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Medication Policy Manual

Policy No: dru351

Topic: Intra-articular Hyaluronic Acid Derivatives: **Date of Origin:** May 09, 2014

- 1% sodium hyaluronate (Euflexxa)
- high molecular weight hyaluronan (Hymovis)
- high molecular weight hyaluronan (Orthovisc)
- hylan G-F 20 (Synvisc, Synvisc-One)
- sodium hyaluronate (Gel-One)
- sodium hyaluronate (Gel-Syn)
- sodium hyaluronate (GenVisc 850)
- sodium hyaluronate (Monovisc)
- sodium hyaluronate (Hyalgan)
- sodium hyaluronate (Supartz)
- sodium hyaluronate (Durolane)

Committee Approval Date: January 31, 2019

Next Review Date: January 2020

Effective Date: April 1, 2019

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

High molecular weight hyaluronan (Orthovisc), high molecular weight hyaluronan (Hymovis), sodium hyaluronate (Gel-One), sodium hyaluronate (Gel-Syn), sodium hyaluronate (GenVisc 850), sodium hyaluronate (Monovisc), sodium hyaluronate (Hyalgan), sodium hyaluronate (Supartz), 1% sodium hyaluronate (Euflexxa), sodium hyaluronate (Durolane), and hylan G-F 20 (Synvisc/Synvisc-One) are hyaluronic acid derivatives that are injected directly into the knee joint to help improve the pain associated with osteoarthritis of the knee.

Policy/Criteria

- I. Hyaluronic acids are considered not medically necessary for osteoarthritis of the knee.
- II. Hyaluronic acids are considered not medically necessary for skin wrinkles or other cosmetic indications.
- III. Hyaluronic acids are considered investigational when used for all other conditions, including but not limited to:
 - A. Osteoarthritis in joints other than the knee
 - B. Temporomandibular joint degenerative disorders
 - C. Trigger finger

Position Statement

- Hyaluronic acids are used as viscosupplementation and are injected directly into the knee joint to improve lubrication and reduce the pain associated with osteoarthritis of the knee.
- Given the inconclusive evidence for safety and efficacy, as well as the lack of support by evidence-based clinical guidelines, the use of hyaluronic acids for osteoarthritis of the knee is considered not medically necessary.
 - * Hyaluronic acids are not recommended by the American Academy of Orthopedic Surgeons (AAOS) guidelines for management of osteoarthritis of the knee. The strength of this recommendation is characterized as “strong” as it is based on multiple high-quality studies. ^[1]
 - * Standard therapies for treatment of knee pain related to arthritis include oral NSAIDs (such as ibuprofen, naproxen, or diclofenac), corticosteroid injections, and physical therapy/exercises. These therapies are effective for providing pain relief for the vast majority of patients.
 - * There is limited evidence demonstrating that hyaluronic acids are more effective than placebo or non-pharmacologic therapy at increasing mobility and reducing pain associated with osteoarthritis of the knee.
 - * There is no evidence that hyaluronic acids are effective in patients who have persistent knee pain and/or functional impairment despite use of these standard therapies. Additionally, hyaluronic acids have not been found to be more effective than all these standard therapies.
- Hyaluronic acids have not been shown to impact quality of life in patients who are not a candidate for surgery. A 2015 AHRQ review noted that there was no significant difference in quality of life measures associated with HLA treatment; the impact on function appears to be minimal based on analysis of secondary endpoints. ^[4]
- There are inadequate data to determine the benefit of multiple treatment courses of hyaluronic acids.

- Retrospective data suggests that use of intra-articular hyaluronic acid injections is associated with an increase in health-care costs and utilization. [2]
- There is inadequate evidence to support the use of hyaluronic acids in temporomandibular joint degenerative disorders or trigger finger.

CLINICAL EFFICACY

- Hyaluronic acids have not been proven in reliable clinical studies to be more effective than non-pharmacologic or generic analgesics such as acetaminophen and NSAIDs.
 - * Systematic reviews of randomized controlled trials evaluating viscosupplementation in patients with osteoarthritis of the knee conclude that there are low quality data available to determine efficacy and safety.
 - * Clinical trials studying the effect of viscosupplementation on knee pain and functional outcomes have reported inconsistent results. Intra-articular injections are associated with a robust placebo-response; it is unclear if hyaluronic acid differs from placebo in a clinically meaningful way.
 - * Several studies have reported no improvement in pain or mobility compared to placebo, simple analgesics, or exercise. [3-6]
- A 2015 Agency for Healthcare Research and Quality (AHRQ) review of clinical trials found no significant association between treatment with HLA and time to total knee arthroplasty (TKA). [4,5] The authors concluded that there is insufficient data to make any conclusions regarding the effect of HLA treatment on time to TKA.
- There is no reliable evidence, based on two comparative trials identified, to differentiate between hyaluronic acid products used for viscosupplementation in terms of safety or efficacy.
 - * One randomized controlled trial in 660 patients with osteoarthritis of the knee did not demonstrate a difference in efficacy or safety of Synvisc compared with Orthovisc. [7]
 - * A randomized trial comparing the effectiveness of Synvisc and Hyalgan is unreliable due to uncertain blinding which may have influenced patient reported outcomes. [8]

