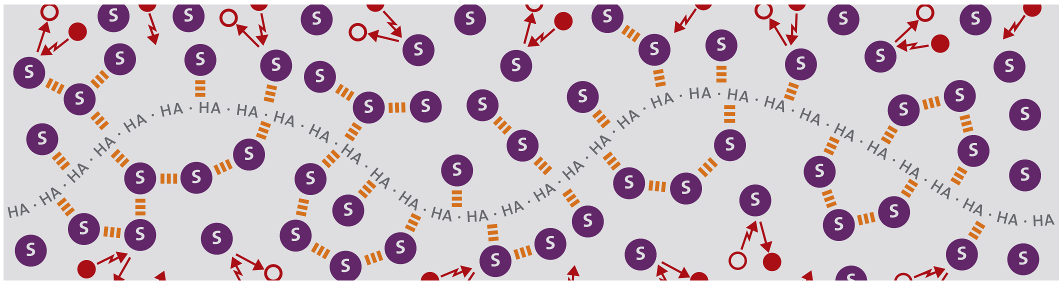
SORBITOL : A KEY INGREDIENT



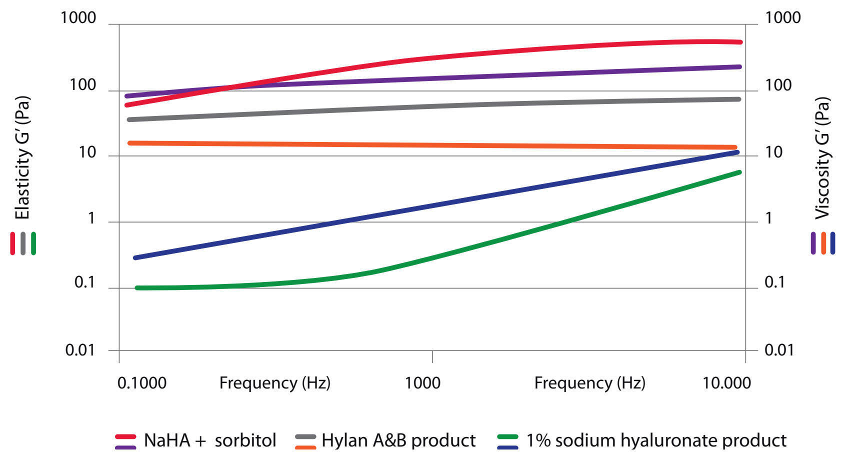
Numerous scientific publications have identified free radicals as deleterious agents that damage tissue and promote inflammation.[1][2] Sorbitol acts as an effective free radical scavenger. By doing so, it has two principal effects:

- Reduces inflammation: Free radicals attract macrophages, a key mediator of inflammatory processes. By lowering the concentration of free radicals, Sorbitol inhibits macrophage migration into the synovial cavity, thereby reducing inflammation and pain.
- Preserves NaHA: Free radicals can directly degrade NaHA. By lowering the concentration of free radicals, Sorbitol maintains NaHA integrity, facilitating the reestablishment of homeostasis and joint mobility.

NATURAL BIOMECHANICAL PROPERTIES

In 1967, medical researcher André Balazs showed that healthy human synovial fluid has a crossing of the elastic and viscous moduli between 0.2 and 0.6 Hz. SYNOLIS **V-A** is a viscosupplement with elastic and viscous moduli crossing at 0.4 Hz, giving it unique rheological properties that mimic those of healthy synovial fluid.[3]

SYNOLIS **V-A** also shows superior viscoelastic moduli than most products on the market.



PRODUCT SPECIFICATIONS

SYNOLIS **V-A** is indicated to significantly reduce pain and improve joint mobility following osteoarthritis in the knee and other synovial joints.

SYNOLIS **V-A** is a patented formulation from Anteis S.A.[6]

FEATURES	DESCRIPTION
NaHA	20 mg/ml, biofermentative origin, pure product, molecular weight > 2.2 MDa in the sterilized product
Sorbitol	40 mg/ml
Volume per syringe	2 ml
Sterilization mode	Steam sterilization
Primary packaging	Glass syringe with ergonomic finger grip and rod
Secondary packaging	Second sterility barrier, in boxes of 1 or 3 syringes
Recommended clinical protocol	1 intra-articular injection per week for 3 consecutive weeks
Storage condition	Room temperature

The SYNOLIS V-A packaging was developed:

- to improve ergonomics and usability with a large finger grip and a rounded rod head
- to ensure sterile conditions with a double sterility barrier, as for surgical products
- to be injected with either a 21G or 18G needle

