I. Policy

A single course of FDA approved intra-articular hyaluronan injections may be considered medically necessary when all of these criteria are met:

- The patient is an adult (18 years of age or older);
- The patient has symptomatic osteoarthritis (OA) of the knee as confirmed by x-ray, MRI or arthroscopic evaluation;
- The patient’s symptoms of pain persist after a trial of treatment with:
  - an anti-inflammatory medication (NSAID or corticosteroid injection) and/or acetaminophen, unless these medications are contraindicated, and
  - a trial of non-pharmacological treatment;
- There are no contraindications to the hyaluronan injections; and
- An FDA-approved medication is used and is administered per the FDA dosage and frequency recommendations.

Bilateral injections may be considered medically necessary if the above criteria are met.

Repeated courses of treatment with intra-articular hyaluronan may be considered medically necessary for the following indications:

- Patient showed response to previous treatment with medical records indicating a significant positive clinical effect from the first course in terms of improvement in pain relief and knee joint functional capacity; and
- Six months have elapsed since previous series of injections.

The use of intra-articular hyaluronan injections into joints other than the knee or for conditions other than osteoarthritis is considered investigational, as there is inadequate data to determine the clinical efficacy of hyaluronan injections in joints other than the knee.
II. PRODUCT VARIATIONS

This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

BlueJourney HMO*  BlueJourney PPO*  FEP PPO**

* Refer to Novitas Solutions Local Coverage Determination (LCD) L35427, Hyaluronan Acid Therapies for Osteoarthritis of the Knee.

** Refer to FEP Medical Policy Manual MP-5.75.09, Hyaluronic Acid Derivatives. The FEP Medical Policy Manual can be found at: www.fepblue.org.

Note for Medicare Advantage:

FDA approved drugs used for indications other than what is indicated on the FDA approved product label may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the Medicare recognized national drug compendia, authoritative medical literature and/or accepted standards of medical practice. Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.2- Unlabeled Use of Drug).


III. DESCRIPTION/BACKGROUND

Knee OA is common, costly, and a cause of substantial disability. Among U.S. adults, the most common causes of disability are arthritis and rheumatic disorders. Currently, no curative therapy is available for OA, and thus the overall goals of management are to reduce pain, disability, and the need for surgery.

Intra-articular hyaluronan injections (IAHA) has been proposed as a means of restoring the normal viscoelasticity of the synovial fluid in patients with OA and improving pain and function. This treatment may also be called viscosupplementation. Hyaluronan (HA) 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; cross-linked hyaluronans are referred to as hylans. In OA, the overall length of HA chains present in cartilage and the HA concentration in the synovial fluid are decreased.

Regulatory Status

Several preparations of intra-articular (IA) hyaluronan have been approved by the U.S. Food and Drug Administration (FDA) as an alternative to nonsteroidal anti-inflammatory drug therapy in the treatment of osteoarthritis (OA) of the knee: Synvisc® and Synvisc-One® (Genzyme); Gel-One®
(Zimmer); Hyalgan® (Fidia); Supartz FX™ (Bioventus); Orthovisc® (Anika); Euflexxa®, previously named Nuflexxa (Savient); Monovisc® (Anika Therapeutics); and Gel-Syn™ (Institut Biochimique SA). All products are manufactured from rooster combs except for Euflexxa, Orthovisc, Monovisc, Gel-Syn, and GenVisc 850, which are produced from bacterial fermentation. Also, Synvisc undergoes additional chemical crosslinking to create hylans with increased molecular weight (6000 kDa) compared with Hyalgan (500-730 kDa) and Supartz (620-1170 kDa). Monovisc is also cross-linked with a proprietary cross-linker. 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.

