

HYALURONIC ACID SODIUM SALT 2.0% FOR INTRA-ARTICULAR INJECTION

INDICATION: **Focusial** a substitute for synovial fluid which, thanks to its visco-elastic and lubricating properties, helps to restore the rheological conditions of the joints, affected by degenerative or post-traumatic diseases. The product, by improving the characteristics of synovial fluid, exerts a protective action on the joints and helps to improve joint function and reduce painful symptoms. **Focusial** acts only at the level of the joint in which it is injected, without exerting any systemic action.

DESCRIPTION: **Focusial** is a sterile injectable, biodegradable and isotonic gel for intra-articular use. Focusial consists of a medium molecular weight hyaluronic acid (3.0 x10⁶ Daltons), produced by *Streptococcus equi* bacteria, formulated at a concentration of 20 mg/ml in a physiological buffer. Focusial is characterized by viscoelastic properties, therefore it helps to normalise the viscosity of the synovial fluid present in the intra-articular cavity. Each pack contains a Focusial ampoule-syringe and a patient information leaflet. It contains two labels bearing the batch number and the expiry date. One of these labels should be attached to the patient's medical record and the other should be given to the patient to ensure traceability.

COMPOSITION: Sodium hyaluronate (20mg/ml), sodium monobasic phosphate dodecahydrate, WFI grade water. A syringe contains 2.0 ml of pyrogenic solution, sterilised by moist heat.

INSTRUCTIONS FOR USE: Remove any joint effusion before injecting Focusial; the same needle must be used for effusion removal and Focusial injection. Remove the protective cap of the syringe taking special care to avoid contact with the opening.

Screw the needle with a diameter between 18 and 22 G firmly onto the Luer-type locking collar following the instructions shown below. Before injection, treat the affected area with a suitable disinfectant. Inject Focusial using an aseptic technique. Only inject into the joint cavity. It is recommended to carry out an initial course of three to five treatment sessions, at intervals of one week from each other possibly followed by maintenance session according to the medical prescription.

INSTRUCTION FOR ATTACHING THE NEEDLE TO THE SYRINGE: A. Carefully unscrew the cap from the tip of the syringe, taking special care to avoid contact with the opening. B. Gently hold the needle guard and attach the needle to the luer-lock attachment, screwing it firmly until a slight back pressure is felt to ensure a watertight seal and prevent gel from leaking during administration.

WARNING PRECAUTIONS FOR USE: Focusial is only indicated for intra-articular injections and should only be administered by a doctor. Before use, check that the syringe is intact and the expiration date. Do not use needles other than those indicated. The product must not be avoided in case of ongoing infections or inflammatory conditions of the skin near the site of the infiltration. It is recommended that the patient, after the intraarticular injection, be advised to avoid any strenuous physical activities involving the joint and to resume normal activities after a couple of days. Focusial has not been tested in pregnant or lactating women. Focusial is a single-use product, quality and sterility are guaranteed only if the syringe is sealed. Any remnants must therefore be disposed of and not reused, even after re-sterilisation. Do not use the product

if the packaging is already open or damaged. After use, dispose of the needle in a suitable container.

SIDE EFFECTS: Some temporary side effects may occur after the injection of Focusial, such as pain, stiffness, warm sensation, redness or swelling. These secondary effects can be reduced using ice pack on the painful treated joint. Normally the same disappear after a short time. If symptoms persist, seek medical advice. Any other undesirable side effects associated with the injection of Focusial should be reported to the doctor.

INCOMPATIBILITY: Incompatibility occurs between sodium hyaluronate and quaternary ammonium compounds, such as benzalkonium chloride solutions. Therefore avoid contact between Focusial and these substances.

STORAGE: Store Focusial at 2-25°C (36-77 °F) in a dry place in the original box. Protect from light, heat and frost. Keep out of the reach of children.

Focusial: is sold only on medical prescription. The intra-articular injection should only be performed by a doctor.

