Hyaluronic Acid

Health Technology Assessment Update
July 26, 2004

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Background

Hyaluronic acid (HA) is an important natural component of synovial fluid. An osteoarthritic joint has a lower concentration and molecular weight of hyaluronic acid, which reduces the viscoelasticity of the joint synovial fluid. Viscosupplementation involves a series of intra-articular injections of HA to increase the viscoelasticity of the synovial fluid in a knee with osteoarthritis (OA).

In 1998, the Department of Labor and Industries (LNI) conducted a technology assessment of HA for OA of the knee. At that time, the department determined that one course of Hyalgan or Synvisc may be considered medically necessary if OA is the accepted condition or is retarding recovery from an accepted condition.[1] At a later date, the department website was updated to include coverage of Supartz. The requesting provider must provide documentation of the existence of OA in the knee and show the patient's failure to benefit from other treatment methods, including physical therapy, nonopioid analgesics, and nonsteroidal anti-inflammatory drugs (NSAIDs). Under rare circumstances, an additional course of HA treatment may be covered. However, additional courses of HA will be covered only when OA is the accepted medical condition, not when it is the condition retarding recovery.[2]

This topic is being revisited because since 1998, two new HA products have been FDA approved and a vast amount of literature has been published on the efficacy of HA for OA of the knee. This update will include information that has been published since the release of the original 1998 Provider Bulletin.

FDA Status

The first two HA products to receive FDA Pre-Market Approval were Hyalgan and Synvisc in 1997.[3,4] Both were indicated for treatment of pain in OA of the knee in patients who have failed to adequately respond to conservative non-pharmacologic therapy and to simple analgesics. FDA approval was later granted to Supartz in 2001,[5] and to Orthovisc in early 2004.[6]

Each HA product is only indicated for intra-articular (IA) injection into the knee to treat OA; Hyalgan and Supartz are approved for five injections, Synvisc and Orthovisc are approved for three injections. The products all have different molecular weights—Hyalgan has the lowest molecular weight (615 kDa), and Synvisc has the highest molecular weight (6000 kDa) due to cross-linked synthetic hylans.[7]

Literature Review

Search methodology included searching existing technology assessment resources, and then doing a PubMed search based on the last search date. Since the last search date was the March 2004 Hayes technology assessment, the search was limited to clinical trials published between March 2004 and July 2004. PubMed search terms included *knee*, *osteoarthritis*, and *hyaluronic acid*. This search found the Wang meta-analysis as well as two other recent studies. Additional studies in this technology assessment were found by searching for articles excluded from the included technology assessment and meta-analysis.

1. Technology Assessment

In March 2004, Hayes Incorporated revisited the HA issue.[8] In looking at peer-reviewed published literature between 1997 and March 2004, they identified studies comparing HA with placebo, nonprescription analgesics, and corticosteroids; different HA preparations; physical therapy; arthroscopic washout; or NSAIDs for treatment of OA of the knee. Studies that provided a randomized comparison to placebo or to another treatment for OA and included at least 50 patients underwent a detailed review. Their technology assessment found that multiple randomized, double-blinded, placebo-controlled studies suggest that HA injections can provide significant pain relief and improved function in individuals suffering from OA of the knee.

a. Findings

The 17 studies included in the assessment were generally well designed, with moderate to large sample sizes, providing randomization to treatment group and either a placebo control or comparison with standard treatment, or both. The study by Petrella, et al. supported a prior report by Altman et al. (1998) in showing that HA provides similar pain relief to NSAIDs but with fewer adverse effects. Different studies also found that HA has a longer duration of pain relief than IA corticosteroids (Frizziero and Pasquali-Ronchetti; Leopold, et al.; Tascioglu and Oner; and Caborn).

Some studies have evaluated molecular weights of HA because of the theory that high molecular weight (HMW) HA is more effective than low molecular weight (LMW) HA. This hypothesis is based on claims that HMW HA normalizes synovial fluid and induces the synovial membrane to synthesize normal HA.[7]

Wobig et al. compared HMW Synvisc to LMW Supartz (also known as Artz or Artzal) and found that Synvisc had statistically significant greater efficacy (the manufacturer of Synvisc funded this study).[9] However, Karlsson et al. compared the same HA formulations and found no difference between the two treatments.[10] With so few high-quality studies evaluating the HMW HA treatments and the presence of heterogeneity among them, the hypothesis that HMW HA has greater efficacy than those of LMW has yet to be confirmed.

