Reference number(s)
2478-A

STANDARD MEDICARE PART B MANAGEMENT

DUROLANE (hyaluronic acid)
EUFLEXXA (1% sodium hyaluronate)
GEL-ONE (cross-linked hyaluronate)
GELSYN-3 (sodium hyaluronate 0.84%)
GENVISC 850 (sodium hyaluronate)
HYALGAN (sodium hyaluronate)
HYMOVIS (high molecular weight viscoelastic hyaluronan)
MONOVISC (high molecular weight hyaluronan)
ORTHOVISC (high molecular weight hyaluronan)
SUPARTZ FX (sodium hyaluronate)
SYNOJOYNT (1% sodium hyaluronate)
SYNVISC (hylan G-F 20)
SYNVISC ONE (hylan G-F 20)
TRILURON (sodium hyaluronate)
TRIVISC (sodium hyaluronate)
VISCO-3 (sodium hyaluronate)
1% sodium hyaluronate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen)

B. Compendial Uses
1. Treatment of pain of arthropathy of the shoulder
2. Treatment of subacromial impingement
3. Treatment of temporomandibular joint disorder

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Osteoarthritis of the Knee or Shoulder
Authorization of 12 months may be granted for treatment of osteoarthritis in the knee or shoulder.

B. Subacromial impingement
Authorization of 3 months may be granted for treatment of subacromial impingement.

C. Temporomandibular joint disorder
Authorization of 3 months may be granted for treatment of temporomandibular joint disorder.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Authorization of 12 months for osteoarthritis of the knee or shoulder may be granted when ALL of the following criteria are met:
   1. The member has previously received therapy in the same joint with a hyaluronate product
   2. The member meets either of the following:
      i. The member will receive the first injection of the retreatment course after at least 6 months from the last injection of the previous completed course and the medication has been effective for treating the diagnosis or condition
      ii. A different hyaluronate product is being requested due to an adverse event with the previous course

B. Authorization of 3 months may be granted for all other indications when ALL of the following criteria are met:
   1. The hyaluronate product is being used to treat an indication enumerated in Section II
   2. The medication has been effective for treating the diagnosis or condition

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for the above referenced hyaluronate products.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. 2019 American College of Rheumatology/Arthritis Foundation Guidelines for the management of osteoarthritis of the hand, hip, and knee.
4. Osteoarthritis Research Society International (OARSI) guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for the above referenced hyaluronate products are covered in addition to the following:
A. Osteoarthritis of the shoulder
B. Subacromial impingement
C. Temporomandibular joint disorder

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for knee osteoarthritis can be found in the OARSI guidelines from 2019. Intra-articular corticosteroids and hyaluronan injections are conditionally recommended in individuals with knee osteoarthritis in all groups. Intra-articular hyaluronic acid may have beneficial effects on pain at beyond 12 weeks of treatment. Hyaluronic acid injections may have a more favorable long-term safety profile compared to repeated intra-articular corticosteroid injections.

Conversely, the American College of Rheumatology and Arthritis Foundation states that intra-articular hyaluronic acid injection are conditionally recommended against in patients with knee osteoarthritis. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, taken into account the risk of bias of the individual primary studies. Our review showed that benefit was restricted to the studies with higher risk of bias: when limited to trials with low risk of bias, meta-analysis has shown that the effect size of hyaluronic acid injections compared to saline injections approaches zero. The finding that best evidence fails to establish a benefit, and that harm may be associated with these injections, motivated the recommendation against use of this treatment.

