Medicare Part B Viscosupplements Prior Authorization Criteria

RI will target the following products Monovisc, Synvisc, Hyalgan, Gelsyn, Supartz FX, Genvisc, Trivisc, Hymovis, Triluron and will require the trial and failure of Euflexxa, Orthovisc and Durolane.

FDA APPROVED INDICATIONS AND DOSAGE[1-15,27,28]

Agent(s)	Indication(s)	Dosage*
Durolane® (sodium hyaluronate) Gel for intra-articular injection	Pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative° non-pharmacologic therapy and to simple analgesics (e.g., acetaminophen)	Inject 1 syringe per knee
Euflexxa® (1% sodium hyaluronate) Viscoelastic solution for intra-articular injection		1 syringe per week per knee; limit of 3 syringes per knee
Gel-One® (cross-linked hyaluronate) Viscoelastic gel for intra-articular injection		1 syringe per knee
GELSYN-3® (sodium hyaluronate) Solution for intra-articular injection		Inject 2mL once a week for a total of 3 injections
GenVisc® 850 (sodium hyaluronate) Viscoelastic solution for intra-articular injection		Inject 25 mg once a week for a total of five injections. Some patients may benefit from three injections given at weekly intervals
Hyalgan® (sodium hyaluronate) Solution for intra-articular injection		1 syringe per week per knee; limit of 5 syringes per knee
Hymovis® (high molecular weight Viscoelastic Hyaluronan) Hydrogel for intra-articular injection		Inject 3 mL (24 mg) once a week for 2 weeks (total of 2 injections)
Monovisc® (cross-linked high molecular weight hyaluronic acid) Viscoelastic solution for intra-articular injection		Inject 88 mg (4 mL) once. Effectiveness of more than one course of treatment has not been established
Orthovisc® (high molecular weight hyaluronan) Viscoelastic solution for intra-articular injection		1 syringe per week per knee; limit of 4 syringes per knee
Sodium Hyaluronate (sodium hyaluronate) Viscoelastic solution for intra-articular injection		1 syringe per week per knee; Limit of 3 injections per knee
Supartz FX® (sodium hyaluronate) Solution for intra-articular injection		Inject 25 mg once a week (one week apart) for a total of five injections.
Synvisc® (hylan G-F 20) Elastoviscous high molecular weight fluid for intra-articular injection		1 syringe per week per knee; limit of 3 syringes per knee
Synvisc-One® (hylan G-F 20)		1 syringe per knee

Elastoviscous high molecular weight fluid for intra-articular injection		
Triluron™ (sodium hyaluronate) Viscous solution for intra-articular injection		1 syringe per week per knee; Limit of 3 injections per knee
TriVisc™ (sodium hyaluronate) Viscoelastic solution for intra-articular injection		Inject 25 mg (1 syringe) per week per knee for a total of 3 injections
Visco-3™ (sodium hyaluronate) Solution for intra-articular injection		1 syringe per week per knee; limit of 3 syringes per knee

* - All viscosupplements should be administered intra-articularly by a healthcare provider.
° - Gel-One also includes non-steroidal anti-inflammatory drugs (NSAIDS)

CLINICAL RATIONALE

Osteoarthritis

The American College of Rheumatology has developed criteria to standardize the definition of osteoarthritis (OA) and help distinguish it from other disorders that also involve joint pain. The patient must have knee joint pain and at least 5 of the following 9 features:

- Greater than 50 years of age
- Morning stiffness for less than 30 minutes
- Crepitus on active motion of the knee
- Bony tenderness
- Bony enlargement
- No palpable warmth
- Erythrocyte sedimentation rate (ESR) less than 40 mm/h
- Rheumatoid factor titer less than 1:40
- Synovial fluid suggestive of OA (clear color, viscous fluid, white blood cell count $<2000/mm^3$

Radiographic data can further the accuracy of the diagnosis. Findings suggestive of OA include: joint space narrowing, sub-chondral sclerosis, osteophytes formation, and sub-chondral cysts.[22-24]

The American College of Rheumatology recommendations a comprehensive plan for the management of osteoarthritis in an individual patient and may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral and intraarticular medications. Goals of management and principles for implementing those goals have broad applicability across patients. However, for some patients at some time points, a single physical, psychosocial, mind-body, or pharmacologic intervention may be adequate to control symptoms; for others, multiple interventions may be used in sequence or in combination. Which interventions and the order in which interventions are used will vary among patients. The American college of Rheumatology has recommended options and not recommended options.[16]