b. Adverse Events

Intra-articular HA injections have led to adverse events in some study participants. Most adverse events are mild reactions such as headache, painful post-injection reaction, local skin problems, and pruritus. The adverse effects are similar to those reported with saline injection. A study by Brandt et al., suggested that because the incidence, type, and severity of adverse events between HA and placebo treatment groups were similar, the adverse events may be attributed to the injection instead of the material injected.[11]

In a briefly mentioned preliminary report, Leopold et al. reported a frequency of acute local reaction eight times greater in patients receiving more than one course of Synvisc than in those treated only once.[12]

c. Limitations

Limitations for different studies included relatively small sample size, high loss to follow-up and dropout rates, and follow-up periods of one year or less. The majority of studies that they reviewed in detail had a follow-up period of 20-26 weeks. Two studies only had a 12-week follow-up period and only four studies had a one-year follow-up period. None of the studies had a follow-up period for longer than 1 year. Six studies had a small sample size (less than 100 patients), and four studies had no comparison to NSAID treatment. Potential study bias sources included differences in method of subject selection, treatment protocols, definitions of response, and lack of adequate blinding for the investigator.[8]

In an included meta-analysis, Lo suggested that a strong placebo effect might exist because many studies reported significant pain improvement in placebo groups. Lo also indicates that a publication bias may overestimate the effect of HA over placebo.[7]

None of the studies provided follow-up for more than 12 months or addressed the benefits and potential adverse effects of long-term use of HA. Furthermore, none of the studies evaluated the efficacy or outcomes of retreatments of HA.

d. Conclusions

There is evidence that IA HA injections can relieve pain and allow increased activity in patients with OA of the knee. A Hayes Rating of B has been assigned for a single course of treatment for patients with OA of the knee with the goal of providing symptomatic relief.[8]

2. Meta-analysis of randomized controlled trials (RCTs)

Wang et al. performed a meta-analysis to reveal the therapeutic efficacy and safety of IA injection of HA for osteoarthritis of the knee.[13] The meta-analysis included twenty blinded randomized controlled trials published between 1996 and 2001 comparing HA to placebo. The selected trials provided data on therapeutic effects for a total of 1647 randomly assigned knees (818 treated with HA, 829 treated with placebo) and data on safety for a total of 2252 knees (1141 treated with HA and 1111 treated with placebo).

The outcome measure of efficacy for the meta-analysis was the mean difference in the efficacy scores between the HA and placebo groups. Outcome end points were classified into three categories: pain with activities, pain without activities, and function. The outcome measure of safety was the relative risk of adverse events.

A subgroup analysis and meta-regression analysis were done with only the non-cross-linked HA trials to avoid a potential drug-class difference comparison with cross-linked HA. The goal of the subgroup analysis was to investigate the effects of several categorical attributes on the estimates of HA efficacy and to assess between-study heterogeneity within each subgroup of trials. Categorical attributes included blinding status, single-center or multi-center trial, intention to treat analysis, use of escape analgesics, mean age of the patients, inclusion of the most advanced radiographic stage of OA, effusion as an inclusion or exclusion criterion, trial duration, sample size, and the status of industry funding.

a. Findings

Injections of cross-linked HA (Synvisc) and of non-cross-linked HA (Hyalgan, Supartz, and Orthovisc) can decrease symptoms of OA of the knee.

The trials involving Synvisc had greater pooled mean differences of HA efficacy than the trials involving non-cross-linked HA. The efficacy differences between cross-linked and non-cross-linked HA are in the table below. The sum of pain intensity differences (SPID) is the difference in pain intensity between one time-point and the baseline. The efficacy scores are SPID% (the overall efficacy in the trial period), ASPID% (the overall efficacy in the trial period after adjustment for the baseline pain intensity) and peak PID% (the maximum efficacy during the trial). The efficacy scores were similarly calculated for function (SFID%, ASFID%, and peak FID%).*

Outcome efficacy scores for cross-linked and non-cross-linked HA

Pain with Activities	*Cross-linked HA*	*Non-cross-linked HA*
SPID%	23.6%	5.4%
ASPID%	34.8%	8.7%
PID%	21.7%	7.4%
Function		
SFID%	21.9%	5.3%
ASFID%	38.3%	11.7%
FID%	26.8%	8.2%

* The sum pain intensity difference (SPID) was the sum of the average of two consecutive pain intensity differences multiplied by the time-interval between two time-points—the area under the pain intensity difference vs. time curve. SPID% = ((SPID)/(maximum scale of pain intensity x trial duration)) x 100%, representing the overall efficacy in the trial period. ASPID% = ((SPID)/(baseline intensity x trial duration)) x 100%, representing the overall efficacy in the trial period after adjustment for the baseline pain intensity. Peak PID% = (maximum pain intensity difference/maximum scale of pain intensity) x 100%, representing the maximum efficacy during the trial.