According to the manufacturer’s prescribing information for Synvisc and Euflexxa, IA hyaluronan 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, eg, acetaminophen.” The product inserts further 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 to 4 weekly injections are recommended for Orthovisc. In February 2009, FDA approved the use of single-dose hylan G-F 20 (Synvisc-One) for the treatment of OA of the knee. In 2011, FDA approved the use of the single-dose cross-linked hyaluronate Gel-One (also known as Gel-200) for the treatment of OA of the knee. In 2014, Monovisc was also approved as a single-dose treatment, while Gel-Syn was approved as a course of 3 weekly injections. In 2015, GenVisc 850 was approved as a course of 3 weekly injections.

In 2000, FDA approved removal of a precautionary statement from the package inserts for Hyalgan and Synvisc that stated that the safety and efficacy of repeat courses have not been established.

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

FDA product code: MOZ.

IV. RATIONALE

The most recent literature review was performed through February 12, 2016.

Knee Osteoarthritis

This evidence review was originally based on a 1998 TEC Assessment on IA hyaluronan injections for OA,¹ and incorporated material from subsequent TEC Assessments and a TEC review for Agency for Healthcare Research and Quality (AHRQ).²-⁴ The 2007 AHRQ report concluded that results from 42 generally showed positive effects of viscosupplementation on pain and function scores compared with placebo for patients with primary OA of the knee.³ However, the evidence on viscosupplementation was accompanied by considerable uncertainty due to variable trial quality, potential publication bias, and unclear clinical significance of the changes.
reported. Trials of hylan G-F 20 (Synvisc, 6000 kDa), the highest molecular weight cross-linked product, generally reported better results than other trials.

The 2014 TEC Assessment involved a systematic review of recent meta-analyses on the treatment of knee OA with IA hyaluronan injections.\(^4\) Included in the assessment were 5 meta-analyses published between 2011 and 2013.\(^5\)\(^-\)\(^9\) Two meta-analyses concluded that IA hyaluronan provides a clinically meaningful benefit and 3 concluded that it did not, due to a lack of supportive evidence. It was not possible from the data to determine the proportions of patients achieving clinically meaningful improvement, although the analysis from the American Academy of Orthopaedic Surgeons determined that is was unlikely that an appreciable number of patients would benefit compared with placebo. It is also possible that the results supporting a clinically meaningful benefit were biased in favor of IA hyaluronan, due to unpublished trial data. When results from unpublished trials were obtained, the magnitude of treatment effect was notably lower compared with published results. Substantial heterogeneity between trials was also evident, increasing uncertainty. The TEC Assessment concluded that the 5 meta-analyses, sampling from a similar collection of published trials and 2 unpublished ones, highlight biases and difficulty ascertaining clinically meaningful patient-level improvement compared with placebo. Although accumulating evidence would be expected to increase certainty about whether a clinically important treatment benefit exists, the current studies do not provide convincing evidence that the net health outcome is improved with IA hyaluronan over placebo.

The 2016 literature review did not identify any additional RCTs evaluating IA hyaluronan for the treatment of knee OA. However, a number of systematic reviews and meta-analyses were published after the 2014 TEC Assessment.\(^10\)\(^-\)\(^17\) Only four of them reported pooled analyses synthesizing results of RCTs that compared IA hyaluronan with placebo, and reported the outcome, pain.\(^10\)\(^-\)\(^12\),\(^14\) Three of the 4 new meta-analyses concluded that IA hyaluronan injections for knee OA provided a clinically meaningful reduction in pain compared with placebo.\(^11\),\(^12\),\(^14\) The other meta-analysis (Jevsevar et al\(^10\)) concluded that evidence from trials at low risk of bias (eg, double-blind, sham-controlled) did not demonstrate a clinically meaningful benefit of IA hyaluronan. (Two of the meta-analyses concluding benefit of IA hyaluronan also limited analysis to trials at low risk of bias.) Only the review by Jevsevar et al reported a minimally clinically important difference with treatment (-0.29). As noted in the 2014 TEC Assessment, “...for a standardized mean difference, a minimally important difference of -0.37 is sometimes cited.”\(^4\)

