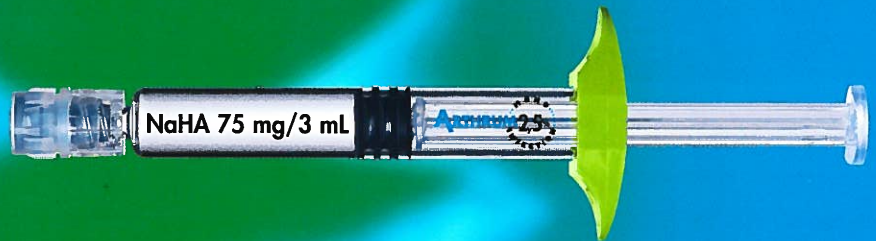


ARTHRUM 2.5% SINGLE INJECTION



ARTHRUM 2.5% SINGLE INJECTION
is a new generation HA-based therapy
for treating **OSTEOARTHRITIS** in a safe,
easy to use, single injection regimen



Pure Sodium Hyaluronate

- No animal origin
- No chemically modified agent

NEW SINGLE INJECTION

NEW

ARTHRUM 2.5%

Sodium Hyaluronate

SINGLE INJECTION

DESCRIPTION

ARTHRUM 2.5% SINGLE INJECTION

is a sterile viscoelastic device whose active ingredient is a natural derivative of hyaluronic acid, sodium hyaluronate, obtained by biofermentation, not chemically modified, with a very high molecular weight of $\geq 2,800,000$ Daltons and a high concentration of 25mg/mL (75 mg per intra-articular injection).

The active ingredient of ARTHRUM 2.5% SINGLE INJECTION does not contain any protein of avian origin and is not cross-linked by a chemical agent, eliminating any risk of allergy and potential cytotoxicity and ensuring a perfect tolerability and safety during long-term use.

ARTHRUM 2.5% SINGLE INJECTION complies with the European Pharmacopoeia, ISO standards and EEC Directive 93/42, which guarantees the perfect safety and biocompatibility of the implantable device.

The high molecular weight combined with a high concentration of sodium hyaluronate in ARTHRUM 2.5% SINGLE INJECTION is the essential factor of long-term efficacy in the symptomatic treatment of osteoarthritis, by replacing for the qualitative and quantitative insufficiency of sodium hyaluronate in the synovial fluid of osteoarthritic joints.

PRESENTATION

ARTHRUM 2.5% SINGLE INJECTION is a sterile, transparent, homogeneous viscoelastic preparation, not chemically modified, composed of highly purified sodium hyaluronate obtained by bacterial fermentation, containing 75 mg of sodium hyaluronate per 3-mL syringe.



ARTHRUM 2.5% SINGLE INJECTION is supplied in a sterile disposable Luer-Lok syringe, prefilled with 3 mL, in one syringe box.



PROPERTIES



Sodium hyaluronate exists naturally in human body and is a major constituent of intercellular matrix.

In joints, it is a structural component of cartilage and synovial fluid that acts as a lubricant, a shock absorber, a filter and a metabolic agent.

ARTHRUM 2.5% SINGLE INJECTION is biologically similar to the sodium hyaluronate of the human body.



THE FUNCTIONS OF **ARTHRUM 2.5% SINGLE INJECTION** ARE AS FOLLOWS :

▶ **Protective effect on cartilage**

- The lubricating properties of sodium hyaluronate molecules in synovial fluid allow the joint surfaces to slide against each other and protect them from mechanical damage.
- By reducing the stress on weight-bearing joints, the elastic properties protect cartilage from compressive forces.

▶ **Metabolism interface**

- Small molecules such as water, electrolytes and nutrients can diffuse readily in the direction of the cartilage and the synovial membrane.

▶ **Structure-modifying effect**

- Sodium hyaluronate provides a protective barrier, masking the pain receptors of the synovial membrane.

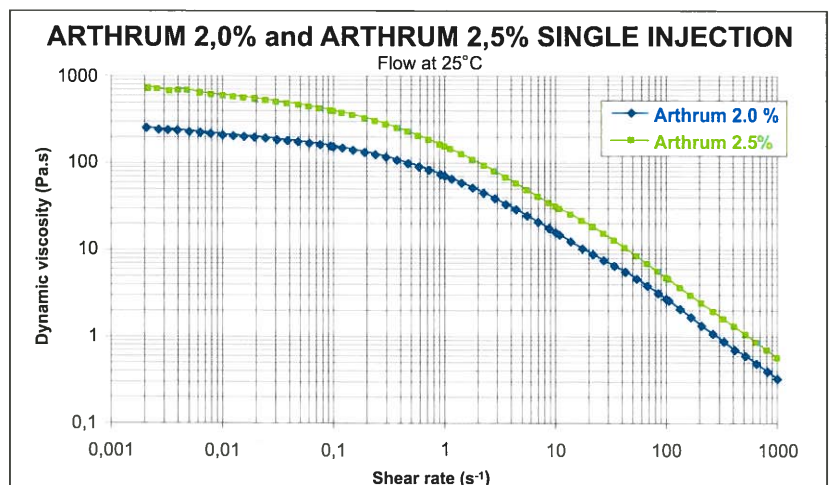


The sodium hyaluronate is normally present in synovial fluid of healthy joints and is deteriorated both in terms of concentration and molecular weight in osteoarthritic joints^{2,3}. In the treatment of osteoarthritis, **ARTHRUM 2.5% SINGLE INJECTION** therefore has the effect of improving the deficient rheological characteristics of the synovial fluid (viscosity and elasticity). These characteristics⁴ are important for shocks absorption and lubrication and protection of cartilage surfaces⁵.