There was significant between-study heterogeneity in the estimates of HA efficacy. The included studies varied in different areas, including characteristics of the patients, inclusion and exclusion criteria, type of HA product, outcome endpoints, outcome instruments, and status with respect to industry funding. More RCTs comparing different types of HA products are needed to clarify the effects of cross-linked status on HA efficacy.

Though all of the non-cross-linked HA trials showed a significant decrease in pain with activities, studies with a lower methodological quality, such as a single-blind or single-center design, resulted in higher estimates of HA efficacy. Furthermore, patients older than sixty-five and patients with the most advanced radiographic stage of OA were less likely to benefit from IA injection of HA.

b. Adverse Events
The pooled relative risk of minor adverse events for all included trials in this meta-analysis was 1.19 (95% confidence interval, 1.01 to 1.41). Although this review showed a low rate of complications, injection of cross-linked HA may be associated with a painful acute local reaction. The aforementioned preliminary report (excluded from this meta-analysis and briefly mentioned in the Hayes technology assessment) by Leopold et al. described acute local reactions in 21% of patients receiving multiple courses of Synvisc.[12] According to Wang et al., this difference could be because all of the Synvisc trials in this meta-analysis were industry-funded; the authors believe that adverse events may be minimally reported in industry-funded trials.

c. Limitations
Many limitations can be noted within this meta-analysis. Unpublished trials were not searched; since trials with "negative" results tend to be unpublished, exclusion of unpublished trials may skew the effect in the positive direction because of publication bias. There may also be a small-trial bias in favor of HA efficacy; some small trials that did not show a positive therapeutic effect of HA may not have been published. Similarly, the effect of HA would be inaccurately skewed in the positive direction.

d. Conclusions
The meta-analysis confirmed that IA injections of cross-linked and non-cross-linked HA could decrease symptoms of OA in the knee. Better designed RCTs with high methodological quality are needed to resolve uncertainty about therapeutic effects of different types of HA on OA of the knee in various clinical situations and patient populations.

3. Published Randomized Controlled Trial with Double-Blinding

Day et al. performed a double blind, randomized, multicenter, parallel group study of Supartz injections between February 1995 and August 1996.[14] This study was not

published until March 2004 and was not included in the Hayes technology assessment or the Wang meta-analysis.

a. Study Population: 240 patients were randomized to two parallel groups, one receiving 5 weekly IA injections of Supartz (Artz) and the other receiving weekly IA injections of placebo. Patients had mild to moderate OA of the knee. The weekly treatment period was followed by 13 weeks of follow-up. Office visits were every four weeks during the follow-up period.

   A significance level of $p < 0.05$ with statistical power of 90% was identified to detect a clinically significant difference in the primary efficacy measure. A reduction of 10% in the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Scale) pain score was considered clinically significant.

   Patients used the WOMAC Osteoarthritis Scale as a primary efficacy measure to assess their pain, stiffness, and physical function. Secondary criteria for evaluation included the Lequesne Index of severity of knee symptoms, knee examinations, physician and patient global assessments, and acetaminophen consumption.

b. Results: For efficacy analyses, 2 study populations were defined:
   1. Modified Intention to Treat (mITT)—all subjects who received a dose of study medication and had at least one efficacy observation recorded after treatment.
   2. Per Protocol (PP) population—all subjects who received at least 3 injections of study medication and did not have significant protocol deviations.

   Of the 240 patients who met study inclusion criteria and were randomized to HA or control treatments, 223 were valid for mITT analysis. Of these 223 patients, 90% of HA patients and 91% of placebo patients completed the study.

   Repeated measures analysis of covariance (ANCOVA) was carried out to consider the difference between the treatment groups in the WOMAC and Lequesne scores recorded at Weeks 6, 10, 14, and 18. The ANCOVA model included factors for treatment, center, and visit number and used the baseline scored as the covariate.

