SYALTEN®

Hyaluronic acid sodium salt (medium molecular weight)

Personalized treatment for degenerative and/or inflammatory pathologies affecting all synovial articulations

INDICATIONS

SYALTEN is a synovial fluid substitute that allows the restoration of the physiological and rheological properties of compromised articulations, in presence of painful states or with reduced mobility, due to affections or post-traumatic conditions.

METHOD OF USE

Aspirate any joint effusion before injecting **SYALTEN**. Remove syringe cap taking special care to avoid contact with the opening. Insert an appropriately sized needle (18 to 22 G), screwing it in tightly to ensure a tight seal and prevent leakage of solution. Inject the device only within the synovial space, at room temperature and under strict asepsis.

POSOLOGY AND MODE OF USE

- Infiltrate **SYALTEN 24 mg/30 mg/40 mg** da **2 ml** intra-articularly. **SYALTEN 24 mg** once weekly for 5 weeks, **SYALTEN 30 mg/40 mg** once weekly for three weeks.
- Infiltrate **SYALTEN 60 mg 4 ml** once weekly for 2 weeks and **SYALTEN 80 mg/4 ml** as a single infiltration.

According to the doctor's discretion and according to the patient's health condition, a different dosing schedule may be followed and several joints may be treated simultaneously. If further courses of treatment are required, an interval of approximately 6 months is recommended.

WARNINGS AND COUNTERINDICATIONS

Do not use after the expiration date indicated on the package. Do not use if the package is open or damaged. The area of injection must be on healthy skin. Do not inject vascularly. Do not inject into the knee joint if there is venous or lymphatic stasis in the limb. Do not inject outside the articular cavity, into synovial tissue or articular capsule. Do not inject in the presence of severe intra-articular effusions. **SYALTEN** should not be injected in the presence of inflammation, infection, or skin conditions in the area to be treated. After intra-articular injection, advise the patient to avoid all intense physical activities and to resume normal activities only after a few days. The content of the syringe is sterile and apyrogenic. Keep at temperature below 25 °C and far from heat sources. Do not freeze. Keep out of the reach of children.

SIDE EFFECTS

Intra-articular infiltration may cause undesirable effects locally. Symptoms such as pain, heat sensation, redness or swelling may occur at the injection site. In this case, it is helpful to apply ice to the treated articulation. Such symptoms under normal conditions disappear after a short time. The doctor must ensure that patients report any undesirable effects after treatment. Do not freeze. Keep out of the reach of children.

1. Curran MP: Hyaluronic Acid (Supartz®): A Review of its Use in Osteoarthritis of the Knee. Drugs Aging 2010; 27 (11): 925-941

2. THERAPEIA – December 2016

Made in Italy

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PHARMALABS HEALTH SOLUTIONS

Table 1. Pharmacological effects of intra-articular administration of hyaluronic acid (Curran 2010)

Bio-mechanical effects	△ synovial fluid viscoelasticityl △ articular lubrication ● cartilage articular surface coating
Analgesic effects	▽ neuromediated algogenic activityarticular lubrication ▽ prostaglandin -or bradykinin- mediated pain
Anti-inflammatory effects	▽ levels of inflammatory mediators (including prostaglandin E2)articular lubrication ▽ leukocyte chemotaxis ● TNFalpha downregulation
Antioxidant effects	▽ oxygen-reactive speciesarticular lubrication ● protection against oxidative damage ● DNA protection against oxidative damage
Chondroprotective effects	▽ release of arachidonic acid from fibroblasts ● stimulates the production of endogenous hyaluronic acid and the biosynthesis of extra-matrix components ● prevents the penetration of fibronectin (by surface coating on the cartilage matrix) ● protects against chondrocyte apoptosis ● inhibits cartilage degradation (by inhibiting the expression of mRNA for glitazone receptor: PPAR gamma, peroxisome proliferator-activated receptor gamma) ● inhibits pericellular fibrinolytic activity mediated by the plasminogen activation system

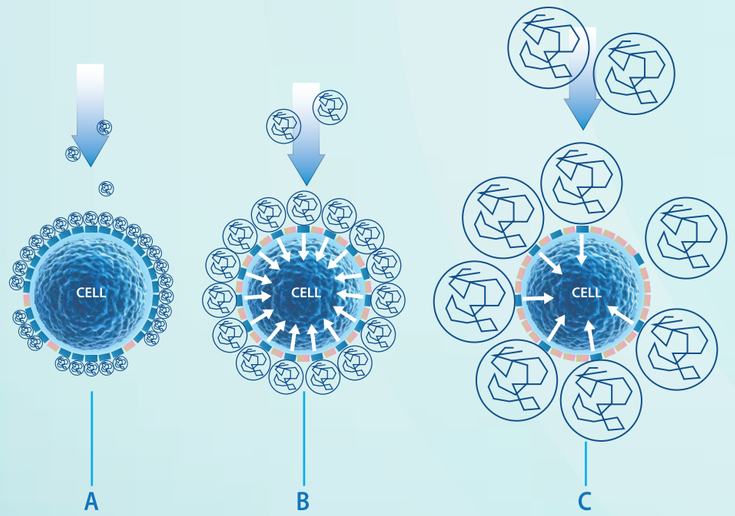
(1)
The exogenous intra-articular administration of hyaluronic acid, called visco-supplementation, recognizes a biodynamic action identifiable in two different moments and processes at the joint site (2)

