

HERC Coverage Guidance – Viscosupplementation for Osteoarthritis of the Knee Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
<i>Orthopedic Surgeon</i> Boston, MA	1	As a practicing orthopedic surgeon and Chair of a former work group for the American Academy of Orthopedic Surgeons (AAOS) that developed the AAOS Guideline for the Treatment of Osteoarthritis of the Knee, I am very familiar with the literature surrounding the use of viscosupplementation for the treatment of osteoarthritis of the knee, the numerous meta-analyses of this literature, and the application of this evidence to the clinical practice of orthopedic surgery.	Thank you for taking the time to comment.
	2	I believe the Health Evidence Review Commission for the State of Oregon has reached the wrong conclusion for their coverage guidance for viscosupplementation in the treatment of osteoarthritis of the knee. Osteoarthritis of the knee has become epidemic in the United States due to high athletic activity, frequent knee injury, and the burgeoning problem that we have with obesity. We are limited in our treatment modalities for this condition. There are no disease modifying treatments and as a practicing physician I am deeply concerned that total knee arthroplasty (TKA) being done on relatively young, overweight patients, will lead to disastrous conclusion with multiple revisions, an astronomical burden of expense for the health care system, and is the wrong course.	HTAS is aware of the epidemic nature of obesity, and consequently, of OA of the knee and hip.
	3	While the literature concerning the use of HA products in the treatment of osteoarthritis of the knee is suboptimal, there are numerous reports outlining its benefit. The majority of insurers and many agencies, including the Washington Health Technology Assessment Clinical Committee, have recommended that viscosupplementation injections into the knee for osteoarthritis be covered with limitations. This is the appropriate recommendation. Clearly, viscosupplementation should not be the first line treatment for osteoarthritis of the knee, but needs to be covered for a limited population set. This population set should include those who have not had adequate response to non-pharmacologic conservative treatment and simple analgesics. It should also include those who are unable to take simple analgesics due to side effects or contraindications, such as hypertension or gastric ulcer disease. Limiting its use to two courses per year is reasonable. Repeated use of viscosupplementation should require documented evidence of the clinical benefit of prior courses of treatment.	HTAS agrees that the literature is suboptimal, and is aware that the WA HTA clinical committee has reached a different conclusion. However, the HTAS does not believe the balance of evidence supports the effectiveness of this therapy.
	4	As I have stated, I believe the Oregon Health Evidence Review Commission has reached the wrong conclusion in its recommendation for non-coverage of viscosupplementation for the treatment of osteoarthritis of the knee. I strongly recommend that the Commission reconsider their coverage guidance and would recommend that they adopt the recommendation of the Washington Health Technology Assessment Clinical Committee, which has been noted in your Draft Coverage Guidance. To leave your coverage guidance as you have proposed will likely lead to an increased use of narcotic analgesics and earlier use of total knee arthroplasty, both of which will be burdens on society for decades to come.	See comment #3
<i>Orthopedic</i>	5	I am writing to comment on your position regarding payment for viscosupplementation as a treatment	Thank you for sharing your experience with this

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Surgeon Portland, OR		for osteoarthritis of the knee that causes pain. This modality for pain control has been an essential part of my practice for alleviating patients' pain and helping them avoid total knee arthroplasty. In conjunction with the literature, which is summarized in the summary of evidence that you presented, my protocol for treating patients begins with non-pharmacologic, activity modification, nonsteroidal anti-inflammatories and then injections. Most patients that come to see a surgeon have already done nonsteroidals and activity modification and, thus, I most often start with a corticosteroid injection.	treatment.
	6	As mentioned in your summary of evidence, I limit that injection to one injection because repeat injections can have harmful effects on the knee joint and can cause significant reactions for the patient. Once they have had a successful injection that eventually fails, my next step typically for these patients is viscosupplementation. And as mentioned in your summary of evidence, the patients tend to get a much longer period of relief from these injections versus corticosteroid injections. I do not repeat these injections more than twice a year and when the patient begins to have symptoms that are not alleviated for greater than six months with these injections or begin having severe limitation of motion, I do, at that point, suggest total knee arthroplasty. Most patients, however, with a treatment of viscosupplementation can avoid total knee arthroplasty for several years, and I think this is a significant benefit in terms of utilization of medical resources.	Thank you for sharing your experience with this treatment.