Guidelines

- Systematic reviews and clinical guidelines have concluded that there is limited evidence to support subsequent treatment courses with hyaluronic acids; however, individual patients may benefit from additional courses of hyaluronic acids. [1,9]
- The American Academy of Orthopaedic Surgeons cannot recommend the use of hyaluronic acid for patients with symptomatic osteoarthritis of the knee. The AAOS graded the recommendation as “Strong,” which means that the strength of the supporting evidence is high. Guidelines state that “Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.” [1]

- * The AAOS position is based on assessment of the clinical meaningfulness of the result. The AAOS analysis concluded that the point estimate for the improvement in pain and function was less than half the pre-defined magnitude for clinically meaningful improvement.
- While there may be differences in efficacy based on the molecular weight of the hyaluronic acid, meta-analyses supporting the AAOS clinical guidelines found that there was no difference between medium- and high-molecular weight hyaluronic acid. The guideline recognized that, while there is the potential for a difference to exist, there is not yet sufficient evidence to recommend use of high molecular weight hyaluronic acid given the aggregate lack of efficacy.^[1]

SAFETY

- The most common adverse events reported with hyaluronic acids include joint pain, stiffness and swelling, as well as injection site reactions. ^[16-23]

INVESTIGATIONAL USES

Use in Joints Other than the Knee

- Hyaluronic acids have been studied in the treatment of osteoarthritis of joints other than the knee, including the hip, shoulder, and ankle.
 - * Small studies in patients with osteoarthritis of the ankle demonstrated that hyaluronic acid may be an effective treatment option; however several larger, well-controlled trials have concluded that hyaluronic acid is not effective in this setting (no different than saline). ^[10-13]
 - * A randomized trial found hyaluronic acid to be no more effective than placebo in the treatment of osteoarthritis of the hip. ^[14]
 - * A randomized trial in patients with osteoarthritis of the shoulder did not demonstrate a significant difference in pain on movement between patients treated with sodium hyaluronate or placebo. ^[15]

Temporomandibular Joint (TMJ) degenerative disorders

- Several small studies have evaluated hyaluronic acids in the treatment of symptoms of TMJ degenerative disorders (pain, range-of-motion, chewing efficiency). Larger, well-controlled studies are needed to confirm the benefit of hyaluronic acids and to determine the optimal frequency, dose, and product.^[24-27]

Trigger finger

- One small randomized, controlled trial (N=36) evaluated patients with a diagnosis of trigger finger. Patients were randomized to hyaluronic acid or steroid injections, after the months of follow-up the percent of patients without triggering effect was numerically lower in the hyaluronic acid group, but not statistically significant. While promising the results must be confirmed in larger studies. Additionally the optimal frequency, dose, and hyaluronic acid product has not been determined.^[28]

Cross References

Intra-articular Hyaluronan Injections for Osteoarthritis, BlueCross BlueShield Association Medical Policy, 2.01.31, Issue 04:2016

Codes	Number	Description
HCPCS	J7323	Hyaluronan or derivative, Euflexxa, for intra-articular injection, per dose
HCPCS	J7321	Hyaluronan or derivative, Hyalgan or Supartz, for intra-articular injection, per dose
HCPCS	J7324	Hyaluronan or derivative, Orthovisc, for intra-articular injection, per dose
HCPCS	J7325	Hyaluronan or derivative, Synvisc or Synvisc-one, for intra-articular injection, 1 mg
HCPCS	J7326	Hyaluronan or derivative, Gel-One, for intra-articular injection, per dose
HCPCS	J7327	Hyaluronan or derivative, Monovisc, for intra-articular injection, per dose
HCPCS	J7328	Hyaluronan or derivative, Gel-Syn, for intra-articular injection, per dose
HCPCS	Q9980	Hyaluronan or derivative, GenVisc 850, for intra-articular injection, per dose
ICD-9	715.16	Osteoarthritis localized primary involving lower leg
ICD-10	M17.0	Bilateral primary osteoarthritis of knee

References

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Revision History

Revision Date	Revision Summary
1/31/2019	No criteria changes with this annual update.
12/14/2018	No criteria changes with this annual update.
12/8/2017	No criteria changes with this annual update. Added sodium hyaluronate (Durolane) to policy.
4/14/2017	No criteria changes with this annual update.
4/8/2016	Added temporomandibular joint disorders and trigger finger as investigational uses
05/09/2014	New policy

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