orthogenRx®
multi-regimen hyaluronic acids

TriVisc®
3 injection hyaluronic acid regimen

Inside Osteoarthritis (OA) of the Knee

NORMAL KNEE

NORMAL CARTILAGE
Provides a smooth surface so bones can move easily across each other

HIGH CONCENTRATION OF HYALURONAN IN SYNOVIAL FLUID
Cushions and lubricates the joint

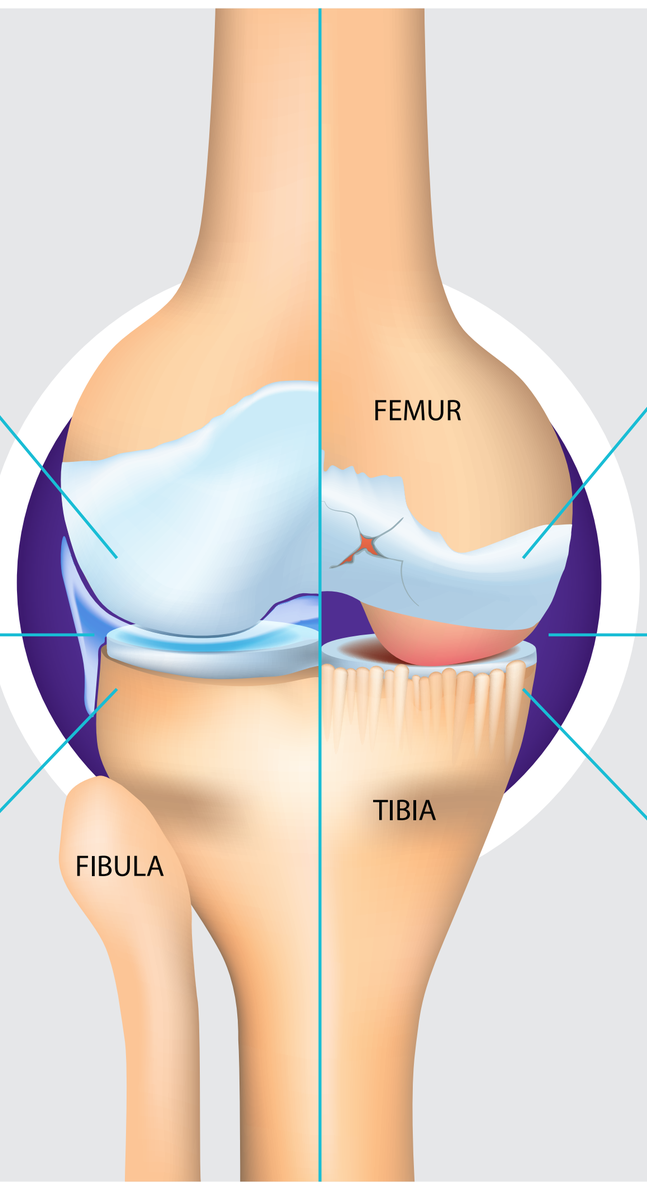
NORMAL BONE

OA KNEE

ERODED CARTILAGE
If completely worn away, bones may scrape painfully against each other

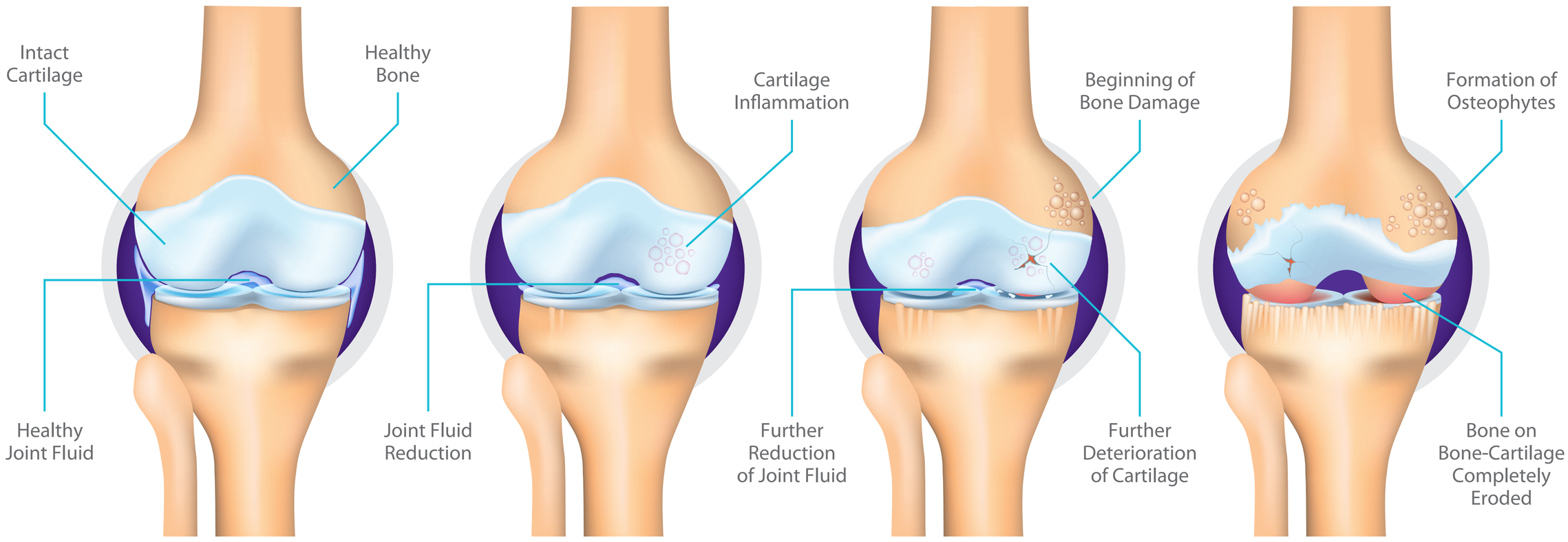
LOW CONCENTRATION OF HYALURONAN IN SYNOVIAL FLUID
Less able to protect the joint