SYNOLIS V-A IS AVAILABLE IN BOXES OF 1 SYRINGE OR 3 SYRINGES, 2 ML PER SYRINGE

SWITCH TO VISCO-ANTALGY

www.anteis.com/Orthopaedics/

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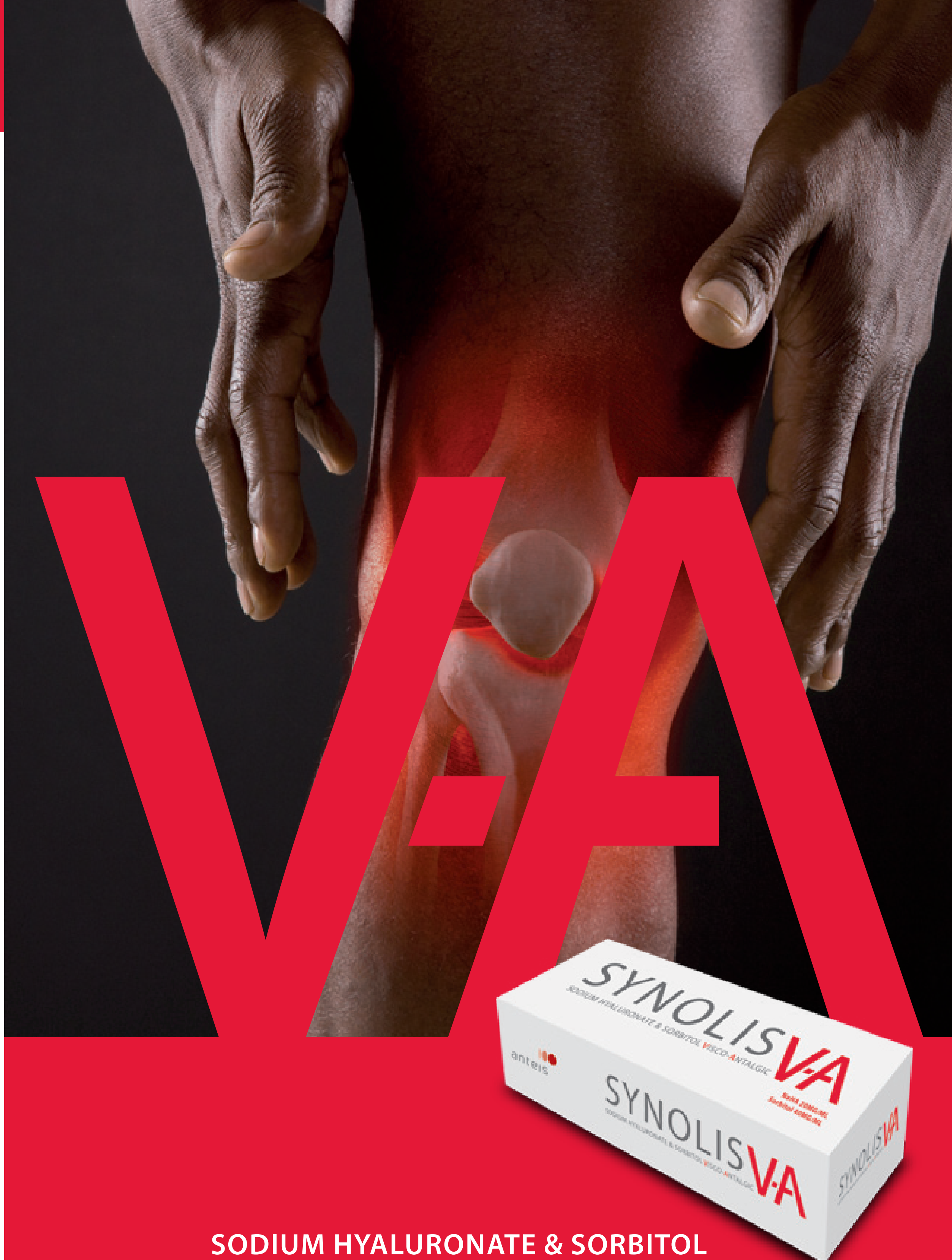
CHANGE STARTS HERE

[1] M. GROOTVELD, E. B. HENDERSON & al : "Oxidative damage to hyaluronate and glucose in synovial fluid during exercise of the inflamed rheumatoid joint" - *Biochem. J.* 1991, Vol. 273, p 459-467
[2] Y. Henrotin and B. Kurz : "Antioxydant to treat osteoarthritis: dream or reality ?" – *Current drug targets,* 2007, Vol. 8, p 347-357
[3] E. Balazs and D.A. Gibbs : "The rheologiocal properties and biological function of hyaluronic acid" – *Chemistry and molecular biology of the intercellular matrix,* 1970, p 1241-1254
[6] S. Gavard and O. Benoit : "HYALURONIC ACID INJECTABLE GEL FOR TREATING JOINT DEGENERATION", 2007, EP2173324



SODIUM HYALURONATE & SORBITOL

THE NEW WINNING COMBINATION !

