SYNVISC ONE
HYLAN G-F 20

6 ml

genzyme EC REP

DESCRIPTION
Hylan G-F 20 is available as
• **Synvisc®**, 2 ml presentation
• **Synvisc-One®**, 6 ml presentation.
Hylan G-F 20 is a sterile, nonpyrogenic, elastoviscous fluid containing hylans. Hylans are derivatives of hyaluronan (sodium salt of hyaluronic acid) and consist of repeating disaccharide units of N-acetylglucosamine and sodium glucuronate. Hylan A has an average molecular weight of approximately 6,000,000 daltons and hylan B is a hydrated gel. Hylan G-F 20 contains hylan A and hylan B (8.0 mg ± 2.0 mg per ml) in buffered physiological sodium chloride solution (pH 7.2 ± 0.3).

CHARACTERISTICS
Hylan G-F 20 is biologically similar to hyaluronan. Hyaluronan is a component of synovial fluid which is responsible for its elastoviscosity. The mechanical (elastoviscous) properties of hylan G-F 20 are, however, superior to those of synovial fluid and hyaluronan solutions of comparable concentration. Hylan G-F 20 has an elasticity (storage modulus G') at 2.5 Hz of 111 ± 13 Pascals (Pa) and a viscosity (loss modulus G") of 25 ± 2 Pa. Elasticity and viscosity of knee synovial fluid of 18- to 27-year-old humans measured with comparable method at 2.5 Hz are G' = 117 ± 13 Pa and G" = 45 ± 8 Pa. Hylans are degraded in the body by the same pathway as hyaluronan, and breakdown products are nontoxic.

INDICATIONS AND USAGE
Hylan G-F 20
- is a temporary replacement and supplement for synovial fluid.
- is beneficial for patients in all stages of joint pathology.
- is most effective in patients who are actively and regularly using the affected joint.
- achieves its therapeutic effect through viscosupplementation, a process whereby the physiological and rheological states of the arthritic joint tissues are restored.

Viscosupplementation with hylan G-F 20 is a treatment to decrease pain and discomfort, allowing more extensive movement of the joint. *In vitro* studies have shown that hylan G-F 20 protects cartilage cells against certain physical and chemical damage.
Synvisc is only intended for intra-articular use by a physician to treat pain associated with osteoarthritis of the knee, hip, ankle, and shoulder.
Synvisc-One is only intended for intra-articular use by a physician to treat pain associated with osteoarthritis of the knee.

CONTRAINDICATIONS
- If venous or lymphatic stasis is present in the relevant limb, hylan G-F 20 should not be injected into the joint.
- Hylan G-F 20 should not be used in infected or severely inflamed joints or in patients having skin diseases or infections in the area of the injection site.

WARNINGS
- Do not inject intravascularly.
- Do not inject extra-articularly or into the synovial tissues and capsule. Adverse events, generally in the area of the injection, have occurred following extra-articular injection of **Synvisc**.
- Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because hyaluronan can precipitate in their presence.

PRECAUTIONS
- Hylan G-F 20 should not be used if there is a large intra-articular effusion prior to the injection.
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities following the intra-articular injection, and resume full activities within a few days.
- Hylan G-F 20 has not been tested in pregnant women or children under 18 years of age.
- Hylan G-F 20 contains small amounts of avian protein and should not be used in patients with related hypersensitivities.

ADVERSE EVENTS
- Adverse events involving the injected joint: transient pain and/or, swelling and/or effusion in the injected joint may occur after intra-articular injections of Hylan G-F 20. Cases of acute inflammation, characterized by joint pain, swelling, effusion and sometimes joint warmth and/or stiffness, have been reported following an intra-articular injection of **Synvisc or Synvisc-One**. Analysis of synovial fluid reveals aseptic fluid with no crystals. This reaction often responds within a few days to treatment with Non Steroidal Anti Inflammatory Drugs (NSAIDS), intra-articular steroids and/or arthrocentesis. Clinical benefit from the treatment may still be apparent after such reactions.
- Intra-articular infections did not occur in any of the clinical trials of **Synvisc/ Synvisc-One** and have been reported only rarely during clinical use of **Synvisc**.
- Hypersensitivity reactions including anaphylactic reaction, anaphylactoid reaction, anaphylactic shock and angioedema have also been reported.
- The post marketing experience has identified the following systemic events to occur rarely with **Synvisc** administration: rash, hives, itching, fever, nausea, headache, dizziness, chills, muscle cramps, paresthesia, peripheral oedema, malaise, respiratory difficulties, flushing and facial swelling.
- In the controlled clinical trials with **Synvisc**, there were no statistically significant differences in the number or types of systemic adverse events between the group of patients that received **Synvisc** and the group that received control treatments.
- In the controlled clinical trial with **Synvisc-One**, the frequency and types of adverse events were similar between the group of patients that received **Synvisc-One** and the group that received placebo.