The rheological properties of 2.5 Hz of **ARTHRUM 2.5% SINGLE INJECTION** exceed those of healthy synovial fluid to anticipate dilution effect within joint. The use of a high molecular weight also increases the residence time in the joint⁶. In addition, different beneficial biological effects are attributed to hyaluronic acid in the joint, as have been expressed in journals^{4,7,8} extract from numerous scientific publications.

The rheological properties of **ARTHRUM 2.5% SINGLE INJECTION** are as follows :

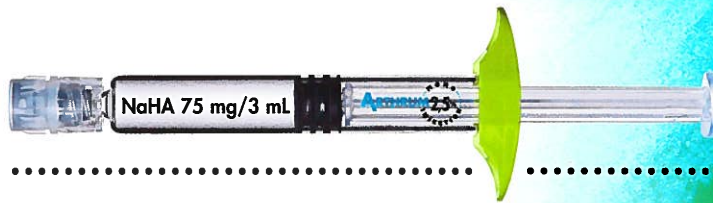
RHEOLOGICAL PROPERTIES ARTHRUM 2.5% SINGLE INJECTION								
Flow at 25°C						Viscoelasticity at 25°C		
Dynamic viscosity (Pa.s)						G' (Pa)	G'' (Pa)	Frequency
at 0,01 s ⁻¹	at 0,1 s ⁻¹	at 1 s ⁻¹	at 10 s ⁻¹	at 100 s ⁻¹	at 1000 s ⁻¹	at 2,5 Hz	at 2,5 Hz	Cutoff (Hz)
848	496	159	33,7	4,79	0,571	407	160	0,11



ARTHRUM 2.5%

Sodium Hyaluronate

SINGLE INJECTION



INDICATIONS



ARTHRUM 2.5% SINGLE INJECTION viscoelastic devices are indicated in the symptomatic treatment of osteoarthritis of the knee, in particular for reducing pain and restoring joint mobility by replacing and supplementing the elastoviscosity of the pathological synovial fluid in osteoarthritic joints.

The therapeutic indications are for all types of painful osteoarthritis of the knee :

- Primary osteoarthritis of the knee (Kellgren radiological stages I, II and III)
- Osteoarthritis of the knee and associated systemic factors :
 - Ineffectiveness of the usual treatments.
 - Intolerance and/or contraindication of NSAIDs or analgesics.
 - Use of anticoagulants, polymedication (hypertension, diabetes, obesity, cardiovascular and gastrointestinal problems).
 - Contraindications related to the placement of a prosthesis : young subjects and various contraindications related to the patient's condition.
- Incipient osteoarthritis of the knee of young subjects.
- Knee osteoarthritis secondary to traumas and sequelae of joint fractures.

BIBLIOGRAPHICAL REFERENCES

1. HASCALL V.C., LAURENT T.C. : Hyaluronan : Structure and Physical Properties Glycoforum / Science of Hyaluronan 1 - <http://www.glycoforum.gr.jp/hyaluronan>
2. BALAZS E.A., WATSON D., DUFF I.F., ROSEMAN S. : Hyaluronic acid in synovial fluid. I. Molecular parameters of hyaluronic acid in normal and arthritis human fluids - *Arthritis Rheum.* 1767; 10 : 357-375
3. PASCARETTI C., MONROCHE A. : L'essor des acides hyaluroniques at usage intra- articulaire - *Cinésiologie (La Revue Internationale des Médecins du Sport)* 2004 Mai-Août ; n° 215-216. 27-30
4. WIK O., AGERUP B., BOTHNER WIK H. : Rheology of hyaluronan products (KENNEDY J., PHILLIPS G., WILLIAMS P., HASCALL V. editors) - Woodhead Publishing Limited. 2002, volume 1, chapter 24. 201-204
5. LEVICK J.R., COLEMAN P.J., SCOTT D., MASON R.M. : Secretory Regulation in vivo. Molecular Reflection & Hydraulic Roles of Synovial Hyaluronan - Hyaluronan - Hyaluronan (KENNEDY J., PHILLIPS G., WILLIAMS P., HASCALL V. editors) - Woodhead Publishing Limited. 2002, volume 2, chapter 46. 329-336
6. MORELAND L.W. : Intra- articular hyaluronan (hyaluronic acid) and Hylans for the treatment of osteoarthritis : mechanisms of action - *Arthritis Research & Therapy* 2003. 5 : 54-67 - <http://arthritis-research.com/content/5/2/54>
7. VITANZO C. Jr, SENNET J. : Hyaluronans : is clinical effectiveness dependent on molecular weight? - *Am J Orthop.* 2006 Sept; 35(9) : 421-8
8. GHOSH P., GUIDOLIN D. : Potential mechanism of action of intra-articular therapy in osteoarthritis : are the effects molecular weight dependent? - *Semin Arthritis Rheum*, 2002 Aug; 32(1) : 10-37

DOSAGE

The dosage schedule of **ARTHRUM 2.5% SINGLE INJECTION** is **ONE INTRA-ARTICULAR INJECTION** in the knee. A second injection may be repeated between the first and third month if this is justified by the painful symptoms of the patient.

LCA PHARMACEUTICAL - 9, Allée Prométhée, F-28000 CHARTRES, FRANCE



Fax
33 2 37 33 39 39

Phone
33 2 37 33 39 30

Email
lca@lca-pharma.com

www.
lca-pharma.com