Clinical Policy: Hyaluronate Derivatives

Reference Number: IL.PHAR.05
Effective Date: 1.1.20
Last Review Date: 04.13.2022
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are hyaluronate derivatives requiring prior authorization: sodium hyaluronate (Euflexxa®, Gelsyn-3™, GenVisc®850, Hyalgan®, Supartz™, Supartz FX™, Synojoynt™, Triluron™, TriVisc™, VISCO-3™), hyaluronic acid (Durolane®), cross-linked hyaluronate (Gel-One®), hyaluronan (Hymovis®, Orthovisc®, Monovisc®), and hylan polymers A and B (Synvisc®, Synvisc One®).

FDA Approved Indication(s)

Hyaluronate 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 and to simple analgesics (e.g., acetaminophen) or non-steroidal anti-inflammatory drugs (NSAIDs).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that hyaluronate derivatives are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Osteoarthritis of the Knee (must meet all)**:**

1. Diagnosis of OA of the knee supported by imaging (e.x., X-ray, MRI);
2. Prescribed* by or in consultation with a rheumatologist, orthopedist, or sports medicine physician;
   **This prescriber requirement does not apply to New Mexico Community Care*
3. Inadequate response to physical therapy as directed by a physical therapist;
4. Failure of a ≥ 4 week trial of one of the following (a or b), as evidenced by claims history, unless all are contraindicated or clinically significant adverse effects are experienced:
   a. Oral NSAID at continuous therapeutic (prescription strength) dosing;
   b. Topical NSAID* if member is ≥ 75 years old or unable to take oral NSAID;
   **Topical NSAID may require prior authorization*
5. Trial of at least one intra-articular glucocorticoid injection with a documented positive but inadequate response *(see Appendix C for examples)* unless contraindicated or history of intolerance;
   **Prior authorization may be required for intra-articular glucocorticoids*

6. Member does not have any of the following (a or b):
   a. Coexistent active inflammatory arthritis other than OA (e.g., rheumatoid arthritis, spondylitis, gouty arthritis) in the targeted knee;
   b. History of total knee arthroplasty in the targeted knee.
7. Dose does not exceed one treatment cycle per knee for a 6 month period.

Approval duration: 6 months (one treatment cycle) (*refer to section V*)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Osteoarthritis of the Knee (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by the following, including but not limited to:
   a. Decrease in pain symptoms as evidenced by improvement in the Visual Analog Scale for pain;
   b. Improvement in ambulation or range of motion;
   c. Improvement in stiffness;
   d. Decrease in rescue pain medication use;
3. Member has not had total knee arthroplasty in the targeted knee;
4. Six or more months have elapsed since the last treatment cycle.
5. Dose does not exceed one treatment cycle per knee.

Approval duration: 6 months (one treatment cycle) *(refer to section V)*

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NSAID: non-steroidal anti-inflammatory drug
OA: osteoarthritis

Appendix B: Contraindications/Boxed Warnings

- Contraindication(s):
    - Durolane, Euflexxa, Gelsyn-3, GenVisc 850, Hyalgan, Supartz, Supartz FX, Synojoynt, Triluron, TriVisc, VISCO-3, Gel-One, Hymovis, Orthovisc, Monovisc, Synvisc, Synvisc One:
        - Known hypersensitivity to hyaluronan preparations
        - Patients with knee joint infections, infections or skin disease in the area of the injection site
    - Hymovis, Monovisc, Orthovisc: do not administer to patients with known hypersensitivity to gram positive bacterial proteins
    - Monovisc: do not administer to patients with known systemic bleeding disorders
- Boxed warning(s): none reported

Appendix C: General Information

- Examples of documented positive but inadequate response to intra-articular glucocorticoid injections include but are not limited to the following: inadequate pain relief, frequent need of rescue medications such as NSAIDs or opioids, need to decrease or inability to increase activity levels, adequate pain relief but with steroid-induced hyperglycemia.
- Per the 2014 Osteoarthritis Research Society International guidelines, hyaluronate derivatives are not appropriate for multiple joint OA subtypes or joint OA other than the knee.
    - In DeGroot et al., single hyaluronic acid was compared to saline injection in a small RCT (N=64). At 6 and 12 weeks, there were no significant differences in improvement between the two groups on the American Orthopedic Foot and Ankle Society clinical rating score, the Ankle Osteoarthritis Scale score, or the patient-reported visual analog pain scale. Migliore et al., conducted a review of seven studies for ankle OA that showed mixed results, but were unable to complete a meta-analysis due to use of study design limitations (e.g., inconsistent use of primary endpoints, varying comparators, small sample size) leading to study heterogeneity.
    - Richette et al. conducted a multicenter, randomized, placebo-controlled trial in hip OA. At 3 months, hyaluronic acid was not more effective than placebo with a treatment difference in pain score of −0.15 (95% CI −11.04, 10.74). Responder rates were 33.3% for hyaluronic acid and 32.6% for placebo (p = 0.94). Additionally, analgesics were taken by 81% of study days by patients on placebo, and 88% of patients in the hyaluronic acid group.
- There are no studies that have evaluated the efficacy of hyaluronate derivatives in patients with OA and coexistent other inflammatory conditions such as rheumatoid arthritis.
- There is no data to suggest efficacy of hyaluronate derivatives in patients who have had total knee arthroplasty in the targeted knee.

