Subject: Hyaluronic Acid (HA) Injections/Viscosupplementation for Knee Osteoarthritis	**Original Effective Date:** 2/28/2008
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Contents

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP document and provide the directive for all Medicare members.

RECOMMENDATION

This policy addresses **Hyaluronic Acid (HA) Injections/Viscosupplementation** when appropriate criteria are met.

Viscosupplementation has been unable to demonstrate clear, consistent, patient centered outcomes, some health plans have discontinued coverage of these products. Molina Healthcare also recognizes that while the evidence and guidelines offer conflicting recommendations for the use viscosupplementation, these products may provide benefit for some. However, due to inconsistent evidence and limited effectiveness data, intraarticular hyaluronans should be reserved when other conservative options and guideline recommended treatments, both non-pharmacologic and pharmacologic, have been exhausted or are contraindicated.

PREFERRED Multiple brands of viscosupplementation are commercially available; however, there is no evidence, to date, that any specific product or brand have superior efficacy or safety. Molina Healthcare may authorize preferred product(s) when applicable.

Molina Healthcare reserves the right to update this policy and revise coverage criteria to include or omit any off-label condition(s) as necessary based on medical literature and clinical studies that may become available.

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Osteoarthritis (OA) of the Knee

- Characterized by articular cartilage loss, bone remodeling, and periarticular muscle weakness resulting in knee joint pain and instability
- The most common type of joint disease, affecting more than 30 million individuals in the United States
- Pathologically in the knee, osteoarthritis is characterized by deterioration and loss of articular cartilage, subchondral sclerosis and osteophyte formation
- No curative therapy available for osteoarthritis. Therapeutic goals in treatment for patients with knee OA include relief of pain and inflammation, and improvement in or maintenance of mobility, enhancing function (including activities of daily living [ADLs]), and improving health-related quality of life (HRQoL).
- Non-pharmacological treatments for patients with symptomatic early-stage knee OA include exercise, weight loss, and education. When these interventions are no longer effective, pharmacological treatments may be prescribed, including oral and topical non-steroidal anti-inflammatory drugs (NSAIDS), opioid analgesics, and topical capsaicin. As the disease progresses, intra-articular injections including corticosteroids and HA may be used. Surgery, including arthroscopy, osteotomy, and uni-compartmental and total joint replacement is generally indicted for end-stage knee OA that is resistant to other measures.

Sodium hyaluronate, also referred to as HA or hyaluronan

- Sodium hyaluronate is found in normal synovial fluid in the joints and has mechanical and biologic mechanisms of action and acts primarily as a joint lubricant and shock absorber. Viscosupplementation involves the intra-articular injection of exogenous HA into the joint to help replace that which is often lost in the synovial fluid of the intra-articular space. (Hayes, 2014, updated 2016)

- HA is a naturally occurring polysaccharide of the glycosaminoglycan family containing repeating disaccharide units of sodium-glucuronate-N-acetylglucosamine. HA, also known as hyaluronan, is a high molecular weight polysaccharide derived from chicken combs and necessary for proper function of the joints and it exerts its effect by replacing the depleted hyaluronan, which acts as a lubricant and shock absorber, in arthritic joints. HA derived from chicken combs, include Gel-One, Hyalgan, Supartz FX, Synvisc, Synvisc-One, Visco-3) or bacterial cells (Euflexxa, Gelsyn-3, Hymovis, Monovisc, Orthovisc.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

FDA-approved indication does not alone dictate coverage. Molina Clinical Policy may not recommend coverage for all FDA-approved indications. Please review this Policy in its entirety for indications covered by Molina Healthcare.

Osteoarthritis of the Knee Treatment of pain in osteoarthritis of the knee in patients who have failed non-pharmacologic treatment and simple analgesics (*Durolane*, *Euflexxa*, *Gel-One*, *Gelsyn-3*, *GenVisc 850*, *Hyalgan*, *Hymovis*, *Monovisc*, *Orthovisc*, *Supartz FX*, *Synvisc*, *Synvisc-One*, *Triluron*, *TriVisc*, *Visco-3*) or nonsteroidal anti-inflammatory drugs (NSAIDs) *(Gel-One)*
**The FDA has not approved intra-articular hyaluronan for joints other than the knee.*

Available as: Several HA agents are available, with varying molecular weights and injections per course of treatment (single injection HAs and those requiring 3 to 5 injections per course of treatment).

