Intra-Articular Hyaluronan Injections

Medicare Advantage Medical Policy #MA-015
Original Effective Date: 03/01/2023
Current Effective Date: 06/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider intra-articular hyaluronan (IAHA) injections (including, but not limited to Gel-Syn™, Genvisc™, Hymovis™, Monovisc®, Hyalgan®, Supartz®, Supartz® FX, OrthoVisc®, Synvisc®, Synvisc-One®, Euflexxa®, Durolane®, Gel-One®, Visco-3™, TriVisc™, Synojoynt™, or Triluron™)‡ for the treatment of painful osteoarthritis of the knee in patients who have insufficient pain relief from conservative non-pharmacologic therapy and simple analgesics to be **eligible for coverage**.**

Initial Treatment

Patient Selection Criteria

The use of intra-articular hyaluronan knee injections for initial treatment will be considered when ALL of the following criteria are met:

- Patient has failed conservative therapy for at least three months with non-steroidal anti-inflammatory drugs (NSAIDs), or acetaminophen, if there is a contraindication to NSAIDs, unless there is clinical evidence or patient history that suggests use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Patient has knee pain and a documented diagnosis of osteoarthritis of the knee with x-ray (radiologic) confirmation of Kellgren-Lawrence Scale score of grade 2 or greater.
- For requests OTHER than Synvisc, Synvisc-One, or Euflexxa: Patient must be prescribed (and subsequently try and fail) Synvisc or Synvisc-One AND Euflexxa prior to other intra-articular knee injection products (unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient).

Repeat Treatment

Patient Selection Criteria
The use of intra-articular hyaluronan knee injections for repeat treatment will be considered when ALL of the following criteria are met:

- Patient has met and continues to meet the initial criteria in this policy regarding diagnosis, pain, imaging, and conservative treatment failures; AND
- Six months or more have elapsed since the prior treatment cycle; AND
- Positive response (i.e., adequate pain relief, increase in or maintenance of function) to the prior course of therapy has been demonstrated and is documented in the medical records (office notes) of the treating physician.
- For requests OTHER than Synvisc, Synvisc-One, or Euflexxa: Patient has tried and failed Synvisc or Synvisc-One AND Euflexxa during prior courses of therapy (unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of intra-articular hyaluronan knee injections when any of the following patient selection criteria are NOT met to be **not medically necessary**:**

- For Initial and Renewal: Patient has failed conservative therapy for at least three months with NSAIDs, or acetaminophen, if there is a contraindication to NSAIDs.
- For Initial: Requests OTHER than Synvisc, Synvisc-One, or Euflexxa - Patient must be prescribed (and subsequently try and fail) Synvisc or Synvisc-One AND Euflexxa prior to other intra-articular hyaluronan knee injection products
- For Renewal: Six months or more have elapsed since the prior treatment cycle.
- For Renewal: Positive response (i.e., adequate pain relief, increase in or maintenance of function) to the prior course of therapy has been demonstrated and is documented in the medical records (office notes) of the treating physician.
- For Renewal: Requests OTHER than Synvisc, Synvisc-One, or Euflexxa - Patient has tried and failed Synvisc or Synvisc-One AND Euflexxa during prior courses of therapy.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of intra-articular hyaluronan injections into joints other than the knee, to be **investigational.***

Based on the review of available data, the Health Plan considers the use of intra-articular hyaluronan injections for diagnoses other than knee pain due to osteoarthritis to be **investigational.***

Based on the review of available data, the Health Plan considers the use of intra-articular hyaluronan injections for patellofemoral syndrome to be **investigational.***

Based on the review of available data, the Health Plan considers the use of intra-articular hyaluronan injections for chondromalacia patellae to be **investigational.***

Based on the review of available data, the Health Plan considers the use of intra-articular hyaluronan injections when the patient does NOT have osteoarthritis of the knee confirmed by x-ray (radiologic) confirmation of Kellgren-Lawrence Scale score of grade 2 or greater to be **investigational.***