   Overall, a significant difference ($p < 0.05$) between the treatment groups was observed in WOMAC pain and WOMAC stiffness, and both variables improved substantially more than the pre-specified effect size of 10%. The ANCOVA analysis identified a significant difference in stiffness scores from Week 10 to Week 14, and a significant difference in pain (WOMAC and Lequesne Index) at Weeks 14 and 18. Statistically significant differences between treatment groups were also observed for the degree of flexion and degree of extension in favor of the HA treated knee.

c. Limitations: There was a short follow-up period in this study of only 18 weeks. Acetaminophen was provided to study participants and was moderately used for pain elsewhere in the body. This therapy was used more frequently by the control patients, which may have reduced the positive effects of HA. Furthermore, the control group may have benefited from the removal of joint effusion prior to saline injection.

d. Conclusions: IA HA treatment was more effective than placebo in mild to moderate OA of the knee for the 13 week, post-injection study period. In contrast to other studies of HA, this study demonstrated a slower onset of effect; a significant difference from control was not observed until 6 weeks into the study.

4. Published Case Series Studies Without Comparison Groups

I. Lee et al. performed a prospective case series study on patients referred by their Chicago area health maintenance organization (HMO) to an orthopedic surgery clinic for OA of the knee.[15] The study recruited consecutive patients from October 1995 to May 1998, but was not published until April 2004.

a. Study Population: 79 patients were recruited, but 5 patients were excluded due to inadequate available medical history. 74 patients were treated and 120 knees were injected with Synvisc. 62% of patients received bilateral knee injections. No patients received more than one series of injections. Follow-up evaluations were scheduled 1 month and 1 year following HA injections.

b. Results: Most patients indicated that their pain improved following HA injections. At 1 month, most patients reported their pain as 'much improved' (81%) or 'improved' (18%). At 1 year, a majority of patients reported their pain as 'much improved' (5.8%) or 'improved' (85%).

Pain relief in treated knees					
Months	<3	3-6	6-9	9-12	>12
Number of knees	7	39	40	25	9
% of knees	5.8%	32.5%	33.3%	20.8%	7.5%

Final evaluation of the patient's perceived duration of relief revealed that 87% of patients experience pain relief between 3 and 12 months, and 62% experienced pain relief for longer than 6 months.

There was a reduced use of pain medication at 1 month and 1 year. A decrease in use of analgesics and NSAIDS was reported at 1 month following HA therapy—analgesics 96% and NSAIDS 75%. At one year, 78% of patients reported less analgesic use. However, a majority of patients (74%) returned to pretreatment NSAID use one year following HA treatment.

Three patients experience localized erythema and irritation around the injection site, but complete resolution of symptoms occurred within 48 hours.

c. Limitations: There were no reported dropouts in this study. Recall bias may have been a factor due to the large gap between the 1-month and 1-year follow-up visits. Further limitations of the study include the lack of assessor blinding and control groups.

d. Conclusions: Pain relief and improved mobility were reported for up to 1 year following HA injections. HA treatment reduced the need for analgesics, NSAIDs, steroid injections, physical therapy, and assistive devices. The authors concluded that Hylan G-F 20 (Synvisc) effectively and safely relieves OA knee pain, facilitates an improved activity level, and decreases the need for pain medication, physical therapy, and assistive devices.

II. Kotz and Kolarz conducted an open-label, multi-center study in Austria between October 1991 and October 1994 to evaluate the effects of HA treatments in patients with OA of the knee.[16]

a. Study Population: 108 patients received weekly injections of Hyalgan and were observed for up to 12 months following the last injection. Pain was measured on a visual analog scale (VAS) of 0-10, with 0 being no pain and 10 being maximum pain. Minor efficacy criteria included pain after exercise, pain at rest, knee motion in degrees, walking distance, acetaminophen consumption, and onset of effect.

Of the 108 patients enrolled, only 73 completed the first treatment cycle. Fifty-nine patients completed the 12-month follow-up; 14 began a new treatment cycle after 4-8 months, and six of these patients completed the second cycle follow-up.

b. Results: Sixty-eight percent of patients experienced relief of symptoms four weeks after treatment. In 55% of these patients, relief was maintained until the end of the 12-month follow-up period. Of the patients requiring a second treatment cycle, 50% also experienced an improvement in symptoms for an additional 12-months. There were 119 adverse events in 108 patients, the most common being back pain (16.8%), injection site reaction (11.8%), and injection site pain (6.7%).

