SYNVISC® (HYLAN G-F 20) 2 mL AND
SYNVISC-ONE® * (HYLAN G-F 20) 6 mL

INSTRUCTIONS FOR USE

DESCRIPTION

Synvisc® / Synvisc-One® (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 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

Synvisc® is biologically similar to hyaluronan. Hyaluronan is a component of synovial fluid which is responsible for its elastoviscosity. The mechanical (elastoviscous) properties of Synvisc are, however, superior to those of synovial fluid and hyaluronan solutions of comparable concentration.

Synvisc 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

- Synvisc is a temporary replacement and supplement for synovial fluid.
- Synvisc is beneficial for patients in all stages of knee pathology.
- Synvisc is most effective in patients who are actively and regularly using the affected knee.
- Synvisc is only intended for intra-articular use by a physician to treat pain associated with osteoarthritis of the knee.

Synvisc achieves its therapeutic effect through viscosupplementation, a process whereby the physiological and rheological states of the arthritic knee tissues are restored. Viscosupplementation with Synvisc is a treatment to decrease pain and discomfort, allowing more extensive movement of the knee. In vitro studies have shown that Synvisc protects cartilage cells against certain physical and chemical damage.
CONTRAINDICATIONS

Synvisc should not be used in patients with known hypersensitivity (allergy) to hyaluronan (sodium hyaluronate) preparations.

If venous or lymphatic stasis is present in the relevant limb, Synvisc should not be injected into the knee.

Synvisc should not be used in infected or severely inflamed knees or in patients having skin diseases or infections in the area of the injection site.

WARNINGS

• Do not inject intravascularly. Intravascular injections may cause systemic adverse events.

• 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

• Synvisc 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.

• Synvisc has not been tested in pregnant women or children under 18 years of age.

• Synvisc contains small amounts of avian protein and should not be used in patients with related hypersensitivities.

ADVERSE EVENTS

Adverse events involving the injected knee: transient pain and/or, swelling and/or effusion in the injected knee may occur after intra-articular injections of Synvisc.

The post marketing experience has identified the following systemic events to occur rarely with Synvisc administration: fever, nausea, headache, dizziness, chills, muscle cramps, paresthesia, peripheral oedema and malaise. Hypersensitivity reactions including anaphylactic reaction, anaphylactoid reaction, anaphylactic shock and angioedema have been reported. In the controlled clinical trials, 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.

Post marketing cases of acute inflammation, characterized by joint pain, swelling, effusion and sometimes joint warmth and/or stiffness have been reported following intra-articular injection; it is important to remove and to analyse the fluid to rule out infection or crystalline arthropathies. 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 and have been reported only rarely during clinical use of Synvisc.

Injection site reactions have been reported post marketing following an intra-articular injection of Synvisc such as pain, bruising, swelling, bleeding, itching, redness, rash and warmth at the injection site.

**DOSAGE AND ADMINISTRATION**

- Do not use Synvisc 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 each Synvisc injection.
- 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 (e.g., 18 to 22 gauge) and length of needle.
- 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.
- The syringe contents are for single use only. The recommended dosage guidelines state to inject the full volume of the syringe. Discard any unused Synvisc.
- 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.
- Do not re-sterilise Synvisc.

**DOSAGE GUIDELINES**

*Synvisc*: The recommended treatment regimen for Synvisc 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 for Synvisc-One is one 6 mL injection in the knee.

The injection may be repeated 6 months after first injection, if justified by the patient’s symptoms.

**DURATION OF EFFECT**

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 or a single Synvisc-One injection.

Synvisc treatment affects only the injected joint; it does not produce a general systemic effect.

1.1 **CONTENT PER ML**

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.

1.2 **HOW SUPPLIED**

**Synvisc** is supplied in a 2.25 mL glass syringe containing 2 mL Synvisc.

**Synvisc-One** is supplied in a 10 mL glass syringe containing 6 mL hylan G-F 20.

The contents of the syringe are sterile and nonpyrogenic.

Store between +2°C and +30°C.

Do not freeze.

*References to “SYNVISC” refer to both SYNVISC and SYNVISC-ONE*
1.2.1 REFERENCES


