

## Hyaluronic Acid Derivatives Clinical Resource

Drug Name	Drug Status
Durolane (sodium hyaluronate injection)	Medical Benefit – Restricted
Euflexxa (sodium hyaluronate injection)	Medical Benefit
Gel-One (sodium hyaluronate injection)	Medical Benefit – Restricted
Gelsyn-3 (sodium hyaluronate injection)	Medical Benefit – Restricted
GenVisc 850 (sodium hyaluronate injection)	Medical Benefit – Restricted
Hyalgan (sodium hyaluronate injection)	Medical Benefit – Restricted
Hymovis (high molecular weight hyaluronan injection)	Medical Benefit – Restricted
Monovisc (high molecular weight hyaluronan injection)	Medical Benefit – Restricted
Orthovisc (high molecular weight hyaluronan injection)	Medical Benefit – Restricted
Supartz FX (sodium hyaluronate injection)	Medical Benefit – Restricted
Sodium hyaluronate 1% injection	Medical Benefit – Restricted
Synojoynt (sodium hyaluronate 1%)	Medical Benefit – Restricted
Synvisc (hylan G-F 20 sodium hyaluronate injection)	Medical Benefit
Synvisc-One (hylan G-F 20 sodium hyaluronate injection)	Medical Benefit
Triluron (sodium hyaluronate injection)	Medical Benefit – Restricted
TriVisc (sodium hyaluronate injection)	Medical Benefit – Restricted
Visco-3 (sodium hyaluronate injection)	Medical Benefit - Restricted

### Overview

Euflexxa, Synvisc, and Synvisc One are covered without prior authorization for Medicare Advantage members.

All other products (Durolane, Euflexxa, Gel-One, Gelsyn-3, GenVisc 850, Hyalgan, Hymovis, Monovisc, Orthovisc, Supartz FX, sodium hyaluronate 1%, Synojoynt, Triluron, TriVisc, Visco-3) are restricted and require step therapy (see the Part B Step Therapy criteria)

Hyaluronic acid derivatives are indicated for the treatment of pain related to knee osteoarthritis in patients who have failed to respond adequately to conservative nonpharmacologic therapy and to simple analgesics (e.g., acetaminophen). The use of intraarticular injections are to restore the normal properties (viscosity and elasticity) of the synovial fluid. Gel-One, Hyalgan, Supartz FX, Synvisc/Synvisc-One, Triluron, and Visco-3 are derived from rooster or chicken combs. The remaining products are derived from non-avian sources and may be useful for patients with allergies to eggs or poultry products. GenVisc 850 has data to support similarity to Supartz FX. All of the products given as a series of five injections (GenVisc 850, Hyalgan, and Supartz FX) have a corresponding product that is equivalent to three injections (TriVisc, Triluron, and Visco-3, respectively). Although retreatment data are limited, all of these products have data concerning efficacy and/or safety of repeat courses. In many cases, at least 6 months was required or a minimum of 6 months had elapsed prior to injection of a repeat course.

### Guidelines

Guidelines for the medical management of osteoarthritis of the hand, hip, and knee are available from the American College of Rheumatology (2019). Multiple non-pharmacological modalities are recommended for knee osteoarthritis, including exercise, self-management programs, weight loss, Tai Chi, and use of assistive devices (i.e., bracing or a cane). Pharmacologic therapy for knee osteoarthritis consists of acetaminophen, oral and topical non-steroidal anti-inflammatory drugs (NSAIDs), tramadol, intraarticular corticosteroid injections, duloxetine, and topical capsaicin. There is limited evidence establishing a benefit of hyaluronic acid intraarticular injections, which contributes to the conditional recommendation against use in knee osteoarthritis. However, when other alternatives have been exhausted or have

failed to provide satisfactory benefit, use of intraarticular hyaluronic acid injections may be viewed more favorably than offering no intervention. In the guidelines, no distinction is made between the available intraarticular hyaluronic acid products or between products with various molecular weights.