	7	I completely agree with the criteria of reserving viscosupplementation for patients who have not had an adequate response to non-pharmacological measures such as activity modification, as well as limiting them to two courses per year, with at least four months in between, and documented evidence of clinical benefit from a prior course of treatment, whether that be viscosupplementation or at least temporary relief from a corticosteroid injection that may or may not include local anesthetic.	Thank you for your comment.
	8	To deny viscosupplementation to all patients with osteoarthritis I think would be doing a disservice to the medical community as well as the patients themselves and potentially cause an increase in cost utilization in terms of the increased usage of total knee arthroplasty as a treatment modality for osteoarthritis.	Thank you for your comment.
	9	In addition to the previously dictated letter regarding the viscosupplementation for patients with osteoarthritis, there is one particular patient population in which there has been a significant amount of literature that does show a positive effect of viscosupplementation in this particular patient group, which includes patients with symptomatic meniscal tears, post arthroscopy, having continued pain as a result of their concomitant osteoarthritis. Several studies show a positive effect that is lasting. In 2007, a study done in the Journal of Knee Surgery and Sports Traumatology and Arthroscopy, author Hempfling shows in a randomized controlled double blind study of 80 patients undergoing arthroscopic knee lavage, 40 patients were given hyaluronan 10 mL and 40 patients were given lavage. Both the control and study groups, the control group being the lavage and the study group being the hyaluronan, showed positive effects in three months. The treatment effect was maintained in the	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available

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		hyaluronan group for a year, as opposed to only three months in the lavage group.	evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	10	In 2008, Bert in the Journal of Arthroscopy and Related Surgery, reported on a prospective multi-center open label study on athletic patients with knee OA, who underwent knee arthroscopy for mechanical symptoms of meniscal pathology. On average, these patients were given Hylan G-F 20 treatments, initiation at an average of 3.4 months after arthroscopy, when they continued to have pain and decreased activity at baseline. At three and six months post injection, the Western Ontario and McMaster University Osteoarthritis Index and International Knee Documentation Committee scores significantly improved. At three months followup, the authors also reported improved activity levels. These were in patients who continued to have significant symptoms on average 3.4 months post knee meniscectomies secondary to the concomitant osteoarthritis.	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	11	Again, in 2008, Huskin et al, in the Journal of Knee Surgery Sports Traumatology and Arthroscopy, also reported on an open label multi-center prospective study in patients who continued to have pain after arthroscopic meniscectomy with concomitant osteoarthritis, starting with injections at a mean time post surgery of 53 days, showing significant improvements in visual analog scale WOMAC scores, visual analog scale walking pain scores, physician global assessment and patient assessment.	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	12	Thus in this population, patients who have mild osteoarthritis in conjunction with meniscal tears that are treated arthroscopically, there has been significant literature that shows an advantage of using viscosupplementation postoperatively in patients that continue to have pain. So, considering 90% of patients that have documented osteoarthritis will have meniscus tears seen on MRI scan, plus patients	Two of the three cited studies were not blinded or controlled. The population of the third study did not have meniscal tears.

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		who have osteoarthritis that does not warrant total knee arthroplasty and have concomitant meniscal tears that are treated arthroscopically, have some relief, but then continue to have pain secondary to osteoarthritis, viscosupplementation is shown to have a benefit for them postoperatively when they continue to have pain.	
	13	I think this patient population should be afforded the advantage of obtaining viscosupplementation to again attempt to reduce their pain and prevent them undergoing total knee arthroplasty.	Thank you for your comment.