- Durolane; Euflexxa; Gel-One; Gelsyn-3; GenVisc 850; Hyalgan; Hymovis; Monovisc; OrthoVisc; Supartz FX; Supartz [discontinued]; Synvisc; Synvisc One; Triluron; TriVisc; Visco-3

- In general, the FDA classifies HA products as medical devices, rather than drug products. A medical device is a product that is intended to affect the structure or function of the body, but which does not achieve its primary intended purposes through the chemical action of a drug, nor is it dependent on being metabolized. These products either create volume and shape (e.g., ophthalmic, or cosmetic products containing these agents) or relieve pain via viscosity and lubrication (e.g., orthopedic products), and thus products containing this component are considered devices.

- HA products are regulated by the FDA as **Class III devices** under product code MOZ (acid, hyaluronic, intraarticular) (Premarket Approval (PMA) Database) and indicated for treatment of osteoarthritis (OA) pain in patients for whom conservative nonpharmacological treatments (e.g., physical therapy) and simple analgesics (e.g., acetaminophen) have failed to provide adequate relief.

Black Box Warning/REMS: None at the time of this writing

COSMETIC USE: NOT A COVERED BENEFIT
The FDA has approved several products containing a transparent HA gel to improve the contours of the skin. These products are used to treat acne, scars and wrinkles on the skin by temporarily adding volume to facial tissue and restoring a smoother appearance to the face (may not be an all-inclusive list):

- Restylane injectable gel received Premarket approval (PMA) approval March 25, 2005
- Perlane injectable gel received PMA approval May 2, 2007
- Hylaform received PMA approval April 22, 2004
- Juvéderm 24HV, Juvéderm 30 & Juvéderm 30HV Gel Implants received PMA approval June 2, 2006

COVERAGE CRITERIA FOR INITIAL AUTHORIZATION

HA Injections/Viscosupplementation may be authorized for members who meet **ALL** the following criteria

1. Prescriber specialty

- ❒ Prescribed by, or in consultation with, a board-certified orthopedic surgeon, pain management specialist, rheumatologist, physical medicine and rehabilitation specialist, or a sports medicine specialist. Submit consultation notes if applicable.

  NOTE: Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.

2. Diagnosis/Indication

Clinical documentation of ALL the following (includes clinical notes from the member's medical records, applicable labs and/or relevant tests supporting the diagnosis):

- ❒ Diagnosis of symptomatic osteoarthritis of the knee **documented** by **ONE** of the following
  - ❍ **Radiologic** evidence of osteoarthritis such as joint space narrowing, subchondral sclerosis, osteophytes, and sub-chondral cysts
    OR
  - ❍ **Symptomatic** osteoarthritis of the knee met by at least **FIVE (5)** of the following:
    **According to the American College of Rheumatology (ACR) clinical and laboratory criteria*
    - Bony enlargement
    - Bony tenderness
    - Crepitus (noisy, grating sound) on active motion
    - Erythrocyte sedimentation rate less than 40 millimeters/hour
    - Less than 30 minutes of morning stiffness (>45 minutes may indicate rheumatoid arthritis)
    - No palpable warmth of the synovium
    - Over 50 years of age
    - Rheumatoid factor less than 1:40 titer (agglutination method)
    - Synovial fluid signs (clear fluid of normal viscosity and white blood cell count less than 2000/millimeters^3

- ❒ Prescriber attestation that member has no evidence of inflammatory arthritis [Including, but not limited to: rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and systemic lupus erythematosus (lupus)] and other causes of musculoskeletal pain, including referred pain, bursitis, and inflammatory rheumatic diseases has been ruled out.
  - *Informational Note: Safety and efficacy in joints with severe inflammation have not been established. 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.*

❒ Affected knee(s): Left, right or both knees to be treated. Documentation of member's medical records, progress notes, and/or physical examination
*__NOTE:__ Bilateral injections may be allowed only if both knees meet criteria.