The Osteoarthritis Research Society International also has guidelines for knee osteoarthritis (2019). These guidelines note that use of intraarticular hyaluronic acid injections are conditionally recommended for patients with knee osteoarthritis. The guidelines comment on the long-term treatment effect with intraarticular hyaluronic acid injections which is associated with symptom improvement beyond 12 weeks and a more favorable safety profile than intraarticular corticosteroid injections.

## Clinical Guidance for Use

### FDA-Approved Indications

#### 1. Osteoarthritis of the Knee

##### A) Initial Therapy. (i, ii, and iii):

- i. Diagnosis of the knee to be treated is confirmed by radiologic evidence of knee osteoarthritis; AND  
Note: Examples of radiographic evidence includes x-ray, magnetic resonance imaging (MRI), computed tomography (CT) scan, ultrasound.
- ii. Patient has tried at least TWO of the following three modalities of therapy for osteoarthritis (i, ii, iii):
  - a) At least one course of physical therapy for knee osteoarthritis;
  - b) At least TWO of the following pharmacologic therapies [(1), (2), (3), (4)]
    - (1) Oral or topical nonsteroidal anti-inflammatory drug(s) [NSAID(s)];  
Note: Examples of oral NSAIDs include naproxen, ibuprofen, celecoxib. Examples of topical NSAIDs include diclofenac solution or diclofenac gel. A trial of two or more NSAIDs (oral and/or topical) counts as one pharmacologic therapy.
    - (2) Acetaminophen;
    - (3) Tramadol (Ultram<sup>®</sup>/XR, generics);
    - (4) Duloxetine (Cymbalta<sup>®</sup>, generics);
  - c) At least TWO injections of intraarticular corticosteroids to the affected knee; AND
- iii. The product is administered by or under the supervision of a physician specializing in rheumatology, orthopedic surgery, or physical medicine and rehabilitation (physiatrist).

##### B) Patient has Already Received One or More Courses of a Hyaluronic Acid Derivative in the Same Knee. (i, ii, and iii):

- i. At least 6 months have elapsed since the last injection with any hyaluronic acid derivative; AND
- ii. According to the prescriber, the patient had a response to the previous course of hyaluronic acid derivative therapy for osteoarthritis of the knee and now requires additional therapy for osteoarthritis symptoms; AND  
Note: Examples of a response include reduced joint pain, tenderness, or morning stiffness, improved mobility.
- iii. The product is administered by or under the supervision of a physician specializing in rheumatology, orthopedic surgery, or physical medicine and rehabilitation (physiatrist).

#### Dosing.

- A) **Durolane, Gel-One, Monovisc, Synvisc-One**: One injection.
- B) **Hymovisc**: Up to two injections given 1 week apart.
- C) **Euflexxa, Gelsyn-3, sodium hyaluronate 1% injection, Synjoynt, Synvisc, Triluron, TriVisc, Visco-3**: Up to three injections given 1 week apart.
- D) **Orthovisc**: up to 4 injections given 1 week apart.
- E) **GenVisc 850, Hyalgan, Supartz FX**: up to 5 injections given 1 week apart.

Note: Dose listed is for one knee. If two knees are being treated, then each knee requires a syringe or vial of product

**CONDITIONS NOT RECOMMENDED FOR USE**

Hyaluronic acid derivatives are not recommended in the following situations:

1. **Acute Ankle Sprain.** More data are needed to determine the role of intraarticular hyaluronic acid products in the treatment of acute ankle sprains.
2. **Pathologic Conditions of the Knee Other than Osteoarthritis** (e.g., chondromalacia patellae, osteochondritis dissecans, patellofemoral syndrome, post-anterior cruciate ligament [ACL] reconstruction). Intraarticular hyaluronic acid derivatives are indicated in knee osteoarthritis. Adequate, well-designed trials have not clearly established the use of these products in other conditions of the knee.

---

Created: 07/22

Effective: 9/1/2022, revised 7/1/2023

Gateway Approval: 9/1/22

P&T Approval: N/A