**Instructions For Use**

**Synvisc® (hylan G-F 20)**

## DESCRIPTION

Synvisc® (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 Nacetylglucosamine and sodium glucuronate. Hylan A has an average molecular weight of approximately 6,000,000 and hylan B is a hydrated gel. Synvisc 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 viscoelasticity. 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 non-toxic.

## INDICATIONS AND USAGE

- Synvisc is a temporary replacement and supplement for synovial fluid.
- Synvisc is beneficial for patients in all stages of joint pathology.
- Synvisc is most effective in patients who are actively and regularly using the affected joint.
- 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 achieves its therapeutic effect through viscosupplementation, a process whereby the physiological and rheological states of the arthritic joint tissues are restored. Viscosupplementation with Synvisc is a treatment to decrease pain and discomfort, allowing more extensive movement of the joint. *In vitro* studies have shown that Synvisc protects cartilage cells against certain physical and chemical damage.

## CONTRAINDICATIONS

- If venous or lymphatic stasis is present in the relevant limb, Synvisc should not be injected into the joint.
- Synvisc 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.
- Some cases of skin necrosis have been reported after intra-articular use of hyaluronic acid. Patients should be instructed to contact their treating physician if signs of skin disorder (such as change of color or open sores) appear.

## PRECAUTIONS

- Synvisc should not be used if there is a large intraarticular 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 joint: transient pain and/or, transient swelling and/or effusion in the injected joint may occur after intra-articular injections of Synvisc. 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. 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 and have been reported only rarely during clinical use of Synvisc.
- Hypersensitivity reactions including anaphylactic reaction, anaphylactoid reaction, anaphylactic shock and angioedema have 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, 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.

## DOSAGE AND ADMINISTRATION

- Remove synovial fluid or effusion before each Synvisc injection.
- Do not use Synvisc if package is opened or damaged.
- 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 minimize product leakage.
- Use an appropriate size of needle (e.g., 18 to 22 gauge) and length of needle, depending on joint to be treated.
- 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.
- Do not resterilize Synvisc.
- 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.
- When using fluoroscopic guidance, ionic or nonionic contrast agent may be utilized. No more than 1 ml of contrast agent should be used for 2 ml of Synvisc.

**DOSAGE GUIDELINES**

The dosage regimen for Synvisc is dependent on the joint being treated.

*Osteoarthritis of the knee:*
The recommended treatment regimen for Synvisc is three injections in the knee, one week apart. 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.

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

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

*Osteoarthritis of the shoulder:*
The recommended initial treatment regimen is a single injection. If however, adequate symptomatic relief is not achieved after this injection, it is recommended to administer a second

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:*
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 OA patients have shown benefit of treatment up to 52 weeks, following a single course of three Synvisc injections. Synvisc treatment affects only the injected joint; it does not produce a general systemic effect.

## 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.

## HOW SUPPLIED

Synvisc is supplied in a 2.25 ml glass syringe containing 2 ml Synvisc. The contents of the syringe are sterile and nonpyrogenic. Store between +2°C and +30°C. Do not freeze.

**IF PACKAGE IS OPENED OR DAMAGED, DO NOT USE.**

**For orders, product information, product and medical complaints call 1-800-265-7927.**

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sanofi-aventis Canada Inc.
1755 Steeles Avenue West, Toronto, ON M2R 3T4

☎1 800 265-7927



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