Many providers want the option of using hyaluronic acid injections when glucocorticoid injections or other interventions fail to adequately control local joint symptoms. In clinical practice, the choice to use hyaluronic acid injections in the knee OA patient who has had an inadequate response to nonpharmacologic therapies, topical and oral NSAIDs, and intraarticular steroids may be viewed more favorably than offering no intervention, particularly given the impact of the contextual effects of intraarticular hyaluronic acid injections. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

Support for shoulder osteoarthritis can be found in a study where patients were administered weekly injection of 25 mg sodium hyaluronate (high molecular weight) into the glenoid cavity or subacromial bursa. The injections improved pain at rest, pain on motion, and pain on pressure in approximately 75% of 62 patients with periarthritis of the shoulder. A series of 5 injections was planned, and further injections were discontinued if pain was resolved. If not, weekly or biweekly injections continued. The mean treatment was 6 ampules injected over 8 weeks, but ranged from 1 to 27 injections given over 2 to 40 weeks. Final global improvement ratings showed 11% markedly improved, 40% moderately improved, 31% slightly improved, and 18% unchanged. None worsened. Among activities of daily living improved more than 60% were hair grooming, tying a sash behind the back, removing upper garments, or being able to touch the opposite shoulder. Range of motion improved in each measure, with the greatest change noted in the angle of abduction.

Support for subacromial impingement can be found in a randomized, single-blind, open-comparator clinical study (n=80). Hyaluronate 20 mg injected into the subacromial space once weekly for 3 weeks was associated with greater self-rated pain relief of subacromial impingement syndrome of the shoulder compared with a single dexamethasone injection, although improvement in functional scores and use of rescue medication were similar. Participants older than 40 years of age who had subacromial impingement syndrome without a rotator cuff tear and who had pain for 3 months or longer without improvement despite conservative treatment with physiotherapy and NSAIDs were randomized to hyaluronate sodium 20 mg subacromial injection once weekly for 3 weeks (n=38; mean age, 55.9 years) or a single subacromial injection of dexamethasone disodium phosphate 5 mg with 4 mL lidocaine 2% (n=42; mean age, 54.1 years). In both treatment arms, the 100-point visual analogue scale (VAS) score decreased significantly from baseline to week 12, from 58.6 to 24.6 in the hyaluronate group (p less than 0.0001) and from 57.2 to 36.9 in the dexamethasone group (p less than 0.0001). The hyaluronate group demonstrated a significantly greater decrease in the VAS score at 12

weeks compared with the dexamethasone group (p=0.018). Functional score from baseline to week 12, assessed by the American Shoulder and Elbow Surgeons (ASES) standardized shoulder assessment form, improved from 18.2 to 22.8 in the hyaluronate group (p=0.0023) and from 17.5 to 21.9 in the dexamethasone group (p=0.0002), although no significant difference was observed between the treatment groups at week 12. The use of acetaminophen for rescue pain relief was similar between the hyaluronate and dexamethasone groups (26 of 38 and 29 of 42, respectively). Adverse events were generally mild, with nasopharyngitis (hyaluronate, 15.38%; dexamethasone, 13.46%) and muscle pain (hyaluronate, 9.62%; dexamethasone, 3.85%) reported most frequently.

Support for temporomandibular joint disorder can be found in a study where patients were injected with sodium hyaluronate into the articular cavities with internal derangement of temporomandibular joints (TMJs). The procedure decreased friction so that, surgically, the articular disc could be retracted and, clinically, degree of mouth opening increased in some patients. After 63 patients were randomized into either a test group of 43 patients (45 TMJs, 29 with disc displacement with reduction and 16 without reduction) or a control group of 20 patients (24 TMJs, 17 with disc displacement with reduction and 7 without reduction), injections were made into the articular cavity. Test-group patients received 0.3 to 1 mL sodium hyaluronate 1% up to 3 times, either into the upper cavity only or into both upper and lower cavities, while control-group patients received 1 mL of lidocaine 2%. At follow-up visits relief of joint pain was evaluated as very good, good, or of no effect. Results were very good for 17 TMJs in the test group and 4 in the control group; good for 19 in the test group and 8 in the control group; and of no effect for 9 in the test group and 12 controls (chi(2)=6.6535, p less than 0.01). The difference between disc displacement with reduction and without reduction was not significant.

VI. REFERENCES

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