Hyalgan®

Qualitative and Quantitative Composition – Each vial or prefilled syringe contains 20mg/2ml of hyaluronic acid sodium salt (Hyalectin®).

Pharmaceutical Form – Hyalgan® is a sterile solution for intra-articular injection for single use only.

Therapeutic Indications – Treatment / sustained relief of pain in osteoarthritis of the knee.

Posology and Method of Administration –
Adults (including the elderly) The contents of one vial (20mg/2ml) or prefilled syringe (20mg/2ml) to be injected into the affected joint once a week for a total of five injections, using a standard technique. No adjustment of dose is required in elderly patients. This can be repeated at not less than 6 monthly intervals.
Children – At present there is not enough evidence to recommend a dosage regimen for use in children.

Contra-indications – Hyalectin®, the active principle in Hyalgan®, is of avian origin. Do not administer to patients with known hypersensitivity to any ingredient of the product or to avian proteins.
Intra-articular injections are contra-indicated in cases of infections or skin diseases in the area of the injection site.

Warnings and Precautions – Hyalgan® should only be administered by medical practitioners qualified in giving intra-articular injections. Remove joint effusion, if present, before injecting. Patients should be carefully examined prior to administration to determine signs of acute inflammation and the physician should evaluate whether Hyalgan® treatment should be initiated when objective signs of inflammation are present. As with any invasive joint procedure, it is recommended that care be taken not to overburden the joint immediately following the intra-articular injection. Use only if the solution is clear.

Interactions with other Medicaments and other forms of Interaction – Since there is limited experience available, Hyalgan® should not be administered simultaneously or mixed with other intra-articular injections.
Do not use concomitantly with disinfectants containing quaternary ammonium salts because hyaluronic acid can precipitate in their presence.

Pregnancy and Lactation – No embryotoxicity or teratogenicity has been observed in animal studies. However, there is no experience of the use of Hyalgan® in pregnant women and therefore the expected benefit to the mother should be weighed against any potential risk to the foetus.
If Hyalgan® is prescribed to a women of child bearing potential, she should be advised to contact her physician regarding discontinuance of the product if she intends to become, or suspects that she is pregnant.
Although it is not expected that Hyalgan® would be present in human milk, because many drugs are excreted by this route, caution should be exercised when Hyalgan® is administered to a nursing mother and the expected benefit to the mother should be weighed against any potential risk to the neonate.

Effects on Ability to Drive and Use Machines – Hyalgan® is not expected to have any effect on the patient's ability to drive or operate machinery.

Undesirable Effects – Pain, swelling, heat and redness may occur sporadically at the injection site. Such symptoms are transient and usually disappear spontaneously within a few days (usually 1-4). If they should occur, rest the affected joint and apply ice locally.
Isolated cases of an anaphylactic-like reaction have been reported. There were only two cases in approximately 950,000 treated patients (approximately 4,750,000 injections) in post-marketing experience and they had favourable outcomes. No case of anaphylactic-like reactions have been reported during clinical trials.
There is the potential for rare allergic reactions, both local and systemic, to occur. The incidence of this (3 out of 5,376 patients treated with Hyalgan® during clinical trials and 3 out of 950,000 patients treated during post-marketing experience), could be attributable to avian proteins, which although present in minimal amounts in Hyalgan® , may induce reactivity in patients with a history of avian allergy.
In a 495-patient US multicentre placebo- and naproxen- controlled clinical study, the following adverse events occurred with a frequency greater than 5% in the Hyalgan® group (versus placebo); headache 18% (17%), rash 7% (9%), ecchymosis 7% (6%) and pruritus 7% (4%). As these events occurred with equal frequency in the placebo group, there is no proven causality in respect of Hyalgan®.

Overdose – Overdose is unlikely given the route of administration and the single use pack of the drug. No case of overdosage has been reported to date.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties - Hyalgan® is a sterile, non-pyrogenic, viscous, aqueous buffered solution of a defined high molecular weight fraction of highly purified hyaluronic acid sodium salt (Hyalectin®). Hyaluronic acid is an important component of the body's extracellular matrix and is present in a particularly high concentration in cartilage and synovial fluid. Endogenous hyaluronic acid provides viscosity and elasticity to synovial fluid, which is fundamental for its lubricating and shock absorbing properties, and it is essential for the correct structure of proteoglycans in articular cartilage. In osteoarthritis there is an insufficient amount of, and a change in the quality of, hyaluronic acid in synovial fluid and cartilage. The intra-articular administration of hyaluronic acid into arthritic joints with degenerating cartilage surfaces and pathologically altered synovial fluid improved joint functions.
The observed beneficial effects of exogenous hyaluronic acid may be related to its interactions with various components of the synovial cavity (synoviocytes and chondrocytes).
In controlled clinical studies, treatment cycles with Hyalgan® have been shown to ameliorate the symptoms of osteoarthritis for up to 6 months following the end of treatment.

