Clinical Policy: Hyaluronate Derivatives

Reference Number: CP. PHAR.05
Effective Date: 10/08
Last Review Date: 08/17
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 FX™), cross-linked hyaluronate (Gel-One®), hyaluronan (Hymovis®, Orthovisc®, Monovisc®), and hylan polymers A and B (Synvisc®, Synvisc One®).

FDA approved indication

Hyaluronate derivatives are indicated for the treatment of pain in osteoarthritis 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 (which may include office chart notes and lab results) 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 osteoarthritis of the knee supported by radiologic imaging;
2. Prescribed by or in consultation with a rheumatologist or an orthopedist;
3. Inadequate response to physical therapy or a physician directed exercise program;
4. Failure of ≥ 2 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 intraarticular glucocorticoid injections with a positive but inadequate response unless contraindicated or history of intolerance.

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

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Six or more months have elapsed since the last treatment cycle.

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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – CP.PHAR.57 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

V. Dosage and Administration

Drug Name	Active Ingredient	Dose of Active Ingredient per Injection	Treatment Cycle*
Euflexxa	Sodium hyaluronate	20 mg (2 mL)	3 injections
Gel One	Cross-linked sodium hyaluronate	30 mg (3 mL)	1 injection
GenVisc 850	Sodium hyaluronate	25 mg (2.5 mL)	3-5 injections
Gelsyn-3	Sodium hyaluronate	16.8 mg (2 mL)	3 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 FX	Sodium hyaluronate	25 mg (2.5 mL)	3-5 injections
Synvisc	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	16 mg (2 mL)	3 injections

Drug Name	Active Ingredient	Dose of Active Ingredient per Injection	Treatment Cycle*
Synvisc One	Cross-linked hylan G-F 20 (hylan A and hylan B polymers)	48 mg (6 mL)	1 injection

*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**
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	2mL syringe
Supartz FX	Sodium hyaluronate	2.5 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

** All syringes/vials are single-use (i.e., one injection/one knee); syringes are pre-filled.

VII. References

1. Euflexxa Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals, Inc. July 2016. Available at http://www.euflexxa.com/. Accessed April 21, 2017.
2. Gel-One Prescribing Information. Warsaw, IN: Zimmer; May 2011. Available at http://www.zimmerbiomet.com/content/dam/zimmer-web/documents/en-US/pdf/medical-professionals/biologics-sports-medicine/Gel-One-Pkg-Insert-Final.pdf. Accessed April 21, 2017.
3. Hyalgan Prescribing Information. Parsippany, NJ: Fidia Pharma USA, Inc.; May 2014. Available at https://hyalgan.com/. Accessed April 21, 2017.
4. Monovisc Prescribing Information. Bedford, MA: Anika Therapeutics, Inc. March 2014. Received from distributor, DePuy Synthes Mitek Sports Medicine, April 21, 2017.
5. Orthovisc Prescribing Information. Woburn, MA: Anika Therapeutics, Inc.; June 2005. Received from distributor, DePuy Synthes Mitek Sports Medicine, April 21, 2017.
6. Supartz FX Prescribing Information. Durhan, NC: Bioventus, LLC; April 2015. Available at http://www.supartzfx.com/wp-content/uploads/2015/07/SUPARTZ_FX_Package_Insert.pdf. Accessed April 21, 2017.
7. Synvisc Prescribing Information. Ridgefield, NJ: Genzyme Biosurgery; September 2014. Available at http://products.sanofi.us/synvisc/synvisc.html. Accessed April 21, 2017.