Background/Overview

Osteoarthritis is the most common form of arthritis and presents with joint pain, stiffness, and locomotor restriction. Symptoms typically present in just one or a few joints. Osteoarthritis is confirmed by radiographic evidence and is classified via the Kellgren-Lawrence Radiographic Criteria for Assessment of Osteoarthritis. The scale ranges from grade 0 to grade 4, with the higher number representing worsening disease. Grade 0 includes no radiographic features of osteoarthritis. Grade 1 represents doubtful narrowing of joint space with possible osteophytic lipping. Grade 2 represents possible narrowing of joint space with definite osteophytes. Grade 3 represents definite narrowing of joint space, moderate multiple osteophytes, some subchondral sclerosis, and possible deformity of bone contour. Grade 4 represents marked narrowing of joint space, large osteophytes, severe subchondral sclerosis, and definite deformity of bone contour.

Intra-articular injection of hyaluronan into osteoarthritic joints is thought to replace hyaluronic acid (HA), restore the viscoelastic properties of the synovial fluid, and improve pain and function. The majority of studies to date have assessed IAHA injections for knee osteoarthritis, and this is the U.S. Food and Drug Administration (FDA) -approved indication. Other joints, such as the hip and shoulder, are currently being investigated for intra-articular HA treatment of osteoarthritis.

Hyaluronan 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 HA increases its molecular weight; crosslinked HAs 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 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Multiple preparations of intra-articular hyaluronans have been approved by the FDA as an alternative to nonsteroidal anti-inflammatory drug therapy in the treatment of osteoarthritis of the knee (Synvisc and Synvisc-One, Sanofi; Supartz, Supartz FX, Gelsyn, and Durolane, Bioventus; OrthoVisc and Monovisc, Johnson and Johnson; Euflexxa, Ferring; Gel-One and Visco-3, Zimmer; Genvisc and TriVisc, Orthogen RX; Hymovis, Hyalgan, and Triluron, Fidia Pharma USA; Synojoynt, Teva). Euflexxa, Gel-Syn, Genvisc, Hymovis, Monovisc, Durolane, Orthovisc, TriVisc, Triluron, and Synojoynt are derived from non-avian sources (bacterial cells), whereas the other products are derived from rooster or chicken combs. The non-avian products may be useful in patients with allergies to eggs or poultry products. Synvisc and Synvisc-One products differ from the others in that they are a viscous mixture of chemically cross-linked HA composed of 80% hylan A and 20% Hylan B. After cross-linking, the preparation is purified.

As mentioned earlier, multiple products have been approved in this space and the products have varying numbers of injections. Single injection products include Monovisc, Synvisc-One, Durolane, and Gel-One. Hymovis uses two injections per course. Gel-Syn, Euflexxa, Synvisc, TriVisc, Triluron, Synojoynt, and Visco-3 call for 3 injections, while Orthovisc calls for 3 to 4 injections per course. Supartz, Hyalgan, and Genvisc call for 5 injections per course of therapy.

The FDA has not approved intra-articular hyaluronan injections for joints other than the knee. Of note, intra-articular HA products have not been approved by the FDA for patellofemoral syndrome or chondromalacia patellae. Further studies are needed in these conditions to definitively prove that intra-articular HAs will significantly delay the need for more invasive treatment.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Knee

Intra-articular hyaluronan (IAHA) products are generally safe and well tolerated. They are also generally considered to have modest improvement in symptoms of osteoarthritis (OA). There is no substantial clinical evidence to support a significant treatment difference between high molecular weight and low molecular weight IAHA products. The Express Scripts Clinical Summary of Hyaluronic Acid Derivatives cited the following meta-analysis: “A 2011 meta-analysis included all randomized controlled trials (RCTs) that enrolled patients and compared an IAHA to placebo when