In addition to the meta-analyses of trials directly comparing IA hyaluronan and placebo, a network meta-analysis by Bannuru et al addressed this comparison indirectly.\(^17\) The investigators included 137 studies examining a number of treatments for knee OA: IA hyaluronan, intra-articular steroids, acetaminophen, diclofenac, ibuprofen, naproxen, and celecoxib.\(^17\) Although none of the included trials compared IA hyaluronan directly with oral placebo, the authors concluded that if IA hyaluronan were to be compared to oral placebo, it would be the most effective of the agents considered in the review. For example, when indirect comparisons were made with oral placebo, the standardized mean difference for pain relief reported at (or nearest) 3 months with IA
hyaluronan was 0.63 (95% credible interval [CrI], 0.39 to 0.88)\(^1\) and with ibuprofen was 0.44 (95% CrI, 0.25 to 0.63). The estimated pain relief effect for IA hyaluronan compared with oral placebo was nearly double that for IA hyaluronan compared with a sham procedure.

However, conclusions that can be drawn from the newer meta-analyses are limited by potential biases with included trials. The presence of publication bias has been documented in the IA hyaluronan literature.\(^5\) Likewise, a small trial bias has been noted with effect estimates from smaller trials (<100 participants) almost 3-fold that of large trials. These observations are consistent with positive results from a small trial having a higher probability of being reported than a small negative one (or possibly a small negative trial having even been completed). In summary, the results from the 2015-2016 meta-analyses, which do not include any new RCTs, do not alter conclusions of the 2014 TEC Assessment on the impact of IA hyaluronan on health outcomes in patients with knee OA.

**Joints Other Than the Knee**

**Ankle Osteoarthritis**

Evidence was examined from RCTs and systematic reviews that have been published. A 2015 Cochrane review by Witteveen et al addressed IA hyaluronan and other conservative treatments for ankle OA.\(^{18}\) The investigators identified 6 RCTs, 3 of which were double-blind and compared IA hyaluronan with placebo. The other trials were single-blind. Two of them compared IA hyaluronan to another treatment (exercise in 1 study and botulinum toxin in the other study) and the sixth study compared different doses of hyaluronan. Five of the 6 studies included patients with unilateral ankle pain. Sample sizes at the time of randomization ranged from 17 to 75, and length of follow-up ranged from 3 to 12 months. The authors pooled findings only for 2 of the 3 studies comparing IA hyaluronan and placebo. Meta-analyses of efficacy outcomes (pain, function) did not find statistically significant benefit of IA hyaluronan over placebo, with the exception of the outcome Ankle Osteoarthritis Scale (AOS) total score at 6 months. For the AOS outcome, the pooled effect size was -12.53 (95% confidence interval [CI], -23.84 to -1.22) in favor of IA hyaluronan; however, the evidence for this analysis was rated as low due to the limitation in study design (ie, unclear risk of bias) and “…imprecision of result (low number of participants).” No serious adverse events were reported and no patient withdrew from the study due to an adverse event.

A 2011 review of IA hyaluronan for ankle OA by Migliore et al considered both RCTs and observational studies.\(^{19}\) The authors identified 3 small RCTs with a total of 75 patients, and 4 case series. In 2 of the RCTs, IA hyaluronan was compared with placebo injection and the third RCT compared IA hyaluronan with exercise therapy. The authors were unable to do a meta-analysis due to the limited number of studies and study heterogeneity.

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\(^1\) The credible interval can be interpreted analogously to a confidence interval.
Foot Osteoarthritis

There is a very limited amount of evidence on IA hyaluronan injections in the foot. Munteanu et al reported on an RCT of a single IA hyaluronan injection in 151 patients with first metatarsophalangeal joint OA. At the 1-, 3-, and 6-month follow-up, there were no significant differences between the IA hyaluronan and placebo groups on the Foot Health Status Questionnaire.