<i>Orthopedic Surgeon</i> Beaverton, OR	14	I must comment in all earnestness regarding the apparent recommendation to discontinue viscosupplementation. This would be devastating to my patients with knee arthritis, who need it. These are: 1) Younger persons who have disabling arthritic knee pain and who are too young for total knee replacement. These people are unable to properly exercise because of their pain, so they gain weight, lose strength, become deconditioned (so they either fall and injure themselves, or require extensive and expensive physical therapy. They tend then to become diabetic, and you know the costs to health and society when that happens.) 2) Older individuals, who by reason of poor health, are unable to obtain a total knee replacement. They are doomed to suffer, until they die, with knee pain, without viscosupplements. It would be cruel to not provide patients such as these with viscosupplements. 3) Those who cannot afford a knee replacement either due to its expense or time away from productive work. Many fall into this category. 4) Unhealthy patients who are younger, eg those on renal dialysis, or type 1 diabetics, etc., ie high risk patients, where arthroplasty is too risky.	Thank you for sharing your experience with this treatment.
	15	I have been using viscosupplements for nearly 14 years, and, with only 2 exceptions, have not had untoward reactions. With Supartz over the last 6 years, I have had no inflammatory reactions. It is thus VERY safe. It is also VERY effective, since my results are superb, ie 90+ % of my patients have sustained relief for 6-12 months, and pain typically improves by greater than 80-90%. Few failures occur, and these are typically those whose arthritis is milder, or those who have concomitant internal derangements, such as meniscus tear.	Thank you for sharing your experience with this treatment.
	16	Base on all the above, I strongly disagree with the results of your studies' conclusions, as they do not correlate to my own very extensive experience, on about 400 patients.	While anecdotal experience has a strong influence on individual opinion, it is inherently susceptible to bias. High quality RCTs are the best way to assess true treatment effects, and the evidence examined by HTAS is inconclusive.
	17	Viscosupplements are very cost effective compared to a knee replacement, which, without viscosupplements, would have to be done at a much earlier age, thus costing the insurer a lot now, when it could have been postponed, and then likely would have avoided the revision knee arthroplasty on the knee which could have waited. Postponing an arthroplasty in the proper patient is obviously in the best interests of patient and insurer alike. To discontinue viscosupplements is assuredly penny wise and pound foolish.	Thank you for your comment.

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	18	I strongly object to discontinuation of viscosupplements for all the above reasons and implore you to avoid all the long term expenses and devastating orthopedic and medical consequences of a very wrong decision.	See comment #3
<i>Orthopedic Surgeon</i> Tigard, OR	19	I have practiced general orthopedics in Oregon since 1991 and the use and application of viscosupplementation for patients with knee arthritis is an important medical treatment. I strongly request that it's use be continued as part of the available spectrum of treatments for the arthritic knee. Many patients are medically contraindicated to proceed with total knee arthroplasty because of medical problems or their youth. Taking away the option will have a negative effect on the health of those patients who need this treatment. Once cortisone is tried and found ineffective arthroscopy is not effective for arthritis pain alone and the only viable option short of a total knee replacement is viscosupplementation, which I have found effective throughout my years in practice. I urge you to continue to allow this treatment to be available for those in need.	Thank you for sharing your experience with the treatment.
<i>Orthopedic Surgeon</i> Corvallis, OR	20	I am an orthopaedic surgeon in practice in Corvallis. I see numerous patients each week that have definitely benefited from the use of viscosupplementation injections. I have seen an increase in mobility and decrease in pain level in those patients which can far outlast just a simple cortisone injection. Additionally, for those patients that can't undergo a knee replacement, these injections can be the only way to reduce their pain. I would implore you to keep them as a treatment option for our patients.	Thank you for sharing your experience with the treatment.
<i>Family Physician</i> Milwaukie, OR	21	I am a family physician practicing in Milwaukie Oregon. I would like to express my extreme concern at the recent decision by this committee to restrict the use of HA into the knee for osteoarthritis. I have seen first hand the benefits of this protocol. I have had patients who I have given viscosupplementation get improved range of motion, strength, and overall function. This is at the savings of a total knee replacement. This will push patients to have more total knees at a cost of tens of thousands of dollars. There is clear evidence that this treatment works and should be a viable option for all patients. There was a recent review by a group in Washington similar to yours and it approved the treatment because of the overall preponderance of evidence showing that it improves mean pain scores and function scores. I implore you to reconsider your position and approve this much needed treatment for the patients of Oregon.	Thank you for sharing your experience with the treatment. HTAS is aware of the different decision reached by the WA HTA clinical committee.