Overall assessment of pain after exercise

Patients who underwent	Baseline VAS	Day 35 VAS	12-month VAS
1st treatment cycle	6.74 cm	2.83 cm	1.94 cm

2nd treatment cycle	5.94 cm	4.56 cm	3.15 cm

c. Limitations: Study limitations included a small sample size, a high dropout rate (32%), and lack of comparison to placebo or other knee OA treatment regimen. Due to the high dropout rate, only 73 patients were actually followed through to the end of the 12-month follow-up period. The lack of assessor blinding was also a limitation, and use of intention to treat analysis was unclear. Authors failed to discuss adverse reactions.

d. Conclusions: Unlike most studies, this study examines a second course of HA treatment for OA of the knee. Unfortunately, because only 14 patients received a second treatment of HA and only six of those completed the 12-month follow-up, it is difficult to conclude anything from these findings.

III. Neustadt evaluated the long-term efficacy and safety of five weekly IA injections of Hyalgan in patients with moderate to severe OA of the knee whose pain was not controlled by conventional measures.[17]

a. Study Population: 76 patients (92 knees). There were 60 males and 16 females; with a combined mean age of 64 years.

Clinical assessment was carried out at baseline, weekly at the time of injections, at the end of the series, at six months, 12 months, and 24 months. This assessment consisted of physical examination and outcome measures of pain using categorical assessment and a VAS of 1-10. Quality of life effects were measured by activities of daily living, such as effects on walking, rising from a low seat, climbing steps, and getting in an out of a car.

b. Results: Following HA treatment, 72% of patients experienced more than 50% improvement for one year or longer, as indicated by a reduction in VAS score. Twelve of 15 patients who had been scheduled for total knee replacement (TKR) surgery no longer considered the procedure necessary. Adverse events were minor and infrequent, but injection site pain was present in 20% of patients.

Number of knees over time according to pain VAS rating (n=92 knees)

Pain	*VAS rating*	*Baseline*	*End of Series*	*6 mo.*	*12 mo.*	*24 mo.*
None	0	0	0	6	5	4
Slight	1-3	0	50	32	25	12
Moderate	4-6	28	38	16	9	7
Severe	7-9	54	3	4	3	1
Extreme	9 or >	10	1	0	0	0
Loss to FU or TKR				34	50	68

Clinical improvement correlated with the stage of disease severity. HA treatment was effective in the majority of patients with Kellgren grade 2 and 3 OA, resulting in clinical improvement of 71% and 62% in those patients, respectively. Only 42% of patients with grade 4 OA experienced clinical improvement.

Thirteen patients (15 knees) received a second course of treatment due to an inadequate initial response or early recurrence of pain. Ten of the 15 knees (67%) exhibited clinical improvement six weeks after a repeat treatment course.

c. Limitations: The author failed to discuss any limitations; however, loss to follow-up, a disproportionate male study population, and the absence of assessor blinding and control groups are all limitations in this study. By the end of the 24-month follow-up period, 74% of the original study population had been lost to follow-up or TKR; it is unclear why these patients were lost to follow-up or how it could have affected the results.

d. Conclusions: The study concluded that IA injection of Hyalgan was effective in the majority of patients, and prevented or delayed TKR in more than 12 patients with severe OA. At the 24-month clinical assessment, 13% of the original study population experienced only slight pain, while most of the patients (74%) had been lost to follow-up.

5. Published Retrospective Data Analysis

Evanich et al. retrospectively reviewed the first 100 knees to receive IA HA at their clinic to determine the efficacy of HA treatment.[18]

a. Study Population: In 19 months, 84 patients (100 knees) received 300 injections of Synvisc; 70 patients (80 knees) were available for clinical follow-up and responded to a detailed patient questionnaire.

The Hospital for Special Surgery knee score was used for pre-injection and post-injection evaluation and knee radiographs were graded based on disease severity. To avoid provider bias, an orthopedic clinic nurse administered a standardized telephone questionnaire to each patient. Clinical efficacy was evaluated by degree of pain relief, increase in activity level, and reported satisfaction. Patients were asked to grade their maximum pain relief on a scale of zero to 10 during follow-up.

b. Results: Of the 55 knees (69% of knees; 52 patients) with some pain relief, the average degree of pain relief was 65%. Average onset of relief occurred 2.3 weeks after the first injection and average duration of pain relief was 4.8 months. Increased activity level was reported in 27 patients (35% of knees; 28 patients) following HA treatment. Satisfaction with overall response to treatment was

found in 36 patients (49% of knees). Adverse events were noted in 15% of knees (11 patients) an average of 1.2 weeks after the first injection.

