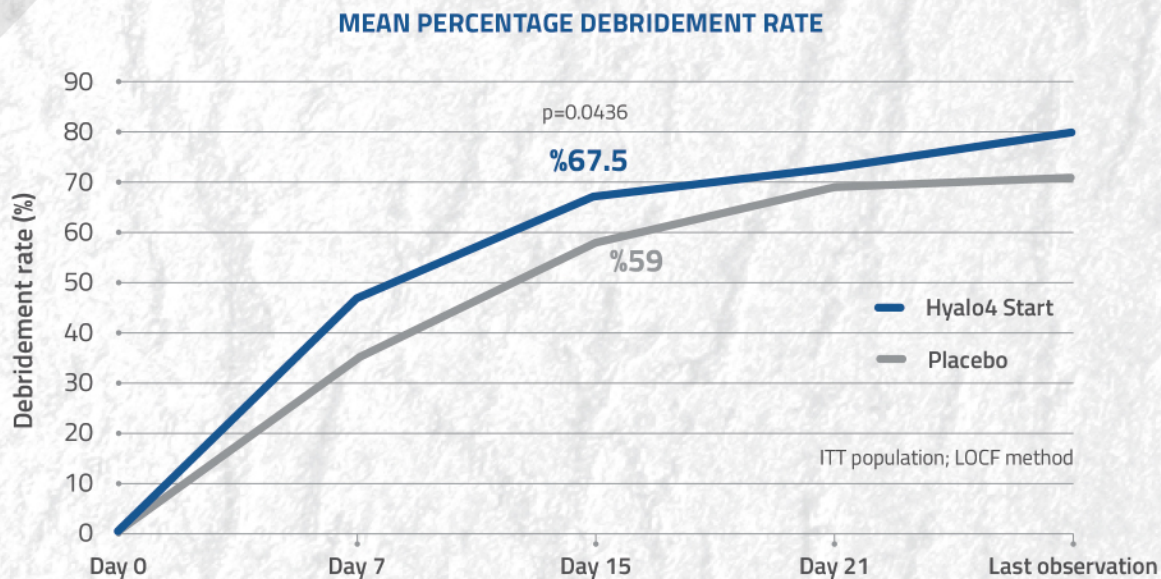
- Hyalo4 Start creates a moist environment and prepares the wound bed to promote natural healing³
- The collagenase in Hyalo4 Start is %99 pure⁴.
The absence of non-specific proteases ensures specific action leaving the peri-lesional site intact
- Hyalo4 Start is very fluid, smooth and simple to apply, with no discomfort or pain⁵



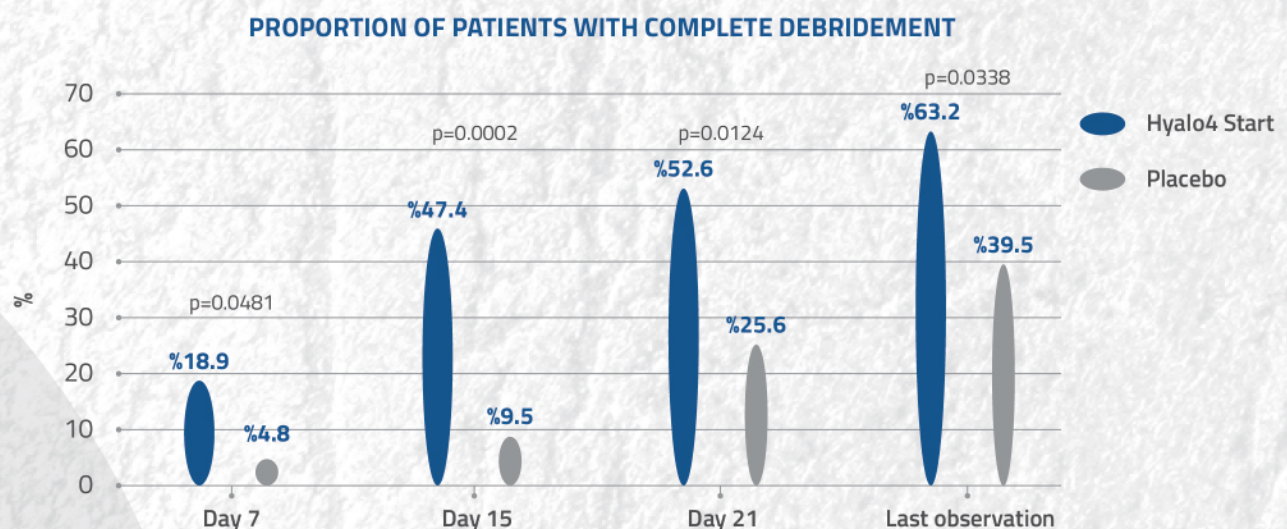
Hyalo4 Start: clinically proven efficacy

Double-blind, multicenter, placebo-controlled clinical trial investigating hyaluronic acid-collagenase applied once a day in 113 patients with chronic venous leg ulcers⁶.

Patients with chronic venous ulcers (CEAP6) for ≥ 6 months and lesion areas up to 30 cm². Hyaluronic acid + collagenase or placebo were applied once a day. Treatment groups were assessed at baseline and at four clinical study visits, every 7 days, up to a maximum of 30 days.