used to treat OA of the knee. Eligible trials were required to report a minimum of one measure of pain, function, or stiffness. The primary endpoint was pain reduction at approximately weeks 2, 4, 8, 12, 16, 20, and 24. A total of 49 reports that included 54 trials (n = 7,545) were included in the analysis. For the analysis, 49 trials (n = 6,962) contributed to pain-related outcomes, 16 trials (n = 2,571) contributed to function-related analysis, and 15 trials (n = 2,488) contributed to stiffness-related outcomes. Throughout the studies, the average age ranged from 45 to 72 years with women making up between 28% and 100% of the patients. The effect size on joint pain was evident by week 4 (0.31 [95% confidence interval {CI}: 0.17, 0.45), peaked at week 8 (0.46 [95% CI: 0.28, 0.65]), and was still evident at week 24 (0.21 [95% CI: 0.10, 0.31]). The effect size was 0.31 (95% CI: 0.11, 0.51) for function-related outcomes and 0.31 (95% CI: 0.12, 0.49) for stiffness-related outcomes with both values favoring IAHA (study time points not provided). Since an effect size of 0.20 has been determined to be clinically relevant for chronic pain, IAHA was found to be an effective agent for OA."

Of course, there are various interpretations of the data, including those that cite that IAHA products do not have any significant effect on OA. Varying practice guidelines from national organizations also exist. The American Medical Society for Sports Medicine in 2016 recommended IAHA for "appropriate" patients (over 60 years of age) with knee OA based on high-quality evidence. The society also "suggests" IAHA for patients under age 60 with knee OA based on moderate-quality indirect evidence. Practice guidelines published in 2021 by The American Academy of Orthopedic Surgeons (AAOS) do not recommend IAHA for routine use in the symptomatic treatment of OA, but state that certain patients can benefit modestly with IAHA treatment. The American College of Rheumatology (ACR) released updated guidelines in 2020 (but titled 2019) that stated IAHA products are conditionally recommended against in patients with knee OA and strongly recommended against in patients with hip OA. The Osteoarthritis Research Society International guidelines, published in 2019, state that IAHA injections are conditionally recommended and may have beneficial effects on pain at and beyond 12 weeks of treatment. The 2014 guidance by the National Institute for Health and Care Excellence stated: "Do not offer intra-articular hyaluronan injections for the management of osteoarthritis." As noted, it is obvious that an argument exists regarding the clinical efficacy of IAHA products.

Joints Except the Knee

Ankle Osteoarthritis

The evidence was examined from published RCTs and systematic reviews. A 2018 review by Vannabouathong and colleagues was published regarding IAHA for the treatment of ankle osteoarthritis. A total of 27 studies were identified (N=1085), including 20 observational studies and 7 small RCTs evaluating hyaluronic acid conducted between 2005 and 2014. Pooled analysis (3 RCTs, 109 patients) demonstrated significantly improved Ankle Osteoarthritis Scale scores with

hyaluronic acid compared to saline at 6 months (mean difference 12.47 points; 95% CI, 1.18 to 23.77; p=.03). Study heterogeneity was low.

A 2015 Cochrane review by Witteveen and colleagues addressed IAHA and other conservative treatments for ankle OA. Reviewers identified 6 RCTs, 3 of which were double-blind and compared IAHA to placebo. The other trials were single-blind. Two of them compared IAHA to another treatment (exercise in 1 study, botulinum toxin in the other) and the sixth trial compared different doses of hyaluronan. Five of the 6 trials included patients with unilateral ankle pain. Sample sizes at 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 IAHA and placebo. Meta-analyses of efficacy outcomes (pain, function) did not find statistically significant benefit favoring IAHA 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% CI: -23.84 to -1.22) in favor of IAHA; however, the evidence for this analysis was rated as low due to the limitation in study design (i.e., unclear risk of bias) and "…imprecision of result (low number of participants)." No serious adverse events were reported and no patient withdrew from the trial due to an adverse event.

A 2011 review of IAHA for ankle OA by Migliore and colleagues considered RCTs and observational studies. They identified 3 small RCTs with a total of 75 patients, and 4 case series. In 2 of the RCTs, IAHA was compared with placebo injection and the third RCT compared IAHA with exercise therapy. Reviewers were unable to conduct a meta-analysis due to the limited number of studies and study heterogeneity.

