

Evidence Based Guideline

Intra Articular Hyaluronan Injections for Treatment of Osteoarthritis of the Knee

File Name: Intra_articular_hyaluronan_injections_for_treatment_of_osteoarthritis_of_the_knee
Origination: 12/1997
Last CAP review 7/2011
Next CAP review 7/2012
Last Review: 7/2011

Description of Procedure or Service

Hyaluronan (HA), also known as hyaluronate or hyaluronic acid, is a naturally occurring macromolecule that is a major component of synovial fluid and is thought to contribute to its viscoelastic properties. Chemical crosslinking of hyaluronan increases its molecular weight; crosslinked hyaluronans are referred to as hylans. In osteoarthritis, the overall length of HA chains present in cartilage and the HA concentration in the synovial fluid are decreased. Intra-articular injection of HA (IA-HA) has been proposed as a means of restoring the normal viscoelasticity of the synovial fluid in patients with osteoarthritis. This treatment has been called viscosupplementation.

Currently, no curative therapy is available for osteoarthritis, and thus the overall goals of management are to reduce pain and prevent disability. In 1995, the American College of Rheumatology published guidelines for the treatment of osteoarthritis of the knee, which recommended acetaminophen as first-line therapy, followed by low-dose ibuprofen and then full-dose non-steroidal anti-inflammatory drugs (NSAIDs), if necessary. Five preparations of intra-articular hyaluronan have been approved by the U.S. Food and Drug Administration (FDA) as an alternative to NSAID therapy in the treatment of osteoarthritis of the knee (Synvisc®, Biomatrix; Hyalgan®, Fidia; Supartz®, Smith and Nephew; OrthoVisc®, OrthoBiotech; and Euflexxa®, previously named Nuflexxa, Savient). All products are manufactured from rooster combs except for Euflexxa, which is the only non-avian derived hyaluronan approved in the United States. Also, Synvisc undergoes additional chemical crosslinking to create hylans with increased molecular weight compared to Hyalgan and Supartz. The differing molecular weights of the products lead to different half-lives; the half-life of Hyalgan or Supartz is estimated at 24 hours, while the half-life of Synvisc may range up to several days.

Intra-articular hyaluronic acid is “indicated for the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy, and to simple analgesics, e.g., acetaminophen.” The product inserts indicate that Synvisc and Euflexxa should be injected intra-articularly into the knee joint once per week for a total of 3 injections over a 2- to 3-week period. In contrast, 5 weekly injections are recommended for the Hyalgan and Supartz products, and 3–4 weekly injections are recommended for OrthoVisc. The FDA approved removal of a precautionary statement from the package inserts for sodium hyaluronate (MW 500-730 kDa) and hylan G-F 20 that stated that the safety and efficacy of repeat courses have not been established. In February 2009, the FDA approved the use of single-dose hylan G-F 20 (Synvisc-One™) for the treatment of osteoarthritis of the knee.

The FDA has not approved intra-articular hyaluronan for joints other than the knee.

*****Note: This Evidence Based Guideline is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Intra Articular Hyaluronan Injections for Treatment of Osteoarthritis of the Knee

Evidence Based Guideline for Intra-Articular Hyaluronan Injections

Intra-articular hyaluronan injections may be appropriate for the treatment of pain in osteoarthritis of the knee when conservative treatment has failed.

The medical record should document conservative therapy as follows:

- Diagnosis of osteoarthritis substantiated by x-ray or other imaging or arthroscopic findings, and
- Complaints of persistent pain while using simple analgesics and non-steroidal anti-inflammatory drugs, and
- Aspiration of the joint resulting in clear viscous aspirate, when effusion is present, followed by injection of steroid that result in unsatisfactory relief of pain or relief of pain that lasts less than three months.

Repeated courses of intra-articular hyaluronan injections may be appropriate when significant pain relief was achieved with the prior course of injections and at least six months have passed since the prior course of treatment.

Medical Evidence regarding Intra-Articular Hyaluronan Injections indicates it is not recommended in the following situations

Intra-articular hyaluronan injections are not recommended for any indication other than osteoarthritis or for treatment of osteoarthritis in any joint but the knee.

Benefits Application

This evidence based guideline relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this guideline.

