Clinical Policy: Hyaluronate Derivatives

Reference Number: IA.PHAR.05
Effective Date: 01.01.23
Last Review Date: 10.22
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description

This policy addresses the use of hyaluronan (hyaluronate derivatives) injections for the replacement of supplementation of intra-articular lubricants in individuals with musculoskeletal conditions. This therapy may also be referred to as viscosupplementation. The hyaluronate derivatives include the following: 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®).

Policy/Criteria

I. Hyaluronate derivative injections:

A. It is the policy of Iowa Total Care® that hyaluronate derivative injections for all joints, but not limited to, the knee, ankle, shoulder, hip, temporomandibular joint, or thumb are **not medically necessary.**

II. Appendices/General Information

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

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral NSAIDs		
diclofenac (Voltaren®)	50 mg PO TID	150 mg/day
etodolac (Lodine®)	400-500 mg PO BID	1,200 mg/day
fenoprofen (Nalfon®)	400 mg PO TID to QID	3,200 mg/day
ibuprofen (Motrin®)	400-800 mg PO TID to QID	3,200 mg/day
indomethacin (Indocin®)	25-50 mg PO BID to TID	200 mg/day
indomethacin SR (Indocin SR®)	75 mg PO QD to BID	150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ketoprofen (Orudis®)	25-75 mg PO TID to QID	300 mg/day
meloxicam (Mobic®)	7.5-15 mg PO QD	15 mg/day
naproxen (Naprosyn®)	250-500 mg PO BID	1,500 mg/day
naproxen sodium (Anaprox®, Anaprox DS®)	275-550 mg PO BID	1,650 mg/day
oxaprozin (Daypro®)	600-1,200 mg PO BID	1,800 mg/day
piroxicam (Feldene®)	10-20 mg PO QD	20 mg/day
salsalate (Disalcid®)	500-750 mg PO TID, titrated up to 30,00 mg QD	3,000 mg/day
sulindac (Clinoril®)	150 mg-200 mg PO BID	400 mg/day
tolmetin DS (Tolectin DS®)	400 mg PO TID, titrated up to 1,800 mg QD	1,800 mg/day
Topical NSAIDs		
diclofenac 1.5% (Pennsaid®)	40 drops QID on each painful knee	320 drops/day
Voltaren® Gel 1% (diclofenac)	2-4 g applied to affected area QID	32 g/day
Intra-articular glucocorticoids		
Kenalog® (triamcinolone acetonide)	40 mg (1 mL) for large joints	80 mg/treatment
Aristospan® (triamcinolone hexacetonide)	10-20 mg for large joints	20 mg/treatment
methylprednisolone acetate (Depo-Medrol®)	20-80 mg for large joints	80 mg/treatment
hydrocortisone acetate	25-50 mg for large joints	75 mg/treatment
Zilretta® (triamcinolone acetonide)	32 mg (5 mL) for large joints	32 mg/treatment

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Osteoarthritis (OA) is a painful condition in which the cartilage between the bones degenerates, no longer providing a smooth, gliding surface for motion or adequate cushioning. Damaged articular cartilage does not tend to heal and may progressively worsen and cause focal lesions and eventually OA. Because OA damages the cartilage and may ultimately damage the bone, it disrupts how components work together, resulting in pain, swelling, inflammation, muscle weakness, impaired quality of life (QOL), and reduced function.
- Hyaluronic acid is a component of synovial fluid, which lubricates the joint and absorbs shock. Hyaluronic acid production is generally reduced and may be of poorer quality with osteoarthritis, which may exacerbate inflammation (Xing et al., 2016). Intra-articular injection of hyaluronic acid is intended to provide mechanical viscosupplementation (e.g., joint lubrication and shock absorption) and induce the body's own production of hyaluronic acid to confer enduring effects and prevent further cartilage breakdown (Nguyen et al., 2016; Xing et al.,2016).