The American College of Rheumatology osteoarthritis guidelines strongly recommend the following approaches to knee osteoarthritis, noting no hierarchy between the recommendations exists.[16]

- Exercise
- Self-Efficiency and Self-Management Programs
- Weight Loss (if appropriate)
- Tai chi
- Cane
- Tibiofemoral knee brace
- Oral nonsteroidal anti-inflammatory drugs (NSAIDs)

- Topical NSAIDs
- Intraarticular Steroids

Intraarticular hyaluronic acid injections are conditionally not recommended by the American College of Rheumatology for patients with knee osteoarthritis. In reviewing intraarticular hyaluronic acid injections, benefit was restricted to the studies with higher risk of bias. When limited to trials with low risk of bias, meta-analysis has shown that the effect seen with hyaluronic acid injections compared to saline injections approaches zero.[16]
The American Academy of Orthopedic Surgeons (2021) recommended the following for treatment of OA of the knee.[21]

- Patients with symptomatic osteoarthritis of the knee participate in self-management programs, strengthening, low-impact aerobic exercises, and neuromuscular education; and engage in physical activity consistent with national guidelines. [Strong recommendation; high level evidence]
- NSAIDs (oral or topical) and acetaminophen are recommended for patients with symptomatic OA of the knee. [Strong recommendation; high level evidence]
- The panel updated the recommendation for tramadol as the following: Oral narcotics, including tramadol, result in a significant increase of adverse events and are not effective at improving pain or function for treatment of osteoarthritis of the knee. [Strong recommendation]

Guidelines from the American Academy of Orthopedic Surgeons does not recommend the routine use of hyaluronic acid products for treatment of symptomatic osteoarthritis of the knee. [Moderate recommendation][21]

A review on treatment of OA (American College of Physicians, 2014) suggests management should always begin with nonpharmacologic and nonsurgical strategies. Two major reasons substantiate this initial approach. First, there is a large body of evidence on the therapeutic efficacy of nonpharmacologic interventions. Second, pharmacologic interventions, particularly NSAID-related injury to the GI, renal, and central nervous systems, have the potential for toxicity. Pharmacologic agents should be offered only when more conservative efforts have failed to improve function. Many prescription and OTC agents are available for medical management of OA. Surgery should be a last resort.[25]

- There are several recommended first-line agents for OA, depending on comorbid conditions, age, and level of pain. Acetaminophen in doses up to 4 g/day is often the first choice for mild to moderate pain associated with OA. Advocacy for its front-line role stems from comparable efficacy to NSAIDs with a safer GI profile. NSAIDs may be added or substituted in patients who respond inadequately to acetaminophen.[25]
- NSAIDs are also considered by many physicians to be the preferred first-line agents in medical management of OA. However, routine use of NSAIDs in OA has disadvantages. All NSAIDs, both non-selective and cyclo-oxygenase (COX)-2 selective, are associated with significant potential toxicity, particularly among the elderly.[25]
- Topical NSAIDs have been found to be effective in relieving pain compared with placebo for both OA of the hand and knee joints. An attractive feature of this approach is reduced adverse GI reactions by maximizing local delivery and minimizing systemic toxicity. Although these topical agents can be associated with local side effects, such as rash, itching, and burning, they are usually minimal. These medications are attractive first-line agents for patients wishing to avoid systemic therapy.[25]

Comparative data on the viscosupplements is available. A meta-analysis comparing hylan and hyaluronic acid products found comparable efficacy between them but an excess of flares and effusion with the hylan products. A randomized, comparative trial comparing hylan and hyaluronic acid products of both avian and bacterial origin found similar efficacy and incidence

of adverse events across all products. A small trial of 92 patients comparing Synvisc® (hylan G-F 20) and Orthovisc® (high molecular weight hyaluronan) found similar improvements in pain for both groups. These data in aggregate indicate that there is no efficacy advantage between the viscosupplements. Additionally, the theory that the higher molecular weight products (hylans) are more effective due to increased residence time in the knee is not supported. Guidelines do not prefer one agent over the others.[17,26]