Billing/Coding/Physician Documentation Information

This guideline may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J7321, J7323, J7324, J7325, J7326

Scientific Background and Reference Sources

MEDLINE search January 1996 through December 1997

USPDI

Consultant Review, March 1997

Medical Policy Advisory Group, 5/28/98

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Specialty Matched Consultant Advisory Group 11/1999

Medical Policy Advisory Group, 12/2/1999

BCBSA Medical Policy Reference Manual 8/18/2000, 2.01.31

Medical Policy Advisory Group - 10/2000

BCBSA Medical Policy Reference Manual 5/31/01; 2.01.31

Specialty Matched Consultant Advisory Panel - 8/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.31, 4/29/03

Hammesfahr JF, Knopt AB, Stitik T. (June 2003). Safety of intra-articular hyaluronates for pain associated with osteoarthritis of the knee. *Am J Orthop*, 32(6), 277-83. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12834190.

Hamburger MI, Lakhanpal S, Mooar PA, Oster D. (April 2003). Intra-articular Hyaluronans: a review of product-specific safety profiles. *Semin Arthritis Rheum*, 32(5), 296-309. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12701040.

Waddell DD, Cefalu CA, Bricker DC. (2003). An open-label study of a second course of hylan G-F 20 for the treatment of pain associated with knee osteoarthritis. *Curr Med Res Opin*, 19(6), 499-507. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14594522.

Waddell DD. (2003). The tolerability of viscosupplementation: low incidence and clinical management of local adverse events. *Curr Med Res Opin*, 19(7), 575-80. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14626291.

Lo GH, LaValley M, McAlindon T, Felson DT. (December 2003). Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. *JAMA*, 290(23), 3115-21. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14679274.

Caborn D, Rush J, Lanzer W, Parenti D, Murray C; Synvisc 901 Study Group. (February 2004). A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol*, 31(2), 333-43. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14760806.

Lee S, Park D, Chmell SJ. (April 2004). Viscosupplementation with hylan G-F 20 (Synvisc): pain and mobility observations from 74 consecutive patients. *J Knee Surg*, 17(2), 73-7. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15124659.

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Goldberg VM, Coutts RD. (February 2004). Pseudoseptic reactions to hylan viscosupplementation: diagnosis and treatment. *Clin Orthop*, (419), 130-7. Retrieved on May 26, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15021143.

Specialty Matched Consultant Advisory Panel - 7/2004

BCBSA TEC Special Report [Electronic Version]. February 2005.

Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. *The Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD005321. DOI: 10.1002/14651858.CD005321.

Samson DJ, Grant MD, Ratko TA, Bonnell CJ, Ziegler KM, Aronson N. Treatment of Primary and Secondary Osteoarthritis of the Knee. Evidence Report/Technology Assessment No. 157 (Prepared by Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-based Practice Center under Contract No. 290-02-0026). AHRQ Publication No. 07-E012. Rockville, MD: Agency for Healthcare Research and Quality. September 2007. Retrieved 5/28/08 from <http://www.ahrq.gov/downloads/pub/evidence/pdf/oaknee.pdf>

Dagenais S. Intra-articular hyaluronic acid (viscosupplementation) for knee osteoarthritis. [Issues in emerging health technologies issue 94]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006. Retrieved 5/20/08 from http://www.cadth.ca/media/pdf/E0010_viscosupplementation_cetap_e.pdf
BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.31, 12/13/07
National Institute for Health and Clinical Excellence (NICE). National Collaborating Centre for Chronic Conditions. Osteoarthritis: national clinical guideline for care and management in adults. London: Royal College of Physicians, 2008. Retrieved 5/20/08 from <http://www.nice.org.uk/nicemedia/pdf/CG059FullGuideline.pdf>

Chevalier X, Jerosch P, Goupille P, et al. (March 2009). Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: a randomised, multicentre, double-blind, placebo controlled trial. *Ann Rheum Dis*. 69(1): 113–119. Retrieved on May 20, 2010 from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2789938/?tool=pubmed>

BCBSA Medical Policy Reference Manual [Electronic Version].2.01.31, 07/09/09

Specialty Matched Consultant Advisory Panel review 7/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.31, 02/10/11

Specialty Matched Consultant Advisory Panel review 7/2011

Policy Implementation/Update Information

12/97 Original policy developed. Reviewed by the Plan's Medical Director and determined investigational.

3/98 Reviewed: Continues to appear investigational due to approval as device and no long term outcomes.