Thumb Osteoarthritis

Two systematic reviews evaluated IA hyaluronan, as well as corticosteroid injections, for treating thumb OA. The 2016 review by Kroon et al identified 3 studies comparing HA and placebo and 6 comparing IA hyaluronan and corticosteroids. Findings of the HA studies were not pooled. Unlike the Kroon et al review, the 2015 systematic review by Trellu et al included only RCTs and pooled study data. Six trials (total N=428 patients) were included in the meta-analyses; 169 patients were treated with HA, 147 with corticosteroids and 74 with placebo. In pooled analyses of studies comparing IA hyaluronan and placebo (74 patients in each arm), there was no significant between-group difference in pain at week 12 (standardized response mean [SRM], -0.95; 95% CI, -3.87 to 1.97); however, functional capacity at week 12 was significantly better after IA hyaluronan than placebo (SRM = -1.14; 95% CI, -1.69 to -0.60). When IA hyaluronan and corticosteroids were compared, there was no significant difference in pain, functional capacity, or pulp pinch force at 12 weeks. At 24 weeks, findings were mixed. There was no significant between IA hyaluronan and corticosteroids in functional capacity, HA was superior on pulp pinch force status (SRM = -1.66; 95% CI, -0.75 to -2.57) and corticosteroids were superior on pain (SRM=1.44; 95% CI, 0.14 to 2.74).

Hip Osteoarthritis

A 2015 systematic review by Lieberman et al included RCTs and observational studies with a minimum of 10 patients evaluating IA hyaluronan for treatment of pain associated with hip OA. A total of 23 studies were identified, 6 of which were RCTs. The studies evaluated 11 different formulations of HA. Duration of follow-up varied; 19 studies followed patients for 6 months or less, 3 studies had between 6 months and 1 year of follow-up and only 1 study followed patients for more than 1 year. The primary efficacy outcome was change from baseline in pain measured by a visual analog scale (VAS). The authors did not report the number of points on the VAS but presumably this differed across studies and the authors appeared to standardize results on a 10-point VAS. A pooled analysis of data from all studies found a statistically significantly lower pain score at follow-up compared to baseline. Mean change was -1.97 points on a VAS (95% CI, -2.83 to -1.12). In a pooled analysis of the 6 RCTs, there was a significantly greater decrease in pain with IA hyaluronan compared with a control intervention (-0.27 points on a VAS; 95% CI, -0.43 to -0.11). Although statistically significant, a between-group difference of 0.27 points on a VAS may not be clinically meaningful.

Shoulder Osteoarthritis

A 2014 systematic review by Colen et al identified RCTs, controlled observational studies, and case series evaluating IA hyaluronan for treatment of glenohumeral OA in adult patients.
studies met the eligibility criteria; 2 were RCTs, 5 were prospective case series, and 1 was a retrospective case control study. Due to heterogeneity among studies and the small number of controlled studies, authors did not pool study findings on the efficacy of IA hyaluronan for treating shoulder OA compared with placebo or an alternative intervention. The RCTs are described next.

Blaine et al (2008) was an industry-sponsored trial of 660 patients with persistent shoulder pain due to glenohumeral joint OA, rotator cuff tear, and/or adhesive capsulitis that compared 3 weekly injections versus 5 weekly injections of sodium hyaluronate (Hyalgan) versus 5 weekly injections of saline. Approximately 60% of patients had OA, although most of those with OA also had rotator cuff disorders or capsulitis. Sixty-nine percent (n=456) of the patients had a follow-up visit at 26 weeks. There was no significant difference among groups in the primary outcome measure, shoulder pain with movement at 13 weeks. Analysis of predefined, stratified subgroups revealed no significant differences in reported pain at 13 weeks but a statistically significant decrease of 7.5 mm and 7.8 mm (on a 100-mm VAS) in reported pain in both treatment groups at 26 weeks compared with placebo among patients with OA. In those without OA, there was no significant improvement with either regimen. Of note, this appears to be an as-treated analysis of the OA subgroup data, and the difference may not be clinically meaningful.

