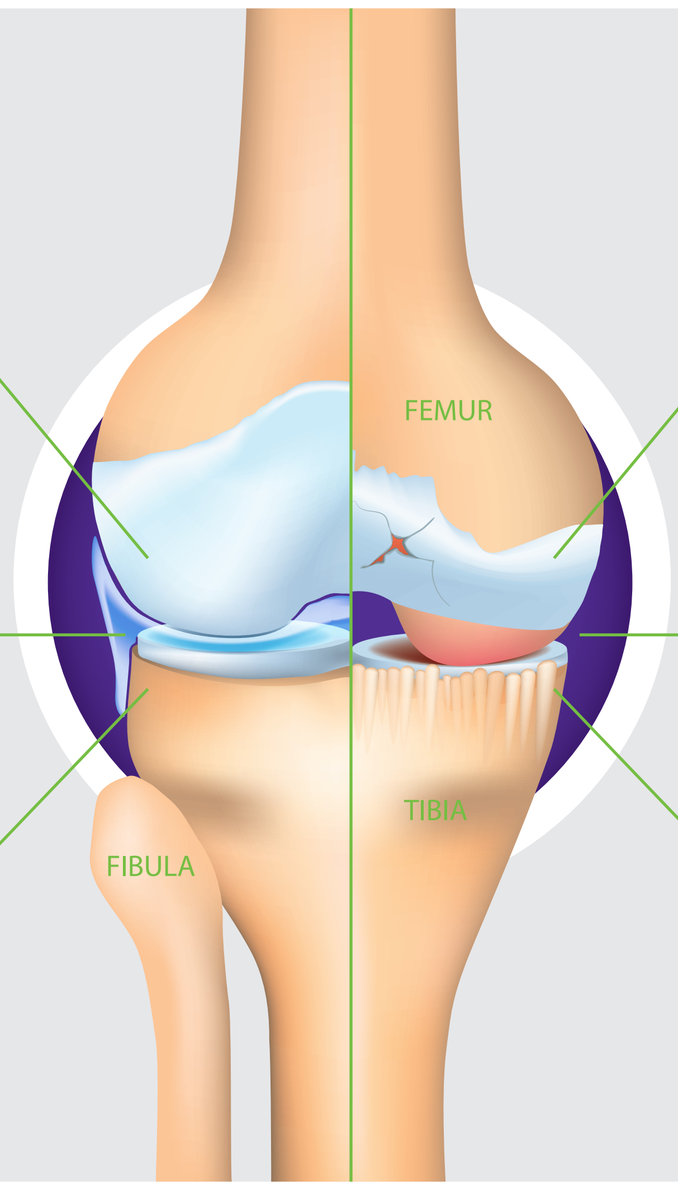
orthogenRx®
multi-regimen hyaluronic acids

GenVisc®850
5 injection hyaluronic acid regimen

Inside Osteoarthritis (OA) of the Knee

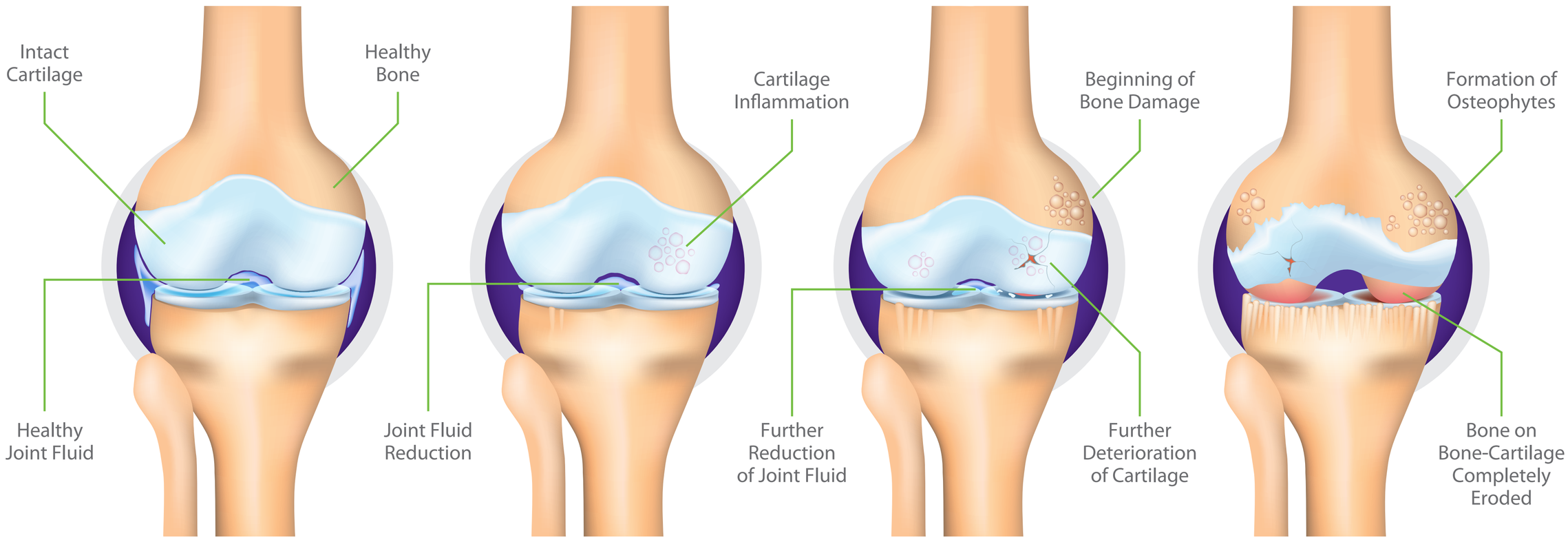
NORMAL KNEE

OA KNEE



TREATMENT WITH GENVISC 850®

When simple pain killers and conservative management (such as weight loss and exercise) no longer work, it may be time for a new approach. GenVisc 850 offers safe, effective treatment of the pain associated with knee osteoarthritis.