Foot Osteoarthritis

There is a very limited amount of evidence on IAHA injections in the foot. Munteanu and colleagues (2011) reported on an RCT of a single IAHA injection in 151 patients with first metatarsophalangeal joint OA. At the 1-, 3-, and 6-month follow-ups, there were no significant differences between the IAHA and placebo groups on the Foot Health Status Questionnaire.

Thumb Osteoarthritis

Three systematic reviews have evaluated IAHA and corticosteroid injections for treating thumb OA. The 2016 review by Kroon and colleagues identified 3 studies comparing IAHA and placebo and 6 comparing IAHA and corticosteroids. Findings from the IAHA studies were not pooled. Unlike the Kroon review, the 2015 systematic review by Trellu and colleagues included only RCTs and pooled study data. Six trials (total n=428 patients) were included in the meta-analyses; 169 patients were treated with IAHA, 147 with corticosteroids, and 74 with placebo. In pooled analyses of trails comparing IAHA 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 IAHA than after placebo (SRM = -1.14; 95% CI, -1.69 to -0.60). When IAHA and corticosteroids were compared, there were

no significant differences in pain, functional capacity, or pulp pinch force at 12 weeks. At 24 weeks, findings were mixed. There was no significant between IAHA and corticosteroids in functional capacity, IAHA 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).

In 2019, Riley and colleagues conducted a systematic review of injection therapies for base of thumb osteoarthritis. Meta-analysis of 2 RCTs that compared corticosteroid injections to intra-articular hyaluronan (92 patients) demonstrated reduced visual analogue scale pain on activity with corticosteroid versus intra-articular hyaluronan (mean difference [MD], −1.32; 95% CI, −2.23 to −0.41) in the medium term (3 to 6 months), but no differences in other measures of pain or function in the short term (1 week to 3 months) or long term (longer than 6 months).

In a 2018 systematic review, Kroon and colleagues updated the evidence on the efficacy and safety on non-pharmacological, pharmacological, and surgical interventions for hand osteoarthritis with a systematic literature review through 2017. No clear beneficial effect was shown for intra-articular thumb base injections of hyaluronic acid. This evidence review informed the 2018 update of the European League Against Rheumatism management recommendations for hand osteoarthritis.

Hip Osteoarthritis

A 2015 systematic review by Lieberman et al included RCTs and observational studies (with a minimum of 10 patients) evaluating IAHA for treatment of pain associated with hip OA. Twenty-three studies were identified, 6 of which were RCTs. The studies evaluated 11 different formulations of IAHA. Durations 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 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). Reviewers 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 the 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 IAHA than 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.

In 2017, Wu and colleagues published a meta-analysis of RCTs investigating the therapeutic effects of hyaluronan injections in patients with hip osteoarthritis. Six studies were selected. To measure the effects of hyaluronan injection, a series of pain and functionality assessments were conducted using a visual analog scale, the Lequesne Index, and the WOMAC. All 6 trials consisted of 2 treatment groups (hyaluronan vs. control). Follow-up ranged from 52 to 180 days. When comparing hyaluronan with control, the pooled effect size of improvement in pain scores was 0.03 (95% CI, -0.20 to 0.26; $p<.05$). The standardized mean difference for improvement in Lequesne Index scores

and WOMAC scores were -0.24 (95% CI, -0.50 to 0.02; p>.05) and -0.13 (95% CI, -0.64 to 0.37; p>.05), respectively. Reviewers noted there were likely no significant differences between hyaluronan injections and saline or other treatments. Limitations included the small sizes of selected studies, selection bias, and expectation bias.