❒ Requested product is FDA indicated for intra-articular injection into the targeted joint

3. Age/Gender/Other restrictions [ALL]

❒ 18 years of age or older
- *Safety and efficacy of HA derivatives have not been established in pediatric patients*

❒ No history of failure on hyaluronic intra-articular injection (applicable to member's medical history prior to, and as a Molina member). Requests will not be authorized for members who have failed to respond to ANY previous viscosupplementation therapy.

NOTE: There is a lack of reliable evidence that any one brand of viscosupplement is more effective to other brands for medically necessary indications. There are also a lack of studies demonstrating that persons who fail to respond to one brand of viscosupplement will respond to other brands of viscosupplements).

4. Step/Conservative Therapy/Other condition Requirements [ALL]

❒ Surgical knee replacement is not a planned treatment option within 6 months of intra-articular viscosupplementation administration
- *There is no data to suggest efficacy of hyaluronate derivatives in patients who have had total knee arthroplasty in the targeted knee.*

❒ **Ineffectiveness/failure** *(defined as symptoms inadequately controlled after an adherent 3-month trial unless specified‡)*, **clinical intolerance** *(defined as an intolerance to the drug or its excipients)*; or **FDA-labeled contraindication(s)*** in the affected joint to the following treatments. Documentation of **ALL** of the following required:

❍ Non-pharmacologic modalities [e.g., weight loss, quadriceps muscle strengthening, other physical therapy modalities, or exercises]

AND

❍ Non-steroidal anti-inflammatory drugs (NSAIDs)
**Contraindications may include: 1) Compromised GI function or at risk of GI bleeding due to the adverse events of NSAIDs, 2) Concomitant anticoagulant therapy for any condition, 3) Cardiovascular or renal risk factors precluding use of COX-2 inhibitors.*

AND

❍ Acetaminophen (up to 1 g 4 times/day)

AND

- ❍ Corticosteroids: ‡Trial of at least **ONE** (1) intra-articular glucocorticoid injection with a documented positive but inadequate response unless contraindicated or history of intolerance **Contraindications may include increase in risk of local or systemic bacterial infection, e.g., diabetes mellitus*

MOLINA STAFF: Verify pharmacy claims data for above medications and compliance. For new members to Molina Healthcare, confirm medications use in medical or chart notes. Non-compliance or non-adherence does not constitute therapeutic failure.

- ❒ Member has no known contraindications to the preferred products: Euflexxa and Visco-3
  OR
- ❒ For member with a contraindication(s) to the preferred products: Submit all relevant clinical documentation for Pharmacy/Medical staff review

PREFERRED Products: Euflexxa and Visco-3 will be authorized for members who meet ALL of criteria in 'Initiation Authorization' section. Multiple brands of viscosupplementation are commercially available (refer to 'Administration, Quantity Limitations, and Authorization Period' section); however, there is no evidence, to date, that any specific product or brand is more effective than other brands for medically necessary indications. Molina Healthcare will authorize preferred product(s), Euflexxa and Visco-3, since other brands of viscosupplementation (e.g., Gel-One, Synvisc-One, Synvisc, Monovisc, Orthovisc) are more costly than Molina's preferred brands, and are likely to produce equivalent therapeutic results. Other brands are of viscosupplementation will be considered not medically necessary unless the member has a contraindication or intolerance to BOTH preferred brands.

5. Contraindications*/Exclusions/Discontinuations

Authorization will not be granted if ANY of the following conditions apply

- ❒ Non-FDA approved indication: Injection of these products for indications other than the diagnosis of osteoarthritis, or use of the requested products for injection into any joint other than the knee
- ❒ Active inflammatory joint disease or synovitis affecting the knee, such as crystal induced synovitis, rheumatoid arthritis
- ❒ Knee joint infections (septic arthritis) or a local skin disease or infection in the area of the injection site
- ❒ Known hypersensitivity to hyaluronan preparations or Allergies to avian or avian-derived products (including eggs, feathers, or poultry) NOTE: Not applicable to Orthovisc
  *HA is derived from chicken combs (Gel-One, Hyalgan, Supartz FX, Synvisc, Synvisc-One, Visco-3) or bacterial cells (Euflexxa, Gelsyn-3, Hymovis, Monovisc, Orthovisc)
- ❒ Hymovis, Monovisc and Orthovisc only: known hypersensitivity to gram positive bacterial proteins
- ❒ Monovisc *and* Durolane *only*: known systemic bleeding disorders
- ❒ Pregnant or nursing women
- ❒ Children under 18 years of age

6. Labs/Reports/Documentation required

All documentation for determination of medical necessity must be submitted for review. Prescriber to submit medical records and specific labs, chart notes, and documentation as indicated in the criteria above. Letters of support and/or explanation are often useful but are not sufficient documentation unless ALL specific information required by this MCP is included.