<i>Arthritis Foundation</i> (Great West Region) Seattle, WA	22	The Arthritis Foundation, Great West Region appreciates the opportunity to offer comments on the Health Evidence Review Commission draft coverage guidance for viscosupplementation for osteoarthritis of the knee. The Arthritis Foundation has participated in and supported the outcome of the Washington Health Technology Assessment Program (WA WHTAP) process referenced in the Health Technology Assessment Subcommittee (OR HTAS) draft, and it is with confusion and dismay that we read the proposal for non-coverage.	Thank you for taking the time to comment.
	23	For people living with osteoarthritis, there are few options between pain management and joint	HTAS is aware of the limited treatment options

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		replacement. Viscosupplementation offers hope for many in staving off joint replacement, and for those whose co-morbidities make surgery too risky, it may be the only option. Furthermore, the relief provided by this therapy may make it easier for people with knee OA to participate in physical activity, an important non-pharmacologic component to managing not only OA, but many other co-morbidities.	available to patients with OA of the knee, but does not believe offering a treatment that does not provide any clinically meaningful improvement in pain is helpful.
	24	We understand that the same reports used as in the Washington determination and the Arthritis Foundation fails to understand how two evidence-based programs can rely on the same report and come to coverage decisions that are so different.	See comment #3. Given the conflicting nature of the evidence base, it is not surprising that different policy making bodies have reached different conclusions regarding efficacy.
	25	<p>The WA HTAP Reimbursement determination found that “based on the evidence about the technologies’ safety, efficacy, and cost-effectiveness, Hyaluronic Acid / Viscosupplementation is a covered benefit for the treatment of pain associated with Osteoarthritis (OA) of the knee when all of the following conditions are met:</p> <ul style="list-style-type: none"> • In patients who have not had an adequate response to non-pharmacological conservative treatment and simple analgesics; • Is limited to two courses per year with at least four months between courses; and • Documented evidence of clinical benefit from the prior course of treatment is required for subsequent treatment courses. <p>The link to the full Washington HTA/HTCC report is: http://www.hta.hca.wa.gov/documents/findings_decision_ha_082010.pdf</p>	HTAS is aware of the WA HTA decision.
	26	<p>Given the decision for coverage with limitations in Washington, we ask that HERC make available a report detailing the evidence it relied upon to come to such a dissimilar decision using what appear to be the same evidence-based materials.</p> <p>We look forward to seeing a report, and strongly urge that the recommendation be changed to “coverage with limitations.”</p>	See comments #3 and 24.
<i>Advocacy for the Improvement in Mobility (AIM)</i> White Plains, NY	27	<p>Advocacy for the Improvement in Mobility (AIM) is a non-profit corporation dedicated to ensuring patient access to appropriate, high quality musculoskeletal health care. We would like to comment on the recent Oregon HERC non-coverage decision for viscosupplementation for osteoarthritis of the knee.</p> <p>As noted in your analysis of the evidence concerning Hyaluronic (HA) supplementation, the Washington State Healthcare Authority has issued a limited coverage decision for this modality. We would agree with that decision based upon the Clinical Practice Guideline (CPG) issued by the American Academy of Orthopedic Surgeons (AAOS) on the treatment of osteoarthritis of the knee in 2008. The AAOS CPG recommendation 16 states: “We cannot recommend for or against the use of intra-articular hyaluronic acid for patients with mild to moderate symptomatic OA of the knee.” Since</p>	<p>Thank you for taking the time to comment. HTAS is aware of the WA HTA decision. Thank you for sharing the AAOS guideline recommendation. HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers’ coverage policies.</p>

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		the strength of recommendation is inconclusive and the treatment is recognized as safe we concur with Washington State and most private health care insurance carriers that HA treatments should be covered in the limited situations outlined by the HTA. In Oregon, the largest private payer, Regence Blue Cross Blue Shield of Oregon has a published medical coverage policy. National payers with Oregon beneficiaries such as Aetna and United Health Group also provide coverage. Attached are the Regence and Aetna coverage policies for viscosupplementation.	