In 2013, Kwon et al published findings from a multicenter, randomized, double-blind, placebo-controlled trial of IA hyaluronan in 300 patients with glenohumeral OA. Intention-to-treat analysis found similar improvement from baseline in 100-mm VAS for pain (19.88 mm for IA hyaluronan, 16.29 mm for sham treatment) and in the Outcome Measures in Rheumatoid Clinical Trials–Osteoarthritis Research Society International (OMERACT–OARSI) high responder rate (40.8% for IA hyaluronan, 34.9% for sham) at 26 weeks. In a subset of IA hyaluronan patients, there was a statistically significant difference of 4.0 mm in VAS score and 8.37% on the OMERACT–OARSI. However, the clinical significance of these differences is uncertain.

Spine Osteoarthritis
The data are limited to small pilot studies and case series.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

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<th>NCT No.</th>
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<td>Mar 2016 (ongoing)</td>
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<td>The Influence of Hyaluronic Acid Injection Following Knee Arthroscopy</td>
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NCT: national clinical trial.
Summary of Evidence
The evidence for intra-articular (IA) hyaluronan injections in individuals who have osteoarthritis of the knee includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Many RCTs have been published over the last 2 decades. While outcomes of these RCTs are mixed, the RCT evidence base is characterized by studies that show small treatment effects of IA hyaluronan treatment. In many cases, these trials are at risk of bias, and it cannot be determined with certainty whether there is a true treatment effect or whether the reported differences are due to bias. Meta-analyses of RCTs have also resulted in mixed findings. Some meta-analyses estimating the magnitude of treatment benefit have concluded that there is no clinically significant benefit; however, others have concluded that there is a clinically significant benefit. These meta-analyses have also highlighted the limitations of this evidence base, most notably publication bias. Overall, given the lack of a definitive treatment benefit despite a large quantity of literature, and given the biases present in the available evidence, it is unlikely there is a treatment benefit that is clinically meaningful. The evidence is sufficient to determine qualitatively that the technology is unlikely to improve the net health outcome.

The evidence for IA hyaluronan injections in individuals who have osteoarthritis of joints other than the knee includes RCTs and systematic reviews of RCTs. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Meta-analyses of RCTs either have not found statistically significant benefits of the technology on health outcomes or have found benefits that were statistically, but likely not clinically, significant (eg, 0.27-point improvement on a 10-point visual analog scale). The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 5 academic medical centers (6 reviewers) and 3 physician specialty societies while this policy was under review in 2011. Most reviewers agreed that IA hyaluronan of the knee was medically necessary. In addition, those providing input supported an interval of 6 months for repeat injections. In response to a question about total number of treatment courses, there was no consensus.

Practice Guidelines and Position Statements

American Medical Society for Sport Medicine
The 2016 scientific statement from the American Medical Society for Sport Medicine (AMSSM) recommended IA hyaluronan for “appropriate” patients with knee osteoarthritis (OA) based on high-quality evidence.12 Patient selection criteria include individuals age 60 and older with
Kellgren-Lawrence grade 2-3 OA. The society also “suggests” IA hyaluronan for patients under age 60 with knee OA based on moderate quality indirect evidence.

**American Academy of Orthopaedic Surgeons**
The 2013 guideline of the American Academy of Orthopaedic Surgeons (AAOS) on treatment of OA of the knee states that they cannot recommend using IA hyaluronan for patients with symptomatic knee OA. This is a strong recommendation, meaning that the quality of the supporting evidence is high. This recommendation was based on a meta-analysis of 3 high-strength and 11 moderate-strength studies that showed that the overall effect was less than 0.5 minimally important different units, indicating a low likelihood that an appreciable number of patients achieved clinically important benefits. AAOS states that practitioners should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present. This replaces a 2008 guideline in which a recommendation could not be made for IA hyaluronan due to inconclusive evidence.