HEALTHY KNEE | MILD OA | MODERATE OA | SEVERE OA

CAUTION: Federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

INDICATIONS AND USAGE: GenVisc 850 is indicated for the treatment of pain in osteoarthritis (DA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen.

CONTRAINDICATIONS: Do not administer to patients with known hypersensitivity (allergy) to sodium hyaluronate preparations. Do not inject this product in the knees of patients with infections or skin diseases in the area of the injection site.

WARNINGS: Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

PRECAUTIONS: Remove joint effusion, if present, before injecting GenVisc 850. Do not use GenVisc 850 if the package is opened or damaged. Store in the original packaging (protected from light) below 86°F (30°C). DO NOT FREEZE. Do not use after expiration date indicated on package. The shelf life of GenVisc 850 is 36 months. The effectiveness of a single treatment cycle of less than 3 injections has not been established. The effectiveness of repeat treatment cycles of GenVisc 850 has not been established. Strict aseptic administration technique must be followed to avoid infections in the injection site. The safety and effectiveness of the use of GenVisc 850 in joints other than the knee have not been established. The safety and effectiveness of the use of GenVisc 850 concomitantly with other intra-articular injectable products have not been established.

INFORMATION FOR PATIENTS: Transient pain and/or swelling of the injected joint may occur after intra articular injection of GenVisc 850. As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within the 48 hours that follow the intra-articular injection. **Use in Specific Populations Pregnancy**: The safety and effectiveness of GenVisc 850 have not been established in pregnant women. **Nursing Mothers**: It is not known if GenVisc 850 is excreted in human milk. The safety and effectiveness of GenVisc 850 have not been established in lactating women. **Pediatrics**: The safety and effectiveness of GenVisc 850 have not been demonstrated in children (21 years of age or younger).

ADVERSE EVENTS: The primary evidence of safety is provided by the comparison of GenVisc 850 to Phosphate Buffered Saline (PBS) in the AMELIA (Navarro, Spain) studystudy, four cycles of 5 injections of GenVisc 850 or PBS were administered with an interval of 6 months for the first three cycles and 1 year for the fourth cycle. Patients were followed for 1 year after the last injection. The population of patients evaluated for the safety of GenVisc 850 included 306 subjects (153 GenVisc 850, 153 PBS). In each treatment group, 127 subjects experienced at least one adverse event during the study and 22 patients (11 in each treatment group) experienced at least one adverse event that was reported as possibly, probably or certainly related to the device, Table 1. None of the related adverse events were assessed as severe. For the first cycle of 5 injections in the GenVisc 850 treatment group, the 15 adverse events reported as related were pain at the injection site (6), allergic reaction (3), arthralgia (2), bleeding at the injection site (2), bleeding (1) and heaviness (1). In the first cycle of 5 injections for the PBS treatment group, the 14 adverse events reported as related were bleeding at the injection site (6), allergic reaction (3), pain at the injection site (2), arthralgia (2), and arthritis (1).

CLINICAL STUDIES: The results of the Yong Ping study and the Bayesian longitudinal analysis summarized below confirm that the clinical performance of GenVisc 850 was superior to a saline placebo control and similar to that of Supartz/Supartz FX. The Yong Ping study was a randomized controlled, multicenter clinical trial that demonstrated non-inferiority of GenVisc 850 to Supartz/-Supartz FX through 6 weeks. The Bayesian longitudinal analysis included data from four randomized controlled trials, two of which included comparisons of GenVisc 850 to saline and two of which included comparisons of Supartz/Supartz FX to saline. The results of this Bayesian longitudinal analysis demonstrated the superiority of GenVisc 850 to a saline placebo control.

DETAILED DEVICE DESCRIPTION: Each 3mL prefilled syringe of GenVisc 850 contains: Sodium Hyaluronate 25.0mg, Sodium Chloride 21.3mg, Disodium Phosphate Dodecahydrate 1.5mg, Sodium Hydroxide q.s. to adjust pH, Hydrochloric acid q.s. to adjust pH, Water for Injection q.s. 2.5mL.

HOW SUPPLIED: GenVisc 850 is supplied as a sterile, non-pyrogenic solution in 3mL pre-filled syringe.

DIRECTIONS FOR USE: GenVisc 850 is administered by intra-articular injection. A treatment cycle consists of five injections given at weekly intervals. Some patients may experience benefit with three injections given at weekly intervals. Injection of subcutaneous lidocaine or similar local anesthetic may be recommended prior to injection of GenVisc 850. **Warning:** Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

Precaution: Do not use GenVisc 850 if the package is opened or damaged. Store in the original packaging (protected from light) below 86°F (30°C). DO NOT FREEZE. Do not use after expiration date indicated on package. The shelf life is 36 months.

Precaution: Strict aseptic administration technique must be followed. **Precaution:** Remove joint effusion, if present, before injection GenVisc 850. Take care to remove the tip cap of the syringe and needle aseptically. Inject GenVisc 850 into the joint through a 21-23 gauge needle. Inject the full 2.5mL in one knee only. If treatment is bilateral, a separate syringe should be used for each knee.

Precaution: The prefilled syringe is intended for single use. The content of the syringe must be used immediately once the container has been opened. Discard any unused GenVisc 850.

MANUFACTURED BY: Meiji Pharma Spain, S.A. Avda. De Madrid 94, 28802 Alcalá de Henares

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