Pharmacokinetic Properties – Hyaluronic acid sodium salt (Hyalectin®) administered intra-articularly is eliminated from the synovial fluid within 2 to 3 days. Pharmacokinetic studies have shown that it is quickly distributed to the synovial membrane. The highest concentrations of labelled hyaluronic acid have been detected in the synovial fluid and the articular capsule, followed by, in decreasing order, the synovial membrane, the ligaments and the adjacent muscle.
Hyaluronic acid in synovial fluid has been shown to be not significantly metabolised. Animal studies have shown that some degradation occurs in the tissue surrounding the joints, but the major site for metabolisation is the liver and excretion is mainly through the kidneys.

Preclinical Safety Data - Hyalectin® (hyaluronic acid sodium salt) was tested in a standard range of toxicological tests, including mutagenicity and reproductive toxicity studies, and produced negative results throughout.

PHARMACEUTICAL PARTICULARS

List of Excipients – Sodium chloride, disodium hydrogen phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate, water for injections.

Incompatibilities – There are currently insufficient data to support the compatibility of Hyalgan® with other drugs administered intra-articularly. Therefore the mixing or simultaneous administration with other intra-articular drugs is not recommended.

Shelf Life - Hyalgan® vials and prefilled syringes have a shelf life of 36 months when in their original package. Hyalgan® should not be used after the expiry date printed on the package.

Special Precautions for Storage – Do not use Hyalgan® if package is opened or damaged. Store in original packaging (protected from light) below 25°C. Do not freeze.

Nature and Contents of Container – Colourless, Type I borosilicate glass vials with rubber stoppers and aluminium seals containing 2 ml of Hyalgan® solution, supplied in packs of 1 and 5 vials.
Sterile, colourless, Type I borosilicate glass syringes with rubber stoppers on which polypropylene plunger rods are tightened up, containing 2ml of Hyalgan® solution, supplied in packs of 1 and 5 prefilled syringes.

Instruction for Use/Handling – Hyalgan® is for intra-articular injection and is supplied as a single-use, ready to use, sterile solution in a 2ml vial or in a 2ml prefilled syringe, and must not be diluted. The contents of the vial and syringe are sterile and must be used immediately once the container has been opened.
Intra-articular injection of Hyalgan® should be made using precise, anatomical localisation into the joint cavity of the knee to be treated. The injection site in the knee is determined by that location which is easier to reach. Usually a lateral approach can be followed, but in some cases a medial approach is preferable. Strict aseptic precautions should be observed during the administration. The solution in the vial requires a suitable sterile disposable syringe and needle while the solution in the prefilled syringe is ready for use and requires only a sterile disposable needle. To ensure sterility the injection site must be carefully cleansed with antiseptic. Care should be taken to expel any trapped air bubbles from the syringe containing Hyalgan® prior to administration.
Joint effusion, if present, should be aspirated by arthrocentesis prior to injection of Hyalgan®. The arthrocentesis should be made using a 20 gauge needle and the joint should be aspirated to almost dryness, but not to a degree that would compromise the accuracy of the subsequent Hyalgan® injection. An appropriate examination of the joint fluid present should be carried out to exclude bacterial infection, prior to injection.
The intra-articular injection of Hyalgan® can be given using the same needle as used for the arthrocentesis by simply detaching the aspirating syringe and attaching the syringe containing Hyalgan®. To make sure the needle is correctly positioned, some synovial fluid should be aspirated prior to the slow injection of Hyalgan®. If the patient experiences pain during injection, the procedure may need to be stopped.
For the first 48 hours after the injection, the patient should be advised to rest the treated knee, with as little exercise as possible, avoiding any strenuous or prolonged activity. Subsequently, they may gradually return to their normal level of activity.
Discard any unused Hyalgan®.

Manufactured by:
Fidia Farmaceutici S.p.A., Abano Terme, Italy.
Distributed by :
TRB Chemedica International S.A., 12 rue Michel-Servet, P.O. Box 352 – 1211 GENEVA 12, Switzerland.