NOTE: Additional documentation, rationale, and/or supporting evidence may be requested for review as deemed necessary or appropriate by Molina Medical/Pharmacy staff

REAUTHORIZATION/CONTINUATION OF THERAPY

HA Injections/Viscosupplementation may be authorized for members who meet ALL the following criteria

1. Initial Coverage Criteria

- ❑ Member currently meets ALL initial coverage criteria

- ❑ Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually. The prescribing physician should periodically reassess the need for continuation of therapy based on the member's condition and continued need. Continuation of therapy requires submission of relevant medical records or chart notes documenting continued efficacy.

2. Compliance

- ❒ At least six (6) months have elapsed since the initial or prior treatment cycle

3. Labs/Reports/Documentation required

Intra-articular injections of sodium hyaluronate has resulted in **clinical improvement** as documented by the following *from baseline***.** Documentation required.

- ❒ Member has not had total or partial joint replacement surgery
  - *There are no clinical trials evaluating the use of sodium hyaluronate in persons following total or partial joint replacement surgery.*

- ❒ Positive response after 3 months of therapy documented by the following: [ALL]

  - ❍ Significant improvement in pain and functional capacity as the result of the previous series of injections as indicated by any type of objective/quantification method, such as Visual Analog Scale for pain, joint mobility, reduction in effusion, and/or patient-response-based questionnaires

- ❍ A significant reduction in the dose/utilization of NSAIDs (or other analgesics or anti-inflammatory medication)

- ❍ A reduction in the number of accompanying intra-articular corticosteroid injections during the six (6) month period following the previous series of injections

NOTE:

- In addition to the documentation required above, the Prescriber additional medical documentation as requested by Medical Reviewer to support the need for repeat courses of treatment may be required.
- If the initial or prior series of injections is not proven or documented as beneficial to the member, it is not considered medically necessary to repeat the therapy and a repeat series of injections will not be authorized.

4. Discontinuation of Treatment

Discontinue treatment if ANY of the following conditions apply:

- ❒ Intolerable adverse effects or absence of unacceptable toxicity from the drug
- ❒ Persistent and uncorrectable problems with adherence to treatment
- ❒ Poor response to treatment as evidenced by physical findings and/or clinical symptoms

Contraindications/Exclusions to therapy

Authorization will not be granted if ANY of the following conditions apply:

- ❒ Non-FDA approved indications
- ❒ Active inflammatory joint disease or synovitis affecting the knee, such as crystal induced synovitis, rheumatoid arthritis
- ❒ Knee joint infections (septic arthritis) or a local skin disease or infection around the injection site
- ❒ Known hypersensitivity to hyaluronan preparations or Allergies to avian or avian-derived products (including eggs, feathers, or poultry) NOTE: Not applicable to Orthovisc

  *HA is derived from chicken combs (Gel-One, Hyalgan, Supartz FX, Synvisc, Synvisc-One, Visco-3) or bacterial cells (Euflexxa, Gelsyn-3, Hymovis, Monovisc, Orthovisc)
- ❒ Hymovis, Monovisc and Orthovisc only: known hypersensitivity to gram positive bacterial proteins
- ❒ Monovisc *and* Durolane *only*: known systemic bleeding disorders
- ❒ Pregnant or nursing women
- ❒ Younger than18 years of age

ADMINISTRATION, QUANTITY LIMITATIONS, AUTHORIZATION PERIOD

Consult the manufacturer's labeling for more detailed information on dosage and administration of this drug, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and monitoring.