DOSAGE AND ADMINISTRATION
- Do not use hylan G-F 20 if package is opened or damaged.
- The contents of the syringe must be used immediately after its packaging is opened.
- Remove synovial fluid or effusion before injecting hylan G-F 20.
- Inject at room temperature.
- To remove the syringe from the blister (or tray), take hold of it by the body, without touching the plunger rod.
- Administer using strict aseptic procedures, taking particular care when removing the tip cap.
- Twist the grey tip cap before pulling it off, as this will minimise product leakage
- Use an appropriate size of needle:
  - **Synvisc** – 18 to 22 gauge

  Depending on the joint to be treated use the appropriate length of needle.
  - **Synvisc-One** – 18 to 20 gauge
- To ensure a tight seal and prevent leakage during administration secure the needle tightly while firmly holding the Luer hub.
- Do not tighten or apply excessive leverage when attaching the needle or removing the needle guard, as this may break the tip of the syringe.
- Inject into the synovial space only, using if necessary, appropriate guidance such as fluoroscopy especially in joints such as the hip and shoulder.
- The syringe contents are for single use only. The recommended dosage guidelines state to inject the full volume (2 mL for Synvisc and 6 ml for Synvisc-One) of the syringe. Discard any unused Synvisc/Synvisc-One.
- Do not re-use the syringe and/or needle. Re-use of syringes, needles and/or product from a used syringe may result in loss of sterility, product contamination and/or incomplete treatment.
- When using fluoroscopic guidance, ionic or non-ionic contrast agent may be utilized. No more than 1 ml of contrast agent should be used per 2 ml of hylan G-F 20.
- Do not resterilise hylan G-F 20.

DOSAGE GUIDELINES
The dosage regimen for hylan G-F 20 is dependent on the joint being treated.

Osteoarthritis of the knee:
Synvisc
The recommended treatment regimen is three 2 mL injections in the knee, with an interval of 1 week between each injection. To achieve maximum effect, it is essential to administer all three injections. The maximum recommended dosage is six injections within six months, with a minimum of four weeks between treatment regimens.
Synvisc-One
The recommended treatment regimen is one 6 mL injection in the knee. The injection may be repeated 6 months after the first injection, if justified by the patient's symptoms.

Osteoarthritis of the hip / ankle / shoulder:
Synvisc
The recommended initial treatment regimen is a single 2 mL injection. If however, adequate symptomatic relief is not achieved after this injection, it is recommended to administer a second 2 mL injection. Clinical data have demonstrated that patients benefit from this second injection when administered between 1 and 3 months after the first injection.

DURATION OF EFFECT
Hylan G-F 20 treatment affects only the injected joint; it does not produce a general systemic effect.
Synvisc
Generally the duration of effect for those patients who respond to treatment has been reported up to 26 weeks, although shorter and longer periods have also been observed. However, prospective clinical data in knee osteoarthritis patients have shown benefit of treatment up to 52 weeks, following a single course of three **Synvisc** injections.
Synvisc-One
Prospective clinical trial data in knee osteoarthritis patients have shown a reduction in pain for up to 52 weeks following a single **Synvisc-One** injection as well as related improvements in stiffness and function.

Clinical data from a double-blind, randomized, controlled trial in knee OA patients have shown a statistically significant and clinically meaningful reduction in pain compared to placebo. A total of 253 patients were treated (124 received **Synvisc-One** and 129 received placebo). Over 26 weeks, patients receiving **Synvisc-One** demonstrated a mean percent change in pain from baseline of 36% while patients in the placebo group had a mean percent change in pain from baseline of 29%.

Additional prospective clinical data from two multi-center, open-label studies in knee OA patients have shown statistically significant improvements in pain relief compared to baseline for up to 52 weeks following a single administration of **Synvisc-One**.

In the first study, 394 patients that received **Synvisc–One** demonstrated a statistically significant change in the WOMAC A1 - pain on walking subscore (-28±19.89 mm on 100 mm VAS) from baseline over Week 26. In addition, statistically significant changes from baseline in WOMAC A1, and WOMAC A, B and C scores were observed over all six observation time periods between week 1 and week 52, demonstrating improvement in pain on walking and pain (WOMAC A1 -32.7±19.95 mm; WOMAC A -29.18±19.158 mm), stiffness (WOMAC B -25.77±22.047 mm), and function (WOMAC C -25.72±19.449 mm) over 52 weeks.

In the second study, 571 patients that received **Synvisc-One**, demonstrated statistically significant improvement in pain over 26 weeks as measured by Verbal Pain Questionnaire (VPQ). The mean pain assessment improved from 3.20 at Baseline to 2.24 at 26 week visit, with 64.6% of patients achieving pain relief. Secondary endpoints demonstrated statistically significant improvement in VPQ scores at all observation time points from 1 week to 52 weeks, with mean VPQ scores declining from 3.20 at baseline to 2.26 at 52 week visit and 61.5% of patients achieving pain relief.

CONTENT PER ml (hylan G-F 20)
Each 1 ml contains: hylan 8.0 mg, sodium chloride 8.5 mg, disodium hydrogen phosphate 0.16 mg, sodium dihydrogen phosphate hydrate 0.04 mg, water for injection q.s.

HOW SUPPLIED
The contents of the each syringe are sterile and nonpyrogenic. Store between +2°C and +30°C. Do not freeze.
Synvisc is supplied in a 2.25 ml glass syringe containing 2 ml hylan G-F 20.
Synvisc-One is supplied in a 10 ml glass syringe containing 6 ml hylan G-F 20.