	28	<p>Medicare and most other private insurers do cover viscosupplementation in osteoarthritic patients with the appropriate symptoms and indications. To deny coverage to Medicaid patients for these procedures creates a potential treatment disparity for the poor and minority patients served by the Medicaid program. Clinical Practice Guidelines are necessary to help improve patient care and make treatment more consistent with the current state of medical knowledge. It is important to have experts examine guidelines to offer necessary insight concerning their relevance and veracity. Attached, please find three additional reference articles HERC might consider in finalizing coverage guidance.</p> <p>We would be happy to advise the HERC on further guidelines concerning musculoskeletal healthcare.</p>	<p>HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies, including Medicare. Only 2 articles attached. Moreland 2003 was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions. Goldberg 2010 is a narrative review only.</p>
<i>Director, Medical Affairs, Sanofi Biosurgery Cambridge, MA</i>	29	<p>OA of the knee is a chronic, progressive disease associated with a substantial public health burden both in terms of personal suffering and use of health care resources. Approximately 16% of adults age 45 years or older have symptomatic OA of the knee. The risk for developing the disease increases with advancing age, and currently 14.6 million Americans are estimated to have symptomatic OA of the knee. The painful symptoms and joint dysfunction associated with OA of the knee make it a leading cause of impaired mobility and disability. Patients with the disease experience significant limitations of activity including difficulty walking, stooping, standing from a seated position, and climbing stairs. Patients with OA of the knee also have poorer social function and worsened health-related quality of</p>	<p>HTAS is aware of the burden of suffering of patients with OA.</p>

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		life.	
	30	The cause of OA of the knee is complex and poorly understood. Degeneration of articular cartilage within the knee joint is accompanied by pathologic changes affecting the entire joint including the underlying bone. One pathologic change involves the reduction of the elastic and viscous qualities of the synovial fluid. The concentration and molecular weight of hyaluronic acid (the substance responsible for the viscoelastic qualities of this fluid) are decreased. One proposed mechanism of pain generation in OA is diminished elastoviscosity of the synovial fluid, which leads to reduced lubrication and protection of joint.	HTAS agrees that the pathogenesis of OA and the mechanism of pain generation are poorly understood.
	31	Currently, there is no treatment that can prevent or cure OA of the knee. Treatment goals include reducing joint pain and stiffness, maintaining and improving joint mobility, reducing physical disability and handicap, improving health-related quality of life, limiting the progression of joint damage, and educating patients about the disorder and its management. Treatment options include non-pharmacologic, pharmacologic, and intra-articular modalities. Many of these patients have risk factors precluding NSAIDs, and/or are not candidates for arthroscopy or total joint arthroplasty. The purpose of intra-articular therapy with viscosupplements is to help replace diseased synovial fluid that has lost its viscoelastic properties. The exact mechanism by which viscosupplements relieve OA pain of the knee is not fully known. Surgical interventions such as total knee replacement are a last resort for patients with severe symptoms who fail to respond to less invasive forms of therapy.	HTAS is aware of the treatment options available to patients with OA of the knee and their limited efficacy.
	32	Several reputable published meta-analyses and systematic reviews have concluded that this class of product is efficacious with a favorable risk-benefit profile. A recent Cochrane review affirmed the role of viscosupplements in treatment of OA of the knee, noting superior efficacy vs placebo, comparable efficacy vs NSAIDs, and longer-term benefits vs intra-articular steroids. As such, intra-articular HA has become a widely accepted treatment option and is included in several professional society guidelines including OARSI and ACR.	The Cochrane review is one of five meta-analyses that were included in the evidence source, with others reaching a different conclusion.
	33	We respect that Oregon HERC chose to commission an independent review of the most recent evidence. However, we wish to note that the Hayes report does not contain data from at least 4 recent publications that might provide more clarity to the questions you are trying to answer. Those publications are listed below.	The WA HTA report included 4 RCTs published after the date of the Hayes report.