6/98 Reviewed: Medical Policy Advisory Group recommends approval of one time treatment cycle for individuals with osteoarthritis of the knee who have failed to respond to conservative therapy. Policy name changed from Sodium Hyaluronate.

9/98 Code changes. J3490 deleted. Codes W5184 and W5179 added.

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- 6/99 Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.
- 12/99 Reaffirmed, Medical Policy Advisory Group
- 10/00 Revised. Changed the indications to include repeat treatment cycles when specific criteria are met. Added comment that treatment cycles should include no more than 3 injections for Synvisc and 5 injections for Hyalgan. System coding changes. Medical Policy Advisory Group - Approved.
- 5/01 Changes in formatting.
- 9/02 Specialty Matched Consultant Advisory Panel meeting 8/2002. Revised policy to include Supartz. Added term Supartz to the Policy Key Word section. Code J7315 deleted and code Q3030 added. System coding changes.
- 3/25/04 Added code J7317 to the Billing/Coding section. Removed code Q3030 from the Billing/Coding section. Benefits Application and Billing/Coding sections updated for consistency.
- 8/12/04 Specialty Matched Consultant Advisory panel review 07/15/2004 with no changes made to policy criteria. References added. Statement added, "e.g., rest, anti-inflammatory medications, physical therapy" to define conservative measures.
- 9/9/04 Title changed from "Intra Articular Hyaluronan Injections for Treatment of Osteoarthritis of the Knee." to "Intra Articular Hyaluronan Injections for Osteoarthritis of the Knee" for purpose of reducing characters.
- 1/05/06 Added policy number to Key Words. CPT Code J7318 added to Billing/Coding section.
- 2/16/06 Deleted code J7318 from Billing/Coding section. This code was never made valid by Centers for Medicare & Medicaid Services (CMS).
- 3/2/06 Statement regarding documentation of conservative therapy moved from Billing/Coding section to section "When Intra-articular Hyaluronan Injections are covered." Statement regarding allergies to chickens or eggs deleted from the "not covered" section. Information regarding Euflexxa added to "Policy Guidelines" section. Euflexxa is free of animal proteins and can be administered to patients who are allergic to chickens, eggs or feathers.
- 8/21/06 References updated. Specialty Matched Consultant Advisory panel review 7/24/06. No changes to policy criteria. (adn)
- 9/18/06 Information regarding repeated treatment cycles deleted from the When Covered section. The following statement added to When Not Covered section: "Repeated treatment cycles are considered investigational." Also added a statement to Policy Guidelines section "There is limited evidence regarding the effectiveness of multiple courses of intra-articular hyaluronan injections, therefore repeated treatment cycles are considered investigational. BCBSNC does not provide coverage for investigational services." Notification date 9/18/06. Effective date 11/27/06. (adn)
- 2/12/07 Billing/Coding section updated to reflect 2007 code changes. (adn)
- 6/18/07 Code J7319 removed from policy. No longer a valid code.
- 12/31/07 Coding update. Deleted codes Q4083, Q4084, Q4085 and Q4086. Added codes J7321, J7322, J7323 and J7324 to Billing/Coding section. (adn)
- 2/11/08 Reformatted the When Covered section into a numbered list and added the following statement: "Repeated courses of intra-articular hyaluronan injections may be considered medically necessary under the following conditions: Significant pain relief was achieved with the prior course of injections; and at least six months have passed since the prior course." The statement regarding repeated treatment cycles was deleted from the Not Covered section. Rationale regarding repeated treatment cycles and use of hyaluronan on joints other than the knee added to the Policy Guidelines section. (adn)
- 8/25/08 Item A.1. in the When Covered section revised to read: Diagnosis of osteoarthritis substantiated by x-ray or other imaging or arthroscopic findings. References updated. Specialty Matched Consultant

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Advisory Panel review 6/17/08. No change to policy statement. (adn)

3/2/09 Description section revised for clarity. Medical Policy changed to Evidence Based Guideline.

1/5/10 HCPCS Code J7322 replaced with Code J7325.

8/17/10 Specialty Matched Consultant Advisory Panel review 7/ 2010. Removed Guideline number. Extensively revised Description section. Updated References.(mco)

4/26/11 References updated. No changes to guideline statements. (mco)

8/16/11 Specialty Matched Consultant Advisory Panel review. No changes to guideline statements. (mco)

12/30/11 New code J7326 added to “Billing/Coding” section. Effective date 1/1/2012. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.