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Focusial

INTRA

VISCOSUPPLEMENTATION

HYALURONIC ACID
AT 2,0% 3.200.000 DA.
FOR INTRA-ARTICULAR USE

New lubrication concept used for the treatment of Osteoarthritis (OA) which helps to restore Viscoelasticity of synovial fluid improving joint functionality



STRENGTHS OF FOCUSIAL INTRA

HYALURONIC ACID

MEDIUM MOLECULAR WEIGHT
FROM **3.200.000 DA** FOR FOCUSIAL H
FROM **1.800.000 DA** FOR FOCUSIAL M

SYNOVIAL MEMBRANE

PRODUCES
HYALURONIC ACID
3.000.000 DA

HYALURONIC ACID

FOCUSIAL USES
HYALURONIC ACID TYPE
PHARMA

FEATURES

EXCELLENT
VISCOSITY

HIGH BIOLOGICAL
COMPATIBILITY

ACTIVATES
C44 RECEPTORS

LONG
HALF-LIFE

OSMOLARITY 300mOsm/Kg BECAUSE HYALURONIDASES ATTACK VERY SLOWLY THE LONG CHAINS OF FOCUSIAL. LONG CHAINS ACTIVATE THE C44 RECEPTORS BETTER OF THE SHORT CHAIN HA

H

It is a medical device based on hyaluronic acid sodium salt, with a constant molecular weight of 3,200,000 Dalton, which allows a perfect diffusion inside of the joint, this means that painful swellings are not created when inoculated. It is obtained by fermentation and this guarantees absolute purity thus minimizing the risks of allergens and inflammatory reactions. It also has a very high persistence and duration of action in situ. It is substitute for synovial fluid which, thanks to visco-elastic and lubricating properties, helps to restore the rheological conditions of the joints, affected by degenerative or post-traumatic diseases. The product, by improving the characteristics of synovial fluid, exerts a protective action on the joints and promotes the improvement of joint function and the reduction of painful symptoms.

FocusIAL H40

2ml 40mg/ high molecular weight

**1 AMPOULE X 3 WEEKS
TO BE REPEATED EVERY 6 MONTHS**

FocusIAL H60

3ml 60mg/ high molecular weight

**1 AMPOULE X 2 WEEKS
TO BE REPEATED EVERY 6 MONTHS**

FocusIAL H80

4ml 80mg/ high molecular weight

**1 AMPOULE
TO BE REPEATED EVERY 6 MONTHS**

FocusIAL M40

2ml 40mg/ medium molecular weight

**1 AMPOULE X 3 WEEKS
TO BE REPEATED EVERY 6 MONTHS**

IT ACTS ONLY AT THE LEVEL OF THE JOINT WHERE IT IS INJECTED, WITHOUT EXERTING ANY SYSTEMIC ACTION.

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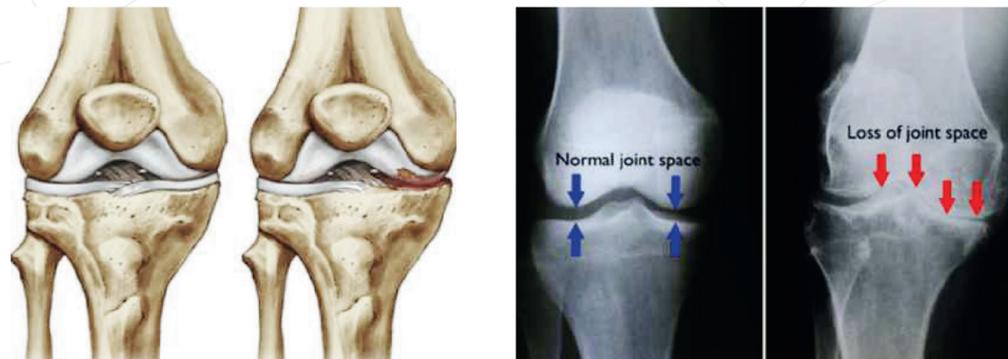
It is a sterile injectable, biodegradable and isotonic gel for intra-articular use. It consist in a hyaluronic acid (1,800,000 DA), produced by Streptococcus equi bacteria, formulated at a concentration of 20mg/ml in a physiological buffer. It is characterized by visco-elastic properties, therefore it helps to normalize of the viscosity of the synovial fluid present in the intra-articular cavity.