The 2009 (reaffirmed 2014) AAOS Clinical Practice Guideline on glenohumeral joint osteoarthritis includes a weak grade C recommendation that “The use of injectable viscosupplementation is an option when treating patients with glenohumeral [shoulder] osteoarthritis.” Grade C recommendations are based on poor-quality evidence. In this instance, the recommendation is based on a single case series of 30 patients with OA of the glenohumeral joint who received 3 weekly IA injections of Synvisc. At 1, 3, and 6 months, clinically significant improvements were seen in pain, function, and quality-of-life measures.

**American College of Rheumatology**
The American College of Rheumatology (ACR) published updated guidelines in 2012 that addressed OA of the hand, hip, and knee. A conditional recommendation was given for IA hyaluronan to treat OA of the knee. ACR recommends not using IA hyaluronan for OA of the hand. For OA of the hip, ACR explicitly made no recommendation regarding treatment with IA hyaluronan due to the lack of RCTs.

**Osteoarthritis Research Society International**
The 2014 Osteoarthritis Research Society International guidelines, developed by consensus after review of existing guidelines and systematic reviews, gave an “uncertain” recommendation for the use of IA hyaluronan for knee OA and a recommendation of “not appropriate” for multiple-joint OA.

**National Institute for Health and Care Excellence**
The 2014 guidelines by the National Institute for Health and Care Excellence state: “Do not offer intra-articular hyaluronan injections for the management of osteoarthritis.”

**U.S. Preventive Services Task Force Recommendations**
Not applicable.
MEDICAL POLICY

INTRA-ARTICULAR HYALURONAN INJECTIONS FOR OSTEOARTHRITIS OF THE KNEE

POLICY NUMBER MP-2.022

Medicare National Coverage
There is no national coverage determination (NCD).

V. DEFINITIONS

INTRA-ARTICULAR refers to within a joint.

OSTEOARTHRITIS is a type of arthritis marked by progressive cartilage deterioration in the synovial joints and vertebrae.

SYNOVIAL FLUID is the clear, viscous lubricating fluid of the joint, bursae, and tendon sheaths secreted by the synovial membrane of a joint.

VI. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member’s contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member’s individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member’s benefit information or contact Capital for benefit information.

VII. DISCLAIMER

Capital’s medical policies are developed to assist in administering a member’s benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member’s benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.
Covered when medically necessary:

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<th>HCPCS Codes</th>
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<td>Hyaluronan or derivative, hyalgan or supartz, for intra-articular injection, per dose</td>
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*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

IX. REFERENCES


MEDICAL POLICY

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<th>INTRA-ARTICULAR HYALURONAN INJECTIONS FOR OSTEOARTHRITIS OF THE KNEE</th>
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<tr>
<td>POLICY NUMBER</td>
<td>MP-2.022</td>
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Other Sources:
Novitas Solutions. Local Coverage Determination (LCD) L35427 - Hyaluronan Acid Therapies for Osteoarthritis of the Knee. Effective 10/1/15

X. POLICY HISTORY

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<td>CAC 4/24/07 Consensus</td>
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<td>Consensus review. Administrative decision to not adopt at this time, the BCBSA coverage position previously approved. References updated. Rationale added.</td>
</tr>
<tr>
<td>CAC 1/27/15</td>
<td>Consensus review. No change to policy statements. References and Rationale updated.</td>
</tr>
<tr>
<td>12/29/2014</td>
<td>Coding reviewed as consensus and no changes.</td>
</tr>
<tr>
<td>01/2015</td>
<td>New 2015 Code added to policy.</td>
</tr>
<tr>
<td>11/2/15</td>
<td>Administrative change. LCD number changed from L32237 to L35427 due to Novitas update to ICD-10.</td>
</tr>
<tr>
<td>CAC 1/26/16</td>
<td>Consensus review. No change to policy statements. Deleted grid with list of FDA products and administration guidelines. Rationale and references reviewed. New 2016 codes added. Coding Reviewed.</td>
</tr>
<tr>
<td>Admin update 1/1/17</td>
<td>Product variation section reformatted. New codes J7320, J7322 added and removed end dated code Q9980; effective 1/1/17.</td>
</tr>
</tbody>
</table>

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