There is limited data available concerning the effectiveness of multiple courses of intra-articular hyaluronan therapy. A 4-week, open, repeat treatment phase of a double blind, randomized, placebo controlled trial assessing the safety and efficacy of a Synvisc-One® (hylan G-F 20) evaluated the safety of an additional course of intra-articular hyaluronan therapy six months after the first course of treatment. This extension study only evaluated safety and not efficacy. The study results indicated that there was no increased risk of adverse events in patients receiving a second injection of hylan G-F 20.[18] This finding contrasted with previous reports from post-marketing studies that suggested an approximate threefold increased risk of local target knee adverse events with a repeat course of hylan G-F 20.[19] A study conducted by Navarro-Sarabia et. al on behalf of the AMELIA project evaluated the efficacy and safety of repeat injections of hyaluronic acid (HA) versus placebo in 309 patients over 40 months. The authors concluded that repeated cycles of intra-articular injections of HA not only improved knee symptoms in between injections but had a carry-over effect for at least 1 year after the last cycle. No safety issues were found.[20]

Safety

Durolane carries the following contraindications:

- Do not inject Durolane with knee joint infections, infections, or skin disease in the area of the injection site.
- Do not administer to patients with known hypersensitivity (allergy) to HA preparations.

Euflexxa carries the following contraindications:

- Hypersensitivity to hyaluronan preparations. Patients with knee joint infections, infections or skin disease in the area of the injection site

Gel-One carries the following contraindications:

- Hypersensitivity (allergy) to Gel-One or sodium hyaluronate preparations. Patients with skin diseases or infections in the area of the injection site

GELSYN-3 carries the following contraindications:

- Do not administer to patients with known hypersensitivity (allergy) to sodium hyaluronate preparations.
- Do not inject Gelsyn into the knees of patients having knee joint infections or skin diseases or infections in the area of the injection site.

GenVisc 850 carries the following contraindications:

- Do not administer to patients with known hypersensitivity (allergy) to hyaluronate preparations
- Do not inject this product in the knees of patients with infections or skin diseases in the area of the injection site

Hyalgan

- Hypersensitivity to hyaluronate preparations. Patients with present infections or skin diseases in the area of the injection site

Hymovis

- Do not administer to patients with known hypersensitivity (allergy) to hyaluronate preparations.
- Do not administer to patients with known hypersensitivity (allergy) to gram positive bacterial proteins.
- Do not administer to patients with infections or skin diseases in the area of the injection site or joint.

Monovisc
- Do not administer to patients with known hypersensitivity (allergy) to hyaluronate preparations.
- Do not administer to patients with known hypersensitivity (allergy) to gram positive bacterial proteins.
- Do not inject Monovisc™ in the knees of patients with infections or skin diseases in the area of the infection site or joint.
- Do not administer to patients with known systemic bleeding disorders

Orthovisc carries the following contraindications:
- Do not administer to patients with known hypersensitivity (allergy) to hyaluronate preparations.
- Do not administer to patients with known allergies to avian or avian-derived products (including eggs, feathers, or poultry).
- Do not inject Orthovisc® in the knees of patients with infections or skin diseases in the area of the injection site or joint.

Sodium Hyaluronate 1% carries the following contraindications:
- Do not use sodium hyaluronate to treat patients who have a known hypersensitivity to hyaluronan preparations
- Do not use to treat patients with knee joint infections or to treat patients with infections or skin disease in the area of the injection site

Supartz carries the following contraindications:
- Hypersensitivity to hyaluronan preparations. Patients with knee joint infections, infections or skin disease in the area of the injection site

Supartz FX carries the following contraindications:
- Do not administer to patients with known hypersensitivity (allergy) to sodium hyaluronate preparations.
- Do not inject this product in the knees of patients with infections or skin diseases in the area of the injection site

Synvisc carries the following contraindications:
- Hypersensitivity to hyaluronan preparations. Patients with knee joint infections, infections or skin disease in the area of the injection site

Synvisc-One carries the following contraindications:
- Hypersensitivity (allergy) to hyaluronan (sodium hyaluronate) preparations. Patients with knee joint infections or skin diseases or infections in the area of the injection site

Triluron carries the following contraindications:
- Do not administer to patients with known hypersensitivity to hyaluronate preparations
- Intra-articular injections are contraindicated in cases of past and present infections or skin diseases in the area of the injection site to reduce the potential for developing septic arthritis

TriVisc carries the following contraindications:

- Hypersensitivity to sodium hyaluronate preparations
- Infections or skin diseases in the area of the injection site

Visco-3 carries the following contraindications:

- Hypersensitivity to sodium hyaluronate preparations
- Infections or skin diseases in the area of the injection site

References

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10. Supartz Prescribing Information. Bioventus. February 2011.
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12. Synvisc One Prescribing Information. Genzyme. September 2014.
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21. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
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27. Triluron Prescribing Information. Fidia Pharma USA Inc. March 2019
28. 1% Sodium Hyaluronate Prescribing Information. Teva Pharmaceuticals USA Inc. March 2019

Document History
Original Prime Standard Part B criteria approved by P&T UM Committee 12/2020
Annual Review Prime Standard Part B criteria approved by P&T UM Committee 12/2021

Medicare Part B Viscosupplements Prior Authorization

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Euflexxa® (sodium hyaluronate) **Durolane®** (sodium hyaluronate) **Gel-One®** (cross-linked hyaluronate) **GELSYN-3®** (sodium hyaluronate) **GenVisc® 850** (sodium hyaluronate) **Hyalgan®** (sodium hyaluronate) **Hymovis®** (high molecular weight viscoelastic hyaluronan) **Monovisc®** (cross-linked high molecular weight hyaluronic acid) **Orthovisc®** (high molecular weight hyaluronan) **Sodium Hyaluronate 1%** **Supartz FX®** (sodium hyaluronate) **Synvisc®** (hylan G-F 20) **Synvisc-One®** (hylan G-F 20) **Triluron™** (sodium hyaluronate) **TriVisc®** (sodium hyaluronate) **Visco-3™** (sodium hyaluronate)	

TARGET AGENTS AND PROGRAM QUANTITY LIMIT

Brand (generic)	GPI (NDC)	Multisource Code	HCPCS Code
Durolane (sodium hyaluronate)			
60 mg/3 mL injection	7580007010E420	M, N, O, or Y	J7318
Euflexxa (sodium hyaluronate)*			
20 mg/2 mL injection	7580007010E520 (55566-4100-01)	M, N, O, or Y	J7323
Gel-One (cross-linked hyaluronate)			
30 mg/3 mL injection	7580002000E420	M, N, O, or Y	J7326
GELSYN-3 (sodium hyaluronate)			
16.8 mg/2 mL injection	7580007010E517	M, N, O, or Y	J7328
GenVisc 850 (sodium hyaluronate)*			
25 mg/2.5 mL	7580007010E525 (50653-0006-01)	M, N, O, or Y	J7320
Hyalgan (sodium hyaluronate)*			
20 mg/2 mL injection	7580007010E520 (89122-0724-20) 75800070102024	M, N, O, or Y	J7321
Hymovis (high molecular weight viscoelastic hyaluronan)			
24 mg/3 mL injection	7580006000E515	M, N, O, or Y	J7322
Monovisc (high molecular weight hyaluronic acid)			

Brand (generic)	GPI (NDC)	Multisource Code	HCPCS Code
88 mg/4 mL injection	7580006000E530	M, N, O, or Y	J7327
Orthovisc (high molecular weight hyaluronan)			
15 mg/mL injection	7580006000E520	M, N, O, or Y	J7324
Sodium Hyaluronate*			
20 mg/2 mL injection	7580007010E520 (57844-0181-13, 57844-0181-21)	M, N, O, or Y	J7317
Supartz FX (sodium hyaluronate)*			
25 mg/2.5 mL injection	7580007010E525 (89130-4444-01)	M, N, O, or Y	J7321
Synvisc (hylan G-F 20)			
8 mg/mL injection (2 mL syringe)	7580004000E530	M, N, O, or Y	J7325
Synvisc-One (hylan G-F 20)			
8 mg/mL injection (6 mL syringe)	7580004000E560	M, N, O, or Y	J7325
Triluron (sodium hyaluronate)*			
20 mg/2 mL prefilled syringe	7580007010E520 (89122-0879-01)	M, N, O, or Y	J7332
TriVisc (sodium hyaluronate)*			
25 mg/2.5 mL	7580007010E525 (50653-0006-04)	M. N, O, or Y	J7329
Visco-3 (sodium hyaluronate)*			
25 mg/2.5 mL injection	7580007010E525 (87541-0301-31, 50016-0957-21)	M, N, O, or Y	J7321, J7333

CRITERIA FOR APPROVAL
Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

AND

2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR

e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

AND

3. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: One course of therapy per knee joint for 6 months