1. Recommended Dosage

Table 1: FDA Labeled Dosage per Treatment Course per Joint

Drug	Dose	Total Injections
Durolane (hyaluronic acid)	60 mg (3 ml) intra-articularly **once**	1 injection
Euflexxa (1% sodium hyaluronate)	20 mg (2 mL) intra-articularly once weekly for 3 weeks	3 injections
Gel-One (Cross-linked Hyaluronate)	30 mg (3 mL) intra-articularly **once**	1 injection
Gelsyn-3 (0.84% sodium hyaluronate)	16.8 mg (2 mL) intra-articularly once weekly for 3 weeks	3 injections
GenVisc 850 (sodium hyaluronate)	25 mg (2.5 mL) intra-articularly once weekly for 5 weeks. Some patients may benefit from 3 injections given at weekly intervals	3 to 5 injections
Hyalgan (sodium hyaluronate)	20 mg (2 mL) intra-articularly once weekly for 5 weeks. Some patients may benefit with 3 injections given at weekly intervals	5 injections
Hymovis (high molecular weight hyaluronan)	24 mg (3 mL) intra-articularly once weekly for 2 weeks (total of 2 injections)	2 injections
Monovisc (high molecular weight hyaluronan)	88 mg (4 mL) intra-articularly once	1 injection
Orthovisc (high molecular weight hyaluronan)	30 mg (2 mL) intra-articularly once weekly for 3 or 4 weeks	3 to 4 injections
Supartz FX	25 mg (2.5 mL) intra-articularly once weekly for 5 weeks. Some patients may benefit with 3 injections given at weekly intervals	
Synvisc One (Hylan G-F 20)	48 mg (6 mL) intra-articularly once	1 injection
Synvisc (Hylan G-F 20)	16 mg (2 mL) intra-articularly once weekly for 3 weeks	3 injections
Triluron (sodium hyaluronate)	20 mg (2 mL) once weekly for 3 weeks	3 injections
TriVisc (sodium hyaluronate)	25 mg (2.5 mL) once weekly for 3 weeks	3 injections
Visco-3	25 mg (2.5 mL) intra-articularly once weekly for 3 weeks	3 injections

2. Authorization Limit

- ❒ **PREFFERED Products: Euflexxa and Visco-3** will be authorized for members who meet ALL of criteria in 'Initiation Authorization' section.
  - Molina Healthcare will authorize preferred product(s) under the applicable benefit since other brands of viscosupplementation (refer to 'Table 1' above) are more costly than Molina's preferred brands and are likely to produce equivalent therapeutic results.
  - Other brands are of viscosupplementation will be considered not medically necessary unless the member has a contraindication or intolerance to BOTH preferred brands.
  - Multiple brands of viscosupplementation are commercially available; however, there is no evidence, to date, that any specific product or brand is more effective than other brands for medically necessary indications.

- ❒ Quantity limit
  - ❍ The dose of an injection and the number of injections per treatment cycle exceeding FDA labeling will **not** be authorized (Table 1)

- ❒ Duration of authorization
  - ❍ Initial authorization: A single course per joint every 6 months
  - ❍ Continuation of treatment: At least **six (6) months** have elapsed since the initial or prior treatment cycle for the respective joint. Re-authorization is required every **6 months** to determine effectiveness of therapy and continued need based on documented positive clinical response. *Refer to 'Continuation of Therapy' section.*

3. Route of Administration

- ❒ Intra-articular injections of sodium hyaluronate is considered a **provider-administered**, **outpatient** treatment by health care providers experienced in the administration of Intra-articular injections of sodium hyaluronate
- ❒ Refer to Specialty Medication Administration Site of Care Policy P&P: MHI Pharm 11

LIMITATIONS

All other uses of intra-articular hyaluronan injections that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy is considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

- ❒ Non-FDA approved indications: The use of intra-articular hyaluronan injections into joints other than the knee or any other indication other than osteoarthritis have **not** been medically proven to be effective are considered investigational, including (but not limited to) the following:
  - ❍ Pain due to OA in any joint other than the knee
  - ❍ Post ACL reconstruction, menisectomy, total knee arthroplasty or temporomandibular disorders
  - ❍ Any other form of arthritis, including:
    - o Rheumatoid Arthritis (RA)
    - o Osteoarthritis of the hand, hip, and temporomandibular joint
    - o Treatment of non-radicular pain in the lumbar spine
  - ❍ Following total or partial knee joint replacement

- ❒ Younger than 18 years of age

- ❒ Non-FDA approved dosing regimen(s)