OSTEOPHYTES
(Bone spurs)



TREATMENT WITH TriVisc®

When simple pain killers and conservative management (such as weight loss and exercise) no longer work, it may be time for a new approach. TriVisc 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: TriVisc 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 TriVisc. Do not use TriVisc 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 TriVisc is 42 months. The effectiveness of a single treatment cycle of less than 3 injections has not been established. Transient increases in inflammation following any intra-articular hyaluronan injection have been reported in some patients with inflammatory joint conditions. The effectiveness of repeat treatment cycles of TriVisc 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 TriVisc in joints other than the knee have not been established. The safety and effectiveness of the use of TriVisc 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 TriVisc. 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 TriVisc have not been established in pregnant women.

Nursing Mothers: It is not known if TriVisc is excreted in human milk. The safety and effectiveness of TriVisc have not been established in lactating women.

Pediatrics: The safety and effectiveness of TriVisc have not been demonstrated in children (21 years of age or younger).

ADVERSE EVENTS: The primary clinical performance testing to assess the safety of TriVisc were two clinical studies, the AMELIA1 and Yong Ping2 studies, used to establish reasonable assurance of the safety of established in the approval of another intra-articular hyaluronan (**if**A) under P1400053 (P140005 **if**A). TriVisc is of identical chemical formulation to this **if**A and differs only in that less of the device is injected (3 weekly injections of 2.5 ml for TriVisc instead of 5 weekly injections). Thus, the clinical studies used to provide evidence of the reasonable assurance of the safety of the **if**A under P140005 are directly applicable to TriVisc as well.The primary evidence of the safety under P140005 was provided by the comparison of the P140005 **if**A to PBS in the AMELIA study. **I**n this study, four cycles of 5 injections of the P140005 **if**A 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 the P140005 **if**A included 306 subjects (153 **if**A, 153 PBS). **I**n 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 (4). **N**one of the related adverse events were assessed as severe. **I**n the **if**A treatment group, the 15 adverse events reported as related adverse events were pain at the injection site (6), allergic reaction (3), arthralgia (2), bleeding at the injection site (2), bleeding (1), and heaviness (1). **I**n 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 primary clinical performance testing to demonstrate effectiveness of TriVisc, as per the application of **S**ection 216 of the Food and Drug Administration Modernization Act (1997), is obtained from the Summary of Safety and Effectiveness Data (SSED) for a viscosupplement approved under Premarket Application (PMA) supplement P980044/S27.
A clinical study was performed to establish a reasonable assurance of safety and effectiveness of three weekly intra-articular injections of the viscosupplement approved under P980044/S27 for the treatment of pain due to **O**A of the knee in patients who had failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics. The study was performed in the **U**nited States (**US**) under **I**DE (**I**nvestigational Exempt Device) G130271. Data from this clinical study were the basis for the approval decision of this viscosupplement under P980044/S27

DETAILED DEVICE DESCRIPTION: Each 3mL prefilled syringe of TrisVisc 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: TriVisc is supplied as a sterile, non-pyrogenic solution in 3mL pre-filled syringe.

DIRECTIONS FOR USE: TriVisc 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 TriVisc. **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 TriVisc 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 42 months.

Precaution: Strict aseptic administration technique must be followed.

Precaution: Remove joint effusion, if present, before injection TriVisc. Take care to remove the tip cap of the syringe and needle aseptically. Inject TriVisc 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 TriVisc.

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