FocusIAL H

Repairs the matrix and slows down osteoarthritis

CHONDROPROTECTION

Osteoarthritis (OA) is a degenerative pathology that affects various tissues in the surrounding joints such as articular cartilage, subchondral bone, synovial membrane and ligaments. The main action of arthrosis is to cause a progressive deterioration of the cartilage (which is not able to reform), and of the bone, with secondary deformation of the same and production of growths, called "Osteophytes", which mechanically hinder joint movement.



The alteration of the ECM, in turn changes the biomechanical environment of the chondrocytes, which further boosts the progression of degeneration in the presence of inflammation

BINDING PATTERNS OF HYALURONIC ACID TO RECEPTORS ON THE SURFACE OF SYNOVIAL CELLS



The endogenous synthesis of hyaluronic acid by synovial fibroblasts is influenced by both the concentration and the molecular weight of hyaluronic acid in the extracellular environment. In vitro studies have shown that in the presence of low molecular weight hyaluronic acid, the binding to the articular cartilage matrix is poor and the endogenous biosynthesis of hyaluronic acid may be insufficiently stimulated.

With intermediate molecular weight hyaluronic acid preparations, on the other hand, binding to the matrix is high and, due to the high number of stimulating receptors, there is an elevation of endogenous hyaluronic acid synthesis.

Finally, in the presence of crosslinked high-molecular-weight hyaluronic acid, binding to receptors is maximal but the large size of these molecules limits the number of sites that can be occupied on the cell surface, negatively interfering with the stimulation of endogenous hyaluronic acid synthesis.

Seminars in Arthritis and Rheumatism, February 2016, page S28-S33

Efficacy and safety of hyaluronic acid in the management of osteoarthritis: Evidence from real-life setting trials and surveys

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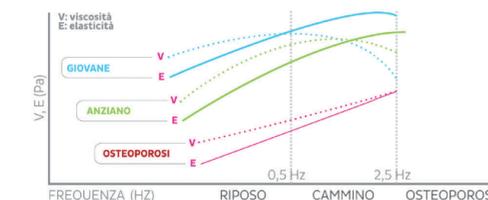
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Focusial hyaluronic acid is a molecule of the extracellular matrix with multiple physical and biological functions present in many tissues, including cartilage.

With the passing of the time the alterations became always more important and the pathology assumes all the characteristics of a chronic condition whose main clinical signs are pain and functional disability of the joint.

The presence of pro-inflammatory cytokines, free radicals and metalloproteases, they modify the joint articular microenvironment, influencing the metabolism of type B synoviocytes, responsible for the production of hyaluronic acid.



INFILTRATION THERAPY

The exogenous HA with a molecular weight between 500 and 4000 dDa increases the viscosity of the synovial fluid and improves the shock absorption and lubricating capacity of the synovial fluid.

In the healthy articulation the liquid is predominantly elastic, in an elderly person or in the course of osteoarthritis, the decrease in concentration and molecular weight of hyaluronic acid, determines a variation of rheological properties of synovial fluid and less protection of the joint from mechanical stress.

The biosynthesis of hyaluronic acid is reduced in terms of concentration and molecular weight. In healthy synovial fluid, AI is made up of linear chains with an average molecular weight of 6 millions Daltons and a concentration of about 3-4 mg / ml, while in the atrophic joint the molecular weight drops to 1.9 millions of Dalton and the concentration is reduced to 1.5 mg / ml.

Since hyaluronic acid is the main responsible for the rheological characteristics of the synovial fluid, there is a reduction in the viscoelasticity of the intra-articular fluid, with impairment of lubrication and protection of the articular cartilage in relation to mechanical stress.