- In 2019, the American College of Rheumatology (ACR) published updated guidelines for the management of osteoarthritis of the hand, hip, and knee (Kolasinski 2019). The guidelines conditionally recommend against intraarticular hyaluronic acid injections in individuals with knee and/or first CMC osteoarthritis. The guideline strongly recommended against intraarticular hyaluronic acid injections in patients with hip OA. ACR states hyaluronic acid injection benefit has been primarily found in studies with higher risk of bias. This supporting meta-analysis showed that the effect size of hyaluronic acid injections compared to saline injections approaches zero.
- The American Academy of Orthopedic Surgeons (AAOS) published their Clinical Practice Guideline for Treatment of Osteoarthritis of the Knee in 2013 (Jevsevar, 2013). AAOS guideline states that they "cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee." The recommendation was based on lack of efficacy, not on potential harm.
- In 2019, Osteoarthritis Research Society International (OARSI) published updated guidelines for the non-surgical management of knee, hip and polyarticular osteoarthritis (Bannuru 2019). The 2019 guidance updated intra-articular hyaluronic acid to conditionally recommended (low consensus) for knee osteoarthritis for longer-term treatment effect (symptom improvement beyond 12 weeks) and favorable safety profile. Although there was a small improvement in pain and function for patients with knee osteoarthritis treated with intra-articular hyaluronic acid, there remained uncertainties about the clinical benefit of this treatment; further high-quality studies were recommended. Treatment modalities with a strong recommendation for knee osteoarthritis include arthritis education, structured land-based exercise programs and topical NSAIDs.
- The American Medical Society for Sport Medicine (AMSSM) published a consensus statement in 2016 concluding that there was a small improvement in pain and function for patients with knee osteoarthritis treated with intra-articular hyaluronic acid, but uncertainties remained about the clinical benefit of this treatment (Trojian, 2016). Potential for bias was present among most studies included in the meta-analysis, including incomplete data reporting, selective reporting, or the absence of blinding of participants and personnel.
- In 2017, a Hayes Technology comparative effectiveness review of hyaluronic acid for knee osteoarthritis concluded that there was uncertainty regarding whether intra-articular hyaluronic acid injections provide clinically significant pain relief relative to saline injections and uncertainty regarding the timing and duration of benefit relative to corticosteroid injections. The assessment gave the use of intra-articular hyaluronic acid to treat knee osteoarthritis in adults with chronic symptoms for whom conservative treatments are contraindicated or have failed to provide adequate relief a Hayes Rating of "C": Potential but unproven benefit. The review found clinically meaningful improvements in function and pain with intra-articular hyaluronic acid but found it unclear whether the incremental value of this effective relative to a saline injection represented a clinical advantage.
- In its 2014 evidence-based guidelines, the National Institute for Health and Care Excellence (NICE) stated that IA-HA injections should not be offered for the management of OA, including OA of the knee (NICE, 2014).

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III. 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.

IV. 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
Supartz	Sodium hyaluronate	2.5 mL syringe

Drug Name	Active Ingredient	Availability**
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	3 mL syringe
Triluron	Sodium hyaluronate	2 mL syringe or 2 mL vial
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.

V. References

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2. Nguyen C, Lefevre-Colau MM, Poiraudeau S, Rannou F. Evidence and recommendations for use of intra-articular injections for knee osteoarthritis. *Ann Phys Rehabil Med.* 2016;59(3):184-189.
3. Jevsevar, D.S. Treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. Journal of the American Academy of Orthopaedic Surgeons. 2013, 21 (9), 571-576. doi: 10.5435/JAAOS-21-09-571..
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6. Trojian TH, Concoff AL, Joy SM, et,al. AMSSM scientific statement concerning viscosupplementation injections for knee osteoarthritis: importance for individual patient outcomes. Br J Sports Med. 2016 Jan;50(2):84-92.
7. DeGroot H, Uzunishvili S, Weir R et al. Intra-articular injection of hyaluronic acid is not superior to saline solution injection for ankle arthritis: a randomized, double-blind, placebo-controlled study. J Bone Joint Surg 2012; 94(1):2-8.
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9. National Institute for Health and Care Excellence (NICE). Osteoarthritis: care and management. London, UK: National Institute for Health and Care Excellence; 2014. Available at: https://www.nice.org.uk/guidance/cg177/resources/osteoarthritis-care-and-management-pdf-35109757272517. Accessed December 5, 2021.

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	Plan Approval Date
New Policy	12.22	12.22

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.