

**Intra-Articular Administration of Hyaluronic Acid or Hylan G-F 20 for Osteoarthritis of the Knee
Criteria for Use
VHA Pharmacy Benefits Management Services, VISN Pharmacist Executives and the Medical Advisory
Panel**

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient. Individual cases that are outside the recommendations should be adjudicated at the local facility according to the policy and procedures of its P&T Committee and Pharmacy Services.

The intra-articular (IA) administration of hyaluronic acid (HA) or hylan (cross-linked hyaluronan chains) is referred to as viscosupplementation. These products are categorized as “Biologic Devices” by the FDA and can be considered for use in patients with OA of the knee who meet the following criteria. *It is strongly recommended that the use of these agents be limited to specialists in Orthopedics, Rheumatology and Physical Medicine and Rehabilitation.* (For details of reviews conducted by the PBM, refer to the PBM websites: <https://vaww.cmopnational.va.gov/cmop/PBM/default.aspx> or www.pbm.va.gov)

EXCLUSION CRITERIA (If one is selected, patient is not eligible)

- Known hypersensitivity or allergy to hyaluronate preparations^a
- Knee joint infection, skin disease or infection in the area of the injection site

INCLUSION CRITERIA (All must be selected for patient to be eligible)

- Documented symptomatic (pain/stiffness) OA of the knee which interferes with functional activities (e.g. ambulation, prolonged standing, etc.) and/or is associated with significant pain.
- Adequate trial (e.g. 2 to 3 months) of non-pharmacologic measures, as appropriate, (e.g. cane/crutches, bracing/orthotics, weight loss, physical therapy/exercise) has not resulted in adequate improvement in pain/function
- Therapeutic trial of at least 3 analgesics (*e.g. acetaminophen, topical capsaicin or topical NSAIDs, oral NSAIDs and other oral analgesics [e.g. tramadol] or narcotic analgesics [in patients with severe pain]*) has not resulted in adequate improvement in pain/function; or patient is unable to tolerate or is not a candidate for NSAIDs or other oral analgesics.
- Intra-articular corticosteroids have not resulted in adequate improvement in pain/function or there are compelling reasons to avoid IA corticosteroids. **Note: VA does not support use of compounded corticosteroids purchased from compounding pharmacies. VA providers should only use commercially available products.**
- Patient and/or provider have elected to continue conservative (nonsurgical) treatment for OA.

PRECAUTIONS

- There is some evidence to suggest that patients with more advanced stages of OA and near complete loss of joint space may be less likely to benefit from this therapy.
- All HA or Hylan products are for intra-articular use only.
- The origin of hyaluronic acid for Gel-One, Hyalgan, Supartz, Synvisc and Synvisc-One is from avian sources (rooster combs). Labeling for Gel-One, Hyalgan, Supartz, Synvisc and Synvisc-One suggest administering with caution in those patients with a known allergy to avian proteins, feathers or eggs. Euflexxa and Orthovisc are not derived from avian sources and can be used in patients with an allergy to avian proteins. Gel-One should be used with caution in patients with an allergy to cinnamon.
- The safety/efficacy of concomitant administration of HA or hylan with other IA agents has not been established.
- The safety/efficacy of administering these agents in pregnant women has not been established.

DOSAGE AND ADMINISTRATION

- Intra-articular administration of HA or hylan should be performed by a physician/provider who is technically proficient at administering drugs via the IA route.
- Strict aseptic administration technique must be used.
- Disinfectants containing quaternary ammonium salts (e.g. benzalkonium chloride or benzethonium chloride) should not be used for skin preparation as hyaluronic acid can precipitate under such conditions. May use isopropyl alcohol or povidone-iodine solutions to thoroughly clean site.

Viscosupplementation
Hyaluronan and Hylan Products

- Remove joint effusion, if present, before injecting HA or hylan.
- Subcutaneous lidocaine or other local anesthetic may be injected prior to IA administration of HA or hylan.

	Euflexxa	Gel-One	Hyalgan	Orthovisc	Supartz FX	Synvisc	Synvisc-One
# Inject/Course	3	1	3 or 5	3	3 or 5	3	1
Response	3 months*	13 weeks	3 inj-60 days* 5 inj-6 months	6 months	3 inj-90 days* 5 inj-6 months	6 months	6 months

*Duration of study follow-up

RECOMMENDED MONITORING/PATIENT INFORMATION

- Transient pain and/or swelling of the injected joint have been reported after intra-articular administration of these agents.
- As with any invasive procedure, it is recommended that patients avoid strenuous activity (e.g. more than 1 hour) or prolonged weight-bearing activities (e.g. jogging or tennis) within 48 hours of procedure.
- Rare, anaphylactoid/allergic reactions have been reported with Hyalgan
- Pseudosepsis or severe acute inflammatory reactions (SAIR) has been reported with Synvisc. Typically with the second or third injection in a course or with subsequent courses.

REPEAT COURSES

- There is evidence to support administering repeat courses of Hyalgan or Synvisc in those patients having experienced a beneficial response with their first course. However, the risk for adverse events does appear to increase in those given repeat courses with Synvisc but not Hyalgan. There is limited safety data for repeat Synvisc-One® courses. The efficacy/safety of giving repeat courses using the other available products has not been established.
- Although the efficacy of repeat treatment courses with Supartz FX has not been established, updated labeling for Supartz FX indicates that no evidence exists for an increase in the frequency or severity of adverse events with repeat courses of treatment versus a single course of treatment with Supartz FX.
- Repeat courses should not be administered within 6 months of the last injection.