TABLE 2
Schematic representation of affinity for specific hyaluronic acid receptors as a function of molecular weight.

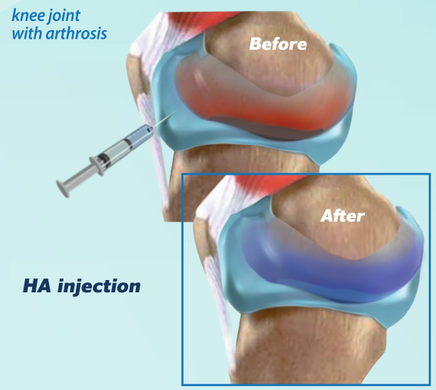
A: Low molecular weight molecules (<500 kDa) fail to fill all receptor sites; this results in reduced biosynthesis of endogenous hyaluronic acid.

B: Medium sized (<500 - 4,000 kDa) lemolecules have an ideal static footprint: they fully saturate receptors and induce effective biosynthesis of endogenous hyaluronic acid.

C: In the case of high molecular weight (>4,000 KDa) the steric bulk is excessive compared to the possibility of saturating the specific receptors; also in this case; as in A, the biosynthesis of hyaluronic acid is defective.



(2)
In a proposed model [Smith and Ghosh 1987] of binding between hyaluronic acid molecules and receptors present on the surface of fibroblasts, the optimal binding condition is constituted by molecules of medium molecular weight, i.e. between average molecular weight, i.e. between 500,000 and 4 million By this is in fact the condition in which the number of simultaneously stimulated receptors is higher.



knee joint after treatment with SYALTEN

With low molecular weight HA molecules (less than 500,000 Da), the ratio between molecules and receptor sites is unbalanced and the biosynthesis of endogenous HA is only weakly stimulated.

On the contrary, high molecular weight molecules (more than 4 million Da) do not allow an optimal binding to receptors, leaving many of them lacking in spatial configuration, ultimately reducing, also in this case, the stimulus to endogenous HA biosynthesis (2).

Hyaluronate infiltrative therapy reduces pain and improves mobility of the treated joint, thus it has a curative but also a preventive action towards the tissues because it reduces the penetration of inflammatory cells and inflammatory mediators.
Hyaluronic acid consists of linear polysaccharide chains responsible for elasticity and energy-absorbing capacity; healthy synovial fluid contains high concentrations of hyaluronic acid.

Due to its ability to retain water, hyaluronic acid can dampen numerous physical stresses that act on the articulation, performing an elastic effect.

Therefore, the same molecule can act both as a lubricant and as a shock absorber depending on the degree of stress to which the joint is subjected.
In the synovial fluid these functions are performed exclusively by endogenous hyaluronic acid.

The graph on the right shows how the **SYALTEN** protocol proved effective in reducing pain after the first administration of the product. After the planned three infiltrations, both flexor and extensor range of motion also increased significantly.
No side effects or systemic reactions were observed.

Infiltration with hyaluronic acid has the immediate effect of restoring synovial fluid, allowing it to function as a lubricant and shock absorber.

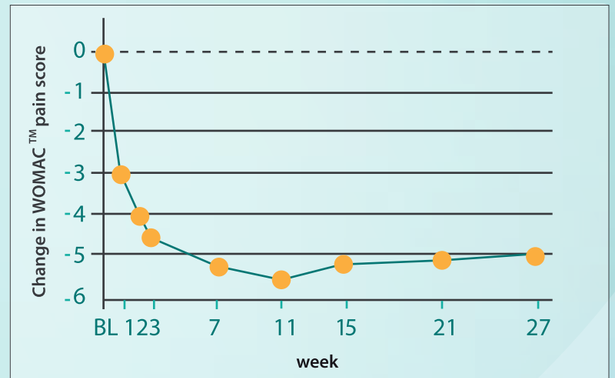


Figure1. thearpeutic effect after three SYALTEN infiltrations.

In cases of arthrosis there is a loss of chemical and physical properties of hyaluronates with a consequent loss of their elasticity and viscosity. The consequence is the interruption of the function of support and nourishment of the cartilage matrix that is progressively altered in a degenerative way.