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Section: Prescription Drugs **Effective Date:** January 1, 2026
Subsection: Neuromuscular Drugs **Original Policy Date:** June 9, 2011
Subject: Hyaluronic Acid Derivatives **Page:** 1 of 7

Last Review Date: December 12, 2025

Hyaluronic Acid Derivatives

Description

Durolane, Euflexxa, GelSyn-3, GenVisc 850, Hyalgan, Sodium Hyaluronate, Supartz, Syn喬ynt, Triluron, TriVisc, **Visco-3** (sodium hyaluronate)

Gel-One, Hymovis, Monovisc, Orthovisc (hyaluronan)

Synvisc, Synvisc-One (hylan G-F 20)

Bolded medications are the preferred products for claims adjudicated through the medical benefit.

Background

Osteoarthritis of the knee is a condition in which the elastoviscous property of the synovial fluid in the knee joint becomes diminished, resulting in less protection and shock absorption.

Durolane, Euflexxa, Gel-One, GelSyn-3, GenVisc 850, Hyalgan, Hymovis, Monovisc, Orthovisc, Sodium Hyaluronate, Synvisc, Synvisc-One, Supartz, Syn喬ynt, Triluron, TriVisc, Visco-3 are hyaluronan derivatives that are injected into the knee joints to increase the elastoviscous properties of arthritic joint fluid and slow its outflow from the joint. The goal of therapy is to restore the viscoelasticity in the affected joints, thereby decreasing pain, improving mobility, and restoring the natural protective functions (1).

The American College of Rheumatology (ACR) updated its guidelines for the treatment of osteoarthritis (OA) of the knee in 2019. In mild symptomatic OA, treatment may be limited to patient education, physical and occupational therapy and other non-pharmacologic modalities.

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Nonpharmacologic modalities strongly recommended for the management of knee OA included exercise, weight loss, self-efficacy and self-management programs, tai chi, the use of a cane and tibiofemoral knee braces. Nonpharmacologic modalities conditionally recommended for knee OA included balance training, yoga, cognitive behavioral therapy, kinesiotaping, acupuncture, thermal interventions, and radiofrequency ablation. Pharmacologic modalities strongly recommended for the management of knee OA included topical NSAIDs, oral NSAIDs and intraarticular glucocorticoid injection. Pharmacologic modalities conditionally recommended for the initial management of patients with knee OA included topical capsaicin, acetaminophen, duloxetine and tramadol (1).

Regulatory Status

FDA-approved indication: Hyaluronic acid derivatives are indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy, simple analgesics (e.g., acetaminophen), NSAIDs, tramadol, or intra-articular steroid injections (2-18).

The hyaluronic acid derivatives are contraindicated for use in patients with known hypersensitivity to hyaluronan (sodium hyaluronate) preparations. Orthovisc lists hypersensitivity to gram positive bacterial proteins as an additional contraindication (4). Caution should be exercised when Gel-One, Hyalgan, Visco-3, Synvisc, Synvisc-One, Supartz, and Triluron are administered to patients with allergies to avian proteins, feathers, and egg products (3-8, 18).

Hyaluronic acid derivatives are contraindicated to treat patients with knee joint infections, infections or skin diseases in the area of the injection site (2-17).

A treatment cycle for most of the hyaluronan derivatives typically involves multiple weekly injections. Euflexxa, GelSyn-3, Sodium Hyaluronate, Synvisc, Triluron, TriVisc, and Visco-3 are given for a total of three injections. Orthovisc is given for three or four injections. GenVisc 850, Supartz and Hyalgan are given for a total of three or five injections. Durolane, Gel-One, Synjoynt, and Synvisc-One differ from the other hyaluronan derivatives in that it only requires one injection. Repeat courses of hyaluronan derivatives may be administered if symptoms return (2-18).

Upon the basis of high-quality supporting evidence, the American Academy of Orthopedic Surgeons cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee (19).

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Related policies

Hyaluronate Powder

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Hyaluronic acid derivatives may be considered **medically necessary** if the conditions indicated below are met.

Hyaluronic acid derivatives may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years or older (22 or older for Synvisc, Synvisc-One, and TriVisc)

Diagnosis

Patient must have the following:

Osteoarthritis of the knee

AND ALL of the following:

1. Inadequate response to **TWO** or more of the following conservative non-pharmacologic therapy:
 - a. Cardiovascular (aerobic) activity, such as: walking, biking, stationary bike, aquatic exercise
 - b. Resistance exercise
 - c. Weight reduction (for persons who are overweight)
 - d. Participation in self-management programs
 - e. Wear of medially directed patellar taping
 - f. Wear of wedged insoles
 - g. Thermal agents
 - h. Walking aids
 - i. Physical therapy