8. Synvisc One Prescribing Information. Ridgefield, NJ: Genzyme Biosurgery; September 2014. Available at http://products.sanofi.us/synviscone/synviscone.html. Accessed April 21, 2017.
9. Hymovis Prescribing Information. Parsippany, NJ: Fidia Pharma USA, Inc.; October 2015. Available at http://www.hymovis.com/. Accessed April 21, 2017.
10. GenVisc 850 Prescribing Information. Doylestown, PA: Orthogen Rx, Inc.; Available at http://genvisc850.com/images/genvisc-850-full-prescribing-information.pdf. Accessed April 21, 2017.
11. Gelsyn-3 Prescribing Information. Durham, NC: Bioventus LLC; 2016. Available at https://www.gelsyn3.com/. Accessed April 21, 2017.
12. Tramadol Drug Monograph. Clinical Pharmacology. Accessed April 2017. http://www.clinicalpharmacology-ip.com
13. Strand V, Baraf HS, Lavin PT, et al. Effectiveness and safety of a multicenter extension and retreatment trial of Gel-200 in patients with knee osteoarthritis. Cartilage. 2012;3(4):297-304.
14. Sun SF, Hsu CW, Hwang CW, et al. Hyaluronate improves pain, physical function and balance in the geriatric osteoarthritic knee: A 6-month follow-up study using clinical tests. Osteoarthritis Cartilage. 2006;14:696-701.
15. Brown GA. American Academy of Orthopaedic Surgeons clinical practice guidelines: Treatment of osteoarthritis of the knee: Evidence-based guideline, 2nd edition. J Am Acad Orthop Surg. September 2013;21(9):577-9. doi: 10.5435/JAAOS-21-09-577.
16. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res. 2012;64(4):465-474.
17. Bannuru RR, Osani M, Vaysbrot EE, McAlindon TE. Comparative safety profile of hyaluronic acid products for knee osteoarthritis: a systematic review and network meta-analysis. Osteoarthritis Cartilage. August 2, 2016. pii: S1063-4584(16)30196-0. doi: 10.1016/j.joca.2016.07.010. [Epub ahead of print]
18. Hyaluronate derivatives: Drug Information. In: UpToDate (Lexicomp), Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed April 21, 2017.
19. Tramadol: Drug Information. In: UpToDate (Lexicomp), Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed April 21, 2017.
20. Rannou F, Peletier JP, Martel-Pelletier J. Efficacy and safety of topical NSAIDs in the management of osteoarthritis: Evidence from real-life setting trials and surveys. Semin Arthritis Rheum. 2016; 45:S18-S21.
21. McAlindon TE, Bannuru RR, Sullivan MC, at al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis Cartilage. 2014; 22:363-388.
Nelson AE, Allen KD, Golightly YM, et al. A systematic review of recommendations and guidelines for the management of osteoarthritis: The chronic osteoarthritis management initiative of the U.S. Bone and Joint Initiative. Semin Arthritis Rheum. 2014; 43:701-712.

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
J7320	Hyaluronan or derivative, GenVisc 850, for intra-articular injection, 1 mg
J7321	Hyaluronan or derivative, Hyalgan or Supartz, for intra-articular injection, per dose
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

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed, specialist reviewed	09/08	10/08
Reviewed with no clinical changes	11/12	12/12
Updated Appendix C for duplicative language	01/14	02/14
Removed requirement for enteric coated formulations Added requirement to fail physical therapy, Monovisc and Gel-One to available therapies Changed approval of Gel-One every 13 weeks and other products every 6 months Added need to document interference with ADLs, failure of tramadol Specialist reviewed	01/15	02/15
Removed limit of two injections Converted to bullet points and new template Removed max dosing of APAP and NSAIDs appendix Combined all safety related appendices into one appendix	08/15	10/15
Converted policy to new template. Added two new products approved in 2015: Hymovis and GenVisc850. Approval duration edited to one treatment course every 6 months rather than every 13 weeks. Removed “interference with ADLs” requirement. Edited step therapy to require an inadequate response to all of the following drugs: a two-week trial of oral NSAIDs if <75 years of age or unable to use oral NSAID, topical NSAID for ≥ 2 weeks, tramadol if no opioid abuse or dependence. Removed acetaminophen requirement.	09/16	10/16
Converted to new template. Added Gelsyn-3 to available therapies and prescriber specialty.	04/17	

Reviews, Revisions, and Approvals	Date	Approval Date
Modified tramadol requirement to exclude members currently receiving an opioid analgesic Removed requirements related to contraindications and hypersensitivity to hyaluronate preparations (initial) and reasons to discontinue (re-auth) per new safety approach/template update; HCPCS codes added. Specialist reviewed.		
Tramadol trial removed. Failure of glucocorticoid injections changed to partial response requirement.	08/17	08/17

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.