Average Degree of Pain Relief

	Age (years)			
Radiographic Grade	<40	40-64	65-79	80+
I	58%	38%	73%	73%
II	--	47%	54%	52%
III	--	31%	28%	65%
IV	--	--	0%	15%

As the radiographic grade became more severe, the average degree of pain relief declined; pain caused by the most severe form of arthritis was unrelieved by HA treatment in most observed cases.

c. Limitations: The authors did not address study limitations. The length of time between HA treatment and follow-up contact was unclear; depending on the time span in a retrospective review, recall bias may have been a factor. Furthermore, only 80% of the knees were available for follow-up.

d. Conclusions: Overall, less than 50% of treated knees in this study achieved satisfactory results. The authors recommend IA HA only for patients who have significant surgical risk factors and for patients with mild radiographic disease in whom conservative treatment has failed.

Other Insurers

Most insurers cover HA injections for OA of the knee, although not every policy has been updated to include the recently approved Orthovisc. Aetna has updated their policy, including Orthovisc as medically necessary for patients with OA of the knee who have not responded to more conservative therapies.[19] Medicare carriers in a few states have also indicated that they will cover Orthovisc.[20,21,22,23]

Excellus BlueCross BlueShield states that:

> Evidence from randomized controlled trials is sufficient to conclude that viscosupplementation improves health outcomes, providing pain relief and functional improvement in patients who have failed conventional conservative management or cannot tolerate alternative medical treatment.[24]

Premera Blue Cross will cover HA injections of Synvisc, Hyalgan, and Supartz if they are medically necessary—the patient has to have failed to adequately respond to pharmacologic and nonpharmacologic treatments. Patients must have failed at least three of the following treatments:

- Exercise when medically appropriate
- Physical therapy when medically appropriate
- Corticosteroid injections, if indicated

- NSAIDs
- Simple analgesics.[25]

For the most part, viscosupplementation of Hyalgan, Supartz, and Synvisc is covered for one treatment course; an additional treatment course may be deemed necessary under individual consideration for coverage. An exception is that the Health Plan of Nevada, which will only cover one course of treatment over a patient's lifetime.[26] Most Medicare carriers reimburse for a second course of HA treatment 5-6 months after the first course of treatment if the beneficiary received pain relief from HA. However, TriSpan Health Services (covering Medicare Part B beneficiaries in Louisiana, Mississippi, and Missouri) will deny repeat treatments of HA injections as not reasonable or necessary because the safety and efficacy of repeat treatment cycles have not been established.[27]

Costs

Under the Fee Schedule, LNI pays the average wholesale price (AWP) for Hyalgan, Supartz, and Synvisc. Orthovisc is paid "by report" as an unclassified biologic because it has yet to receive a unique HCPCS code. The average wholesale price (AWP) for each HA injection effective January 2004:

- Hyalgan, Supartz: $146.01/injection; $730.05/five-injection treatment course.
- Synvisc: $235/injection; $705/three-injection treatment course.[28]

The cost of Orthovisc is $250.91 per injection, $752.73 for a three-injection treatment course.[29]

In 2001, Waddell et al. used a hypothetical cohort of 3835 patients in a managed care plan with OA of the knee to illustrate the potential cost savings associated with viscosupplementation in a managed care setting.[30] They found that the 3-year savings associated with adding one or more courses of Synvisc to the standard treatment for OA of the knee was $8,810,771. The total savings per OA patient receiving HA treatment was $4706, and 808 total knee replacements were avoided.

In 2003, LNI paid for 907 HA injections, for a total of 296 patients. The total amount paid for HA treatment in 2003 was $192,034.54; most of the cost came from treatments of Synvisc ($157,158). Only five patients were covered for repeat treatments in 2003 (four for Synvisc, one for Hyalgan or Supartz).

Billing Codes

The current HCPCS billing codes for HA treatments are:

J7317: each injection of Supartz or Hyalgan,
J7320: each injection of Synvisc, and
J3590: each injection of Orthovisc (this is a miscellaneous code for "unclassified biologics," the manufacturer is awaiting a unique HCPCS code).

Conclusions

Literature published since 1998 does indicate that HA injections can provide pain relief in patients with OA of the knee. However, the literature does not conclusively determine the safety or efficacy of repeated HA treatments.

The newest HA product of Orthovisc should be considered an equivalent formulation of HA and should be included under coverage. Although it has not been as extensively studied as the other HA products, it appears to be a comparable product.

Resources

[1] Department of Labor and Industries (LNI). "Hyaluronic Acid." *Medical Coverage Decisions*. Available from Hhttp://www.lni.wa.gov/ClaimsInsurance/Providers/TreatmentGuidelines/Covered/default.aspH. Last accessed on May 24, 2004.
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