Zhao and colleagues published a systematic review and meta-analysis in 2020 evaluating various intra-articular injections for hip osteoarthritis, including platelet-rich plasma, hyaluronic acid, corticosteroids, and hyaluronic acid with platelet-rich plasma. A literature review through April 2018 was performed identifying 11 RCTs, representing 1060 patients. Mean follow-up duration ranged from 3 to 12 months. Studies varied with regard to imaging method used for guidance (ultrasound vs. fluoroscopy). A pair-wise meta-analysis indicated that corticosteroids and hyaluronic acid were superior to control in reducing visual analog scale score at 1 and 3 months (p<.05) and that a corticosteroid injection was superior to hyaluronic acid in reducing visual analog scale score at 1 month (p<.05). The authors recommend corticosteroid injections as the most efficient agent for hip osteoarthritis in the short-term.

A 2019 systematic review and meta-analysis by Liao and colleagues included 5 high quality RCTs representing 591 patients with hip osteoarthritis treated with intra-articular viscosupplementation. Although several trials demonstrated a significant decrease in visual analog scale pain scores from baseline, meta-analysis did not indicate viscosupplementation was superior to placebo at follow-up time windows of 7 to 14 days, 28 to 30 days, or final visit.

Gazendam and colleagues published a 2021 systematic review and network meta-analysis of RCTs investigating the efficacy of intra-articular corticosteroid, hyaluronic acid, and platelet-rich plasma injections for the treatment of hip osteoarthritis. A literature search through 2019 identified 11 studies for inclusion, representing 1353 patients. For both pain and functional outcomes at 2 to 4 and 6 months, none of the interventions significantly outperformed intra-articular saline injections. All interventions (including placebo) led to a clinically important improvement in pain and function from baseline, except for the combination of hyaluronic acid and platelet-rich plasma.

Shoulder Osteoarthritis

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

Zhang and colleagues published a systematic review and meta-analysis in 2019 of studies of intra-articular hyaluronan for treatment of glenohumeral osteoarthritis that found reductions in pain and

functional outcomes at 3 and 6 months with intra-articular hyaluronan treatment. However, similar clinical improvements were seen in control groups, suggesting a significant placebo effect. The reviewers concluded that further RCTs are necessary to evaluate efficacy of the treatment.

Blaine and colleagues study (2008) was an industry-sponsored trial, 3-arm of 660 patients with persistent shoulder pain due to glenohumeral joint OA, rotator cuff tear, and/or adhesive capsulitis that compared 3 weekly injections to 5 weekly injections of Hyalgan and to 5 weekly injections of saline. Approximately 60% of patients had OA, although most 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 were no significant improvements 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 and colleagues published findings from a multicenter, randomized, double-blind, placebo-controlled trial of IAHA in 300 patients with glenohumeral OA. Intention-to-treat analysis found similar improvements from baseline in 100-mm VAS for pain (19.88 mm for IAHA, 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 IAHA, 34.9% for sham) at 26 weeks. In a subset of IAHA patients, there were statistically significant differences 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.

Summary
For individuals who have osteoarthritis of the knee who receive intra-articular hyaluronan injections, the evidence includes 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 have been mixed, the RCT evidence base is characterized by studies showing small treatment effects of intra-articular hyaluronan injections. 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 had mixed findings. Some meta-analyses, estimating the magnitude of treatment benefit, have concluded there is no clinically significant benefit; others have concluded there is a clinically significant benefit. These meta-analyses have also highlighted the limitations of this evidence base,

most notably publication bias and small trial bias. For example, a meta-analysis (2016) found more than a 3-fold larger treatment effect in small trials than in larger trials (ie, >100 participants). 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 insufficient to determine that the technology results in an improvement in the net health outcome.

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

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Policy History

Original Effective Date: 03/01/2023
Current Effective Date: 12/01/2024
03/28/2023 Chief Medical Officer review and approval.
04/16/2024 UM Committee review.
11/19/2024 UM Committee review. Format revision.
12/30/2024 Coding update
03/18/2025 UM Committee review. Added criteria that preferred products (Synvisc or Synvisc One and Euflexxa) must be tried and failed.
Next Scheduled Review Date: 03/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	20610, 20611
HCPCS	J7318, J7320, J7321, J7322, J7323, J7324, J7325, J7326, J7327, J7328,

	J7329, J7331, J7332, Delete code effective 01/01/2025: J3590
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.