THE FIRST VISCO-ANTALGIC

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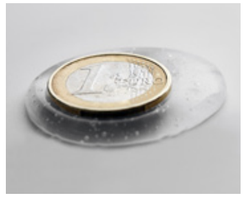
CHANGE STARTS HERE

A NEW GENERATION TREATMENT FOR SYMPTOMATIC OSTEOARTHRITIS

1



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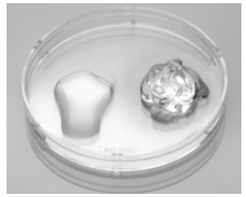


3

SYNOLIS **V-A** is an innovative, new-generation treatment for osteoarthritis. It addresses not only the mechanical background of the disease but also the underlying inflammatory processes. **A unique combination of 2% Sodium Hyaluronate (NaHA) and 4% Sorbitol,** SYNOLIS **V-A** addresses the limits of traditional viscosupplements, significantly reducing pain throughout the therapy.

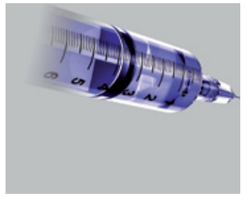
The aim of SYNOLIS V-A treatment is to :

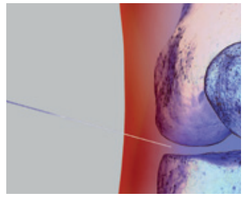
- slow down inflammatory processes
- provide rapid pain relief
- improve joint mobility

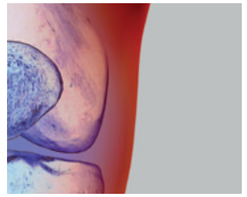
KEY BENEFITS

- SYNOLIS **V-A** leads to rapid pain relief, with 50% of the reduction occurring after the first injection [5], whereas with other viscosupplements, pain relief can take several weeks to achieve.
- SYNOLIS **V-A** acts more effectively on the inflammatory background of osteoarthritis than regular viscosupplements through the anti-inflammatory properties of Sorbitol, a free radical scavenger.
- SYNOLIS **V-A** restores the viscoelastic properties of the synovial fluid more rapidly and effectively than regular viscosupplements, as Sorbitol protects the NaHA from degradation by free radicals.
- SYNOLIS **V-A** significantly reduces osteoarthritic pain and improves mobility in the knee and other synovial joints.

THE FIRST VISCO-ANTALGIC ON THE MARKET







Anteis S.A. has designed an intra-articular NaHA injection with the capacity to significantly reduce pain after the first shot and for up to 1 year. [5]

With its free radical scavenger effect, SYNOLIS **V-A** possesses anti-inflammatory properties through a non-pharmacological route.

DECREASE IN KNEE PAIN AFTER INTRA-ARTICULAR INJECTION IN PATIENTS SUFFERING FROM KNEE OSTEOARTHRITIS

	WEEK 1	WEEK 4	WEEK 8	WEEK 24
Injection of traditional NaHA viscosupplement [4]	+	+	++	+++
Injection of corticosteroid [4]	+++	+	0	0
Injection of SYNOLIS **V-A** [5]	+++	+++	+++	+++

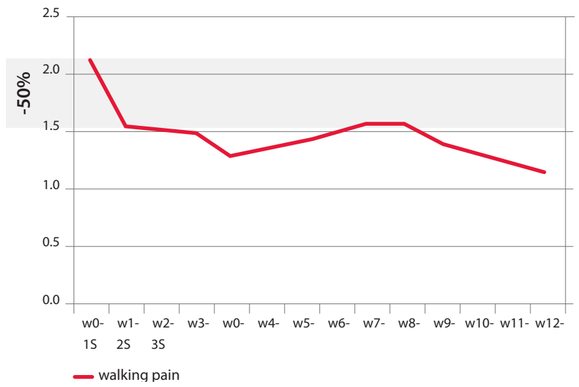
SYNOLIS V-A combines :

- the mid- and long-term efficacy of a very good viscosupplement
- the immediate, short-term efficacy of intra-articular corticosteroids

50 % OF THE PAIN RELIEF IS GAINED AFTER THE FIRST INTRA-ARTICULAR INJECTION

SIGNIFICANT CLINICAL STUDY RESULTS

MEAN WALKING PAIN ASSESSMENT BY THE PATIENT [5]



DESIGN [5]

Prospective, open-label, 13-week study in patients suffering from knee osteoarthritis.

CLINICAL PROTOCOL : 1 INTRA-ARTICULAR INJECTION PER WEEK FOR 3 CONSECUTIVE WEEKS.

RESULTS [5]

Pain reduction

- 50% of the reduction in pain is gained after the first injection
- 7 out of 10 patients experience pain relief after the first injection
- Continuous improvement in pain control until the end of the study

Safety

- Excellent safety and tolerance profile.

1 SYNOLIS **V-A**
2 SYNOLIS **V-A**
3 SYNOLIS **V-A** compared to a regular viscosupplement

[4] R. Bannuru, N Natov, I Obadan & al: "Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: A systematic review and meta-analysis" - *Arthritis and Rheum,* 2009, Vol 61, p 1704–1711
[5] T. Conrozier & al : « Early efficacy of a novel viscosupplement combining hyaluronic acid and sorbitol, ANTI-OX-VS (Synolis) in patients with knee osteoarthritis » - *ECCEO (2011).*