Hyalo4 Start removes devitalized tissue more effectively than the control group after 15 days⁶



Hyalo4 Start promotes the healing process by anticipating the transition to the re-epithelialization phase⁶

Clinically-demonstrated efficacy

Woman, -48years-old, with persistent lesions for 7 months

RESULTS



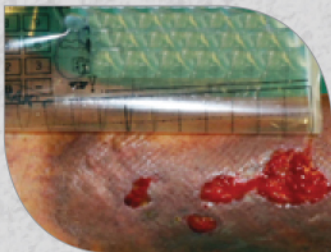
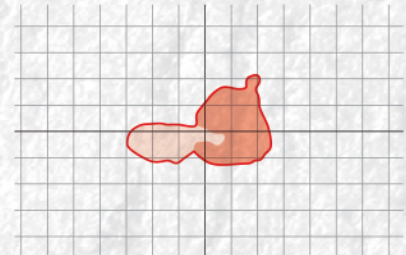
Baseline

Lesion total area 10.5 cm²
Devitalized area cm² %63.8) 6.7)

Granulation tissue

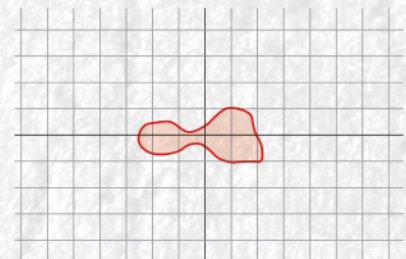


Devitalized area



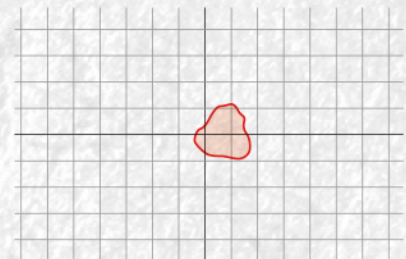
After 15 days

Lesion total area 5.2 cm²
Devitalized area 0.0 cm²



Final visit (21 days)

Lesion total area 2.8 cm²
Devitalized area 0.0 cm²
In advanced epithelialization stage



Key points

Hyalo4 Start

- Combines the **protective effect of hyaluronic acid** to improve wound bed preparation with the **proteolytic action of collagenase from *Vibrio alginolyticus***^{1,2}
- Hyalo4 Start **removes devitalized tissue more effectively**⁶
- Hyalo4 Start: **promotes the healing process** by anticipating the transition to the re-epithelialization phase⁶
- Well tolerated and easy to apply**⁵

Hyalo4 Start

Product description¹

Hyalo4 Start is a fluid ointment for topical use containing sodium hyaluronate obtained by bacterial fermentation, as the principal component, and bacterial collagenase obtained from a non-pathogenic *Vibrio alginolyticus* strain, as an incorporated medicinal substance. Hyalo4 Start allows the preparation of the wound bed, thanks to the hydrating properties of hyaluronic acid that promotes the natural repair process and protects the new viable tissue. In fact the process of cicatrization of the lesions takes place more rapidly in a moist environment. The bacterial collagenase assists in the wound bed preparation.

Indications¹

Local management of chronic ulcers (i.e. pressure sores, vascular ulcers of the legs, diabetic ulcers). In particular, it is intended to provide an optimal moist environment and wound bed preparation that supports the natural healing process.

Advantages¹

- The Hyalo4 Start collagenase is %99 pure. The absence of aspecific protease entails a totally specific action leaving the perilesional site intact.
- Hyaluronic acid maximises the effectiveness of the collagenase, and stimulates the healing processes which are faster and improved.
- As Hyalo4 Start is so fluid and smooth, it is very simple to apply with no discomfort or pain for the patient.

Mechanism of action²

Collagenase from *Vibrio alginolyticus* is effective towards the native collagen, or type 1 collagen, which is responsible of eschar's "anchoring" on the bottom of the lesion. HA facilitates the migration of fibroblasts and endothelial cells in the natural process of re-epithelialization. Hyaluronic acid moderates the inflammatory phase, by acting as scavenger of the free radicals and activating a negative feedback. Consequently HA decreases the fibrosis in the remodelling phase.

Composition

Principal component: sodium hyaluronate %0.2

Other components: collagenase (not less than 2.0 nkat/g of ointment*), light liquid paraffin, white petrolatum.

*The katal (symbol: kat) is the SI unit of catalytic activity. [Nomenclature Committee of the International Union of Biochemistry (NC-IUB) (1979)].

Product description	Format	Articles per pack
Hyalo4 Start	15g tube	1
Hyalo4 Start	30g tube	1
Hyalo4 Start	50g tube	1



REFERENCES: 1. Hyalo4 Start. Technical data sheet. 2. Onesti MG, et al. A new association between hyaluronic acid and collagenase in wound repair: an open study. Eur Rev Med Pharmacol Sci 6- 17:210;2013. 3. Chen WY, Abatangelo G. Functions of hyaluronan in wound repair. Wound Repair Regen 89-79;(2)7;1999. 4. Cortivo R, et al. Bionect start: the biological synergy for the evolution of enzymatic debridement. J Wound Technol. -13;1;2011 6. 5. Onesti MG, et al. Effect of enzymatic debridement with two different collagenases versus mechanical debridement on chronic hard-to-heal wounds. Int Wound J 2015 Feb 3. doi: 10.1111/iwj.12421. 6. Scalise A, et al. Enzymatic debridement: is HA-collagenase the right synergy? Results from a randomized double-blind controlled clinical trial in venous leg ulcers. Manuscript submitted for publication.