V. Dosage and Administration

Drug Name	Active Ingredient	Dose of Active Ingredient per Injection	Treatment Cycle*
Durolane	Hyaluronic acid	60 mg (3 mL)	1 injection
Euflexxa	Sodium hyaluronate	20 mg (2 mL)	3 injections
Gel-One	Cross-linked sodium hyaluronate	30 mg (3 mL)	1 injection
Gelsyn-3	Sodium hyaluronate	16.8 mg (2 mL)	3 injections
GenVisc 850	Sodium hyaluronate	25 mg (2.5 mL)	3-5 injections
Hyalgan	Sodium hyaluronate (Hyalectin®)	20 mg (2 mL)	3-5 injections
Hymovis	Sodium hyaluronate (HYADD®4)	24 mg (3 mL)	2 injections
Monovisc‡	Cross-linked sodium hyaluronate	88 mg (4 mL)	1 injection
Orthovisc‡	Sodium hyaluronate	30 mg (2 mL)	3-4 injections
Supartz, Supartz FX	Sodium hyaluronate	25 mg (2.5 mL)	3-5 injections
Synojoynt	Sodium hyaluronate	20 mg (2 mL)	3 injections
Synvisc	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	16 mg (2 mL)	3 injections
Synvisc One	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	48 mg (6 mL)	1 injection
Triluron	Sodium hyaluronate	20 mg (2 mL)	3 injections
TriVisc	Sodium hyaluronate	25 mg (2.5 mL)	3 injections
VISCO-3	Sodium hyaluronate	25 mg (2.5 mL)	3 injections

*Treatment cycle: Total number of injection per cycle per knee (if treating both knees, double the number of injections per treatment cycle).
‡Per product label, one injection of Monovisc is equivalent to 3 injections of Orthovisc.

VI. Product Availability

Drug Name	Active Ingredient	Availability**
Durolane	Hyaluronic acid	3 mL syringe
Euflexxa	Sodium hyaluronate	2.25 mL syringe
Gel-One	Cross-linked sodium hyaluronate	3 mL syringe
GenVisc 850	Sodium hyaluronate	3 mL syringe
Gelsyn-3	Sodium hyaluronate	2.25 mL syringe
Hyalgan	Sodium hyaluronate (Hyalectin®)	2 mL vial or 2 mL syringe
Hymovis	Sodium hyaluronate (HYADD®4)	5 mL syringe
Monovisc‡	Cross-linked sodium hyaluronate	5 mL syringe
Orthovisc‡	Sodium hyaluronate	3 mL syringe

Drug Name	Active Ingredient	Availability**
Supartz	Sodium hyaluronate	2.5 mL syringe
Supartz FX	Sodium hyaluronate	2.5 mL syringe
Synojoynt	Sodium hyaluronate	3 mL syringe
Synvisc	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	2.25 mL syringe
Synvisc One	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	10 mL syringe
TriVisc	Sodium hyaluronate	2.5 mL syringe
Triluron	Sodium hyaluronate	2 mL syringe
VISCO-3	Sodium hyaluronate	2.5 mL syringe

** All syringes/vials are single-use (i.e., one injection/one knee); syringes are pre-filled.
‡Per product label, one injection of Monovisc is equivalent to 3 injections of Orthovisc.

VII. References

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7318	Hyaluronan or derivative, Durolane, for intra-articular injection, 1 mg
J7320	Hyaluronan or derivative, GenVisc 850, for intra-articular injection, 1 mg
J7321	Hyaluronan or derivative, Hyalgan or Supartz FX, for intra-articular injection, per dose (Hyalgan dose is 20 mg/2 mL, Supartz dose is 25 mg/2.5 mL)
J7322	Hyaluronan or derivative, Hymovis, for intra-articular injection, 1 mg
J7323	Hyaluronan or derivative, Euflexxa, for intra-articular injection, per dose
J7324	Hyaluronan or derivative, Orthovisc, for intra-articular injection, per dose
J7325	Hyaluronan or derivative, Synvisc or Synvisc-One, for intra-articular injection, 1 mg
J7326	Hyaluronan or derivative, Gel-One, for intra-articular injection, per dose
J7327	Hyaluronan or derivative, Monovisc, for intra-articular injection, per dose
J7328	Hyaluronan or derivative, Gel-Syn, for intra-articular injection, 0.1 mg
J7329	Hyaluronan or derivative, Trivisc, for intra-articular injection, 1 mg
J7331	Hyaluronan or derivative, Synojoynt, for intra-articular injection, 1 mg
J7332	Hyaluronan or derivative, Triluron, for intra-articular injection, 1 mg
J7333	Hyaluronan or derivative, Visco-3, for intra-articular injection, per dose

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted CP.PHAR.05 Hyaluronate derivatives policy.	12.17.19	1.7.20
1Q 2021 Annual review - Revised requirement for diagnosis confirmation by radiologic imaging – generalized to imaging beyond just radiologic type (i.e., to include MRIs); imaging reference added. added sports medicine physician as acceptable specialist; references reviewed and updated.	3.10.2021	

HCPCS Codes	Description		
	2Q 2022 Annual Review: added allowable treatment number per duration to initial and continued criteria; Clarified physical therapy should be supervised by a physical therapist; Revised requirement for diagnosis confirmation by radiologic imaging – generalized to imaging beyond just radiologic type (i.e., to include MRIs); updated Appendix C: General Information; Updated Appendix B: Contraindications/Boxed Warnings; references reviewed and updated.	4.13.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.