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- j. Occupational therapy
2. Inadequate response, intolerance, or contraindication to **TWO** or more of the following:
 - a. Acetaminophen
 - b. Oral NSAIDs
 - c. Topical NSAIDs
3. Inadequate response, intolerance, or contraindication to intra-articular steroid injections in which efficacy lasted less than 8 weeks
4. Radiologic confirmation of Kellgren-Lawrence Scale score of grade 2 or greater
5. **NO** dual therapy with another hyaluronic acid injectable
6. **Non-preferred medications only:** Inadequate treatment response, intolerance, or contraindication to **ONE** of the preferred products (Gel-One, Synvisc, Synvisc-One, or Visco-3)

Prior – Approval Renewal Requirements

Age 18 years or older (22 or older for Synvisc, Synvisc-One, and TriVisc)

Diagnosis

Patient must have the following:

Osteoarthritis of the knee

AND ALL of the following:

1. Documentation of improvement in pain with previous course of treatment
2. At least 12 months has elapsed since last injection of the prior treatment cycle
3. Documentation of reduction of dosing of NSAIDs or other analgesics during the 12 month period following the last injection of the prior treatment cycle
4. **NO** dual therapy with another hyaluronic acid injectable

Policy Guidelines

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Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Quantity One course of therapy for each knee

Prior – Approval Renewal Limits

Same as above

Rationale

Summary

Osteoarthritis of the knee is a condition in which the elastoviscous property of the synovial fluid in the knee joint becomes diminished, resulting in less protection and shock absorption.

Durolane, Euflexxa, Gel-One, GelSyn-3, GenVisc 850, Hyalgan, Hymovis, Monovisc, Orthovisc, Sodium Hyaluronate, Synvisc, Synvisc-One, Supartz, Synojoyn, Triluron, TriVisc, Visco-3 are hyaluronan derivatives that are injected into the knee joints to increase the elastoviscous properties of arthritic joint fluid and slow its outflow from the joint. The goal of therapy is to restore the viscoelasticity in the affected joints, thereby decreasing pain, improving mobility, and restoring the natural protective functions (1-18).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of the hyaluronic acid derivatives while maintaining optimal therapeutic outcomes.

References

1. American College of Rheumatology, Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee: 2019 update. *Arthritis Care & Research* 2019; 72(2):149-162.
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6. Synvisc [package insert]. Ridgefield, NJ: Genzyme Corp.; December 2014.
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11. GenVisc 850 [package insert]. Doylestown, PA: OrthogenRx Inc.; January 2015.
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14. Visco-3 [package insert]. Warsaw, IN: Zimmer, Inc.; May 2017.
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17. TriVisc [package insert]. Doylestown, PA: OrthogenRx, Inc.; September 2018.
18. Triluron [package insert]. Florham Park, NJ: Fidia Pharma USA Inc.; July 2019.
19. American Academy of Orthopaedic Surgeons. Treatment of osteoarthritis of the knee. Evidence-based guideline 2nd edition. May 2013.

Policy History

Date	Action	Reason
January 2012	Added minimum age - only approved for adults	
December 2012	Annual editorial review and reference update	
December 2013	Annual editorial review and reference update	
March 2014	Annual editorial review	
	Addition of examples of non-pharmacological agents and agents of prior failure medications.	
April 2014	Line-Addition of Monovisc to PA	
March 2015	Annual criteria review and reference update	
March 2016	Change from one tried and failed to two tried and failed non-pharmacologic and pharmacologic therapies and addition of the tried and failed of intra-articular steroid and radiologic confirmation of Kellgren-Lawrence Scale score of grade 2 or greater	
	Addition of Hymovis	
	Policy # change from 5.11.04 to 5.75.09	
May 2016	Addition of GelSyn-3 and GenVisc 850	
December 2016	Annual editorial review and reference update	
	Added: no dual therapy with another hyaluronic acid injectable	
March 2017	Bolded preferred products in the title page	
July 2017	GelSyn-3 has been changed to preferred	
September 2017	Annual review	
December 2017	Addition of Durolane and Visco-3	

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March 2018	Annual editorial review Removal of Tramadol from the T/F list
September 2019	Annual review and reference update. Addition of Sodium Hyaluronate, Synojoyn, and TriVisc
December 2019	Annual review. Addition of requirement to trial preferred products
January 2020	Addition of Triluron
March 2020	Annual review
March 2021	Annual editorial review and reference update. Clarification added to the t/f, intolerance, C/I to preferred products requirement indicating that it only applies to claims adjudicated through the pharmacy benefit
June 2022	Annual review and reference update
June 2023	Annual review. Changed policy number to 5.75.009
December 2023	Annual review
June 2024	Annual review
December 2024	Annual review
June 2025	Annual review
December 2025	Annual review. Removed Medex requirement and switched to t/f only one preferred. Changed preferred products to Gel-One, Synvisc, Synvisc-One, and Visco-3

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January1, 2026.