- ❒ Known hypersensitivity to hyaluronan preparations or Allergies to avian or avian-derived products (including eggs, feathers, or poultry) NOTE: Not applicable to Orthovisc
  *HA is derived from chicken combs (Gel-One, Hyalgan, Supartz FX, Synvisc, Synvisc-One, Visco-3) or bacterial cells (Euflexxa, Gelsyn-3, Hymovis, Monovisc, Orthovisc)

- ❒ Hymovis, Monovisc and Orthovisc only: known hypersensitivity to gram positive bacterial proteins

- ❒ Monovisc *and* Durolane *only*: known systemic bleeding disorders

- ❒ Administration in any manner other than the FDA-approved administration will not be authorized

SUMMARY OF CLINICAL EVIDENCE

HA Injections/Viscosupplementation

Viscosupplementation is a therapeutic modality for the treatment of osteoarthritis based on the physiologic importance of hyaluronan in synovial joints (Bellamy, 2002)

- Viscosupplements contain hyaluronate. Hyaluronates are also referred to as HA or hyaluronan.
- HA is a naturally occurring polysaccharide of the glycosaminoglycan family containing repeating disaccharide units of sodium-glucuronate-N-acetylglucosamine. HA is a large viscoelastic glycosaminoglycan molecule that is found naturally in synovial fluid and cartilage, important for shock absorption, traumatic energy dissipation, protective coating of the articular cartilage surface, and lubrication. Individuals with knee OA tend to have lower concentrations of HA.
- Its therapeutic goal is to restore the visco-elasticity of synovial hyaluronan, thereby decreasing pain, improving mobility and restoring the natural protective functions of hyaluronan in the joint.

Clinical studies of sodium hyaluronate and hylan G-F-20 have demonstrated that injection of these agents into the joint space of osteoarthritic knees is sometimes marginally more effective than placebo procedures in reduction of pain and improvement in functional capacity in some patients. These marginal beneficial results are more pronounced with the larger molecular weight compound hylan G-F20.

There is no data indicating that these agents reverse or delay the osteoarthritic process in the injected joints. The long-term effects of repeated injections are unknown.

Clinical Practice Guidelines

- The majority of guidelines did not find sufficient evidence to make a recommendation for or against the use of HA for knee OA. [APPENDIX 1: GUIDELINES AND RESOURCES (references as stated in section)]
- There is inconsistent evidence and limited effectiveness data that viscosupplementation, or HA products, produces clinically relevant improvements in pain and functioning for OA of the knee and no evidence to suggest it delays the progression of OA nor the progression to knee replacement.

- Several major practice guidelines have been unable to recommend intraarticular hyaluronan (IA HA), with others recommending against its use with several other major organizations.

American Academy of Orthopedic Surgeons (AAOS) In the second edition of the evidence-based guidelines on treatment of OA of the knee, the AAOS issued a "Strong" recommendation against the use of HA for knee OA due to lack of efficacy (AAOS, 2013).

National Institute for Health and Care Excellence (NICE 2014) recommended against HA for knee OA

American College of Rheumatology (ACR 2012) clinical practice guidelines on osteoarthritis indicate they have no recommendations regarding the use of IAHA in the knee. Recommendations for the use of pharmacologic therapies in knee OA include acetaminophen, oral and topical NSAIDs, tramadol and intra-articular corticosteroid injections. The ACR conditionally recommends IA-HA for patients who had inadequate relief with initial treatment for knee OA in evidence-based guidelines (Hochberg et al., 2012). An update of this guideline is anticipated in 2018 (Osteoarthritis: Call for Public Comment on Project Plan).

American Medical Society for Sports Medicine (AMSSM) Based on findings from their systematic review with network meta-analysis, the AMSSM recommended IA-HA for appropriate patients with knee OA. Criteria for appropriate patients were not reported. (Trojian et al., 2016)

Osteoarthritis Research Society International (OARSI) 2014 guideline update provided an "uncertain" recommendation for IAHA, indicating an overall small effect size on pain, inconsistent results among the available meta-analyses, and one meta-analysis signaling potential for serious safety concerns, influenced their recommendation.

ECRI Institute. Viscosupplementation for Treating Osteoarthritic Knee Pain A 2019 ECRI report on viscosupplementation summarized evidence from 8 systematic reviews and 6 RCTs (total patients = 12,775) to be inconclusive for treating knee pain due to OA. While IA HA injections may provide relief in some patients, uncertainty remains about the most effective formulations, which populations benefit most, and whether HA should be combined with other agents to increase efficacy. (ECRI; 2019)

APPENDIX

Appendix 1: Guidelines and Resources

Guideline Comparison

- Comparison of 2 guidelines (AAOS 2013, VA/DoD 2014) on nonsurgical management of osteoarthritis of the knee Reference: National Guideline Clearinghouse 2016 Jun 13:50210
- Comparison of 16 guidelines on the management of osteoarthritis
  Reference: Semin Arthritis Rheum 2014 Jun;43(6):701

CODING INFORMATION

The codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is covered or non-covered. coverage is determined by the benefit document. this list of codes may not be all inclusive.

HCPCS	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, supartz or visco-3, for intra-articular injection, per dose Effective Date: 04/01/2021

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, GelSyn-3, 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--Effective July 1, 2020 Discontinue existing HCPCS code J7333 "Hyaluronan or derivative, visco-3, for intra-articular injection, per dose." --Effective Date: 03/31/2021	

REFERENCES

Government Agencies, Drug Compendia

Durolane (sodium hyaluronate) [prescribing information]. Durham, NC: Bioventus LLC; October 2017

Euflexxa (sodium hyaluronate) [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals Inc; July 2016.

Hyalgan (hyaluronic acid derivative) [prescribing information]. Parsippany, NJ: Fidia Pharma; May 2014.

Hymovis (hyaluronic acid derivative) [prescribing information]. Parsippany, NJ: Fidia Pharma; October 2015.

Gel-One [prescribing information]. Warsaw, IN: Zimmer; May 2011.

Gelsyn-3 (sodium hyaluronate) [prescribing information]. Durham, NC: Bioventus; 2016.

GenVisc 850 (sodium hyaluronate) [prescribing information]. Doylestown, PA: OrthogenRx Inc; no date.

Monovisc [prescribing information]. Bedford, MA: Anika Therapeutics; December 2013.

Orthovisc [prescribing information]. Raynham, MA: Anika Therapeutics; June 2005.

Synvisc [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.

Synvisc One [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.

Supartz FX (sodium hyaluronate) [prescribing information]. Durham, NC: Bioventus; April 2015.

Triluron (sodium hyaluronate) [prescribing information]. Florham Park, NJ: Fidia Pharma USA Inc.; July 2019.

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Policy History	Approval
Policy Developed	MCPC 2/28/2008
Review Date(s): 10/26/2011, 12/16/2015, 6/15/2016, 3/21/2017, 9/13/2018	MCPC
Revision IRO Specialist Peer Review: Practicing Physician. Board certified in Orthopedic Surgery. Date completed: 8/21/2018.	MCPC 9/13/2018
Revision IRO Specialist Peer Review: Practicing Physician. Board certified in Orthopedic Surgery, Surgery Spine. Date completed: 9/10/2019	P&T Q4 2019
Revision IRO Specialist Peer Review: Practicing Physician. Board certified in Orthopedic Surgery, Surgery Spine. Date completed: 3/24/2020 Notable revisions: 1) Added 'no history of failure' criterion (under 'Age/Gender/Other restrictions' on page 5 of 14); 2) Added 'preferred brand' criterion (under #4 Step/Conservative Therapy/Other condition Requirements on page 6 of 14); updated the 'Preferred Products' criterion language (in the 'Administration, Quantity Limitations, and Authorization Period' section) to reflect the 'preferred' language (under #4 Step/Conservative Therapy/Other condition Requirements on page 6 of 14)	P&T Q2 2020
Annual Review The medical necessity criteria were not revised with this annual review. Clarifications and updates made throughout policy includes: • Removed Supartz product, which was discontinued from policy • Updated 'Table 1: FDA Labeled Dosage per Treatment Course per Joint'	MCPC 4/5/2021

**All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections reviewed and revised with the most recent medical literature and available evidence for both 'Annual Reviews' and 'Policy Revisions.' Annual Reviews without notable changes to coverage criteria or position may not require Peer Review. Policy Revisions include notable content updates or revisions that which may have affected criteria or requires review by a practicing specialist, Peer Reviewer.*