	34	The Hayes report also excluded the Phase III (Synvisc-One) hylan G-F 20 single-injection trial called SOUND that led to the February, 2009 FDA approval of Synvisc-One. The SOUND trial was published online in March, 2009 and appeared in print earlier this year. It featured a 26-week, double-blinded, and placebo-controlled design, and was also intent-to-treat analyzed for both improvement and responders. These data withstood a full panel review by the FDA. The primary pain improvement endpoint was reached, and, 71% of hylan G-F 20 patients experienced clinically meaningful pain reduction versus 53% of controls. The repeat treatment phase demonstrated that a second injection	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does

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		of hylan G-F 20 did not increase the frequency of adverse events. Synvisc-One can provide 6 months of analgesia with as little as one office visit.	not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	35	Trials have demonstrated the efficacy of hylan G-F 20 against treatment with intra-articular steroid, NSAIDs, and appropriate care.	HTAS agrees that there is some evidence of equivalency to other treatment modalities, but is unclear what is meant by “appropriate care.”
	36	Determination of the magnitude of benefit in the Hayes report relied heavily on Effect Size. A published consensus statement from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials, or IMMPACT group, urged considering improvements within treatment groups or patients in chronic pain trials, in addition to Effect Size, which is statistical in nature. IMMPACT considered pain reductions of 30% or more to be moderately clinically important. Mean pain was reduced 36% over 26 weeks in patients treated with Synvisc-One.	Citation not provided. Not clear which trial this is referring to. If referring to the SOUND trial, see comment #29
	37	There may have been valid evidence omitted for other products in the class as well. In general, while some may believe the efficacy data across the class to be inconsistent, viscosupplements have a safer systemic toxicity profile than NSAIDs/COX-2, and longer-lasting efficacy than an intra-articular corticosteroid. Adverse events are typically infrequent, local, mild to moderate, and generally consist of injection site reactions and knee pain or swelling. The GI, cardiovascular, and renal adverse events that can occur with NSAIDs/COX-2 do not happen with viscosupplements.	HTAS agrees that the efficacy data across this class of products is inconsistent.
	38	It would greatly benefit patients with OA knee pain who are not surgical candidates and are searching for treatment options with less harmful systemic side effects if they had continued access to viscosupplements. Sanofi will follow up with a review of the viscosupplement class in another letter. 1. Hochberg M, Altman R, April KT, Benkhalti M, Guyatt G, McGowan J et al. American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. <i>Arthritis Care & Res</i> 2012;64(4):465-474. 2. Bannuru R, Natov N, Dasi U, Schmid C, McAlindon T. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis - meta-analysis. <i>Osteoarthritis Cartilage</i> . Jun 2011;19(6):611-619. 3. Chevalier X, Jerosch J, Goupille P, van Dijk N, Luyten FP, Scott DL, Bailleul F, Pavelka K. Single, intra-articular treatment with 6 mL of hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: A randomised, multi-centre, double-blind, placebo-controlled trial. <i>Ann Rheum Dis</i>	Articles not attached. No additional letter submitted.

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		<p>2010;69:113-119.</p> <p>4. Zhang W, Nuki G, Moskowitz RW et al. OARS recommendations for the management of hip and knee osteoarthritis Part III: changes in evidence following systematic cumulative update of research published through January 2009. <i>Osteoarthritis Cartilage</i> 2010;18:476-499.</p>	
Zimmer, Inc. Minneapolis, MN	39	<p>Zimmer appreciates this opportunity to comment on the draft guidance on viscosupplementation for osteoarthritis of the knee. We strongly encourage HERC to reconsider its proposal to not cover viscosupplementation for the treatment of pain associated with osteoarthritis (OA) of the knee. This treatment is one of only a handful of non-surgical treatments that reduces pain and may delay eventual arthroplasty. The additional benefit of minimal potential side effects makes this an important treatment alternative.</p> <p>We are greatly concerned that, if finalized, this non-coverage guidance reduces the viable therapy options to publicly insured Oregon residents.</p>	Thank you for taking the time to comment.
	40	<p>Zimmer recently introduced a new single injection viscosupplement for OA of the knee to the market called Gel-One® Cross-linked Hyaluronate, which was approved by the FDA. The following link provides an abstract of the published peer reviewed study showing the statistically significant benefit of this product (referenced as “Gel-200” in the publication) for patients who suffer from OA of the knee. http://www.sciencedirect.com/science/article/pii/S1063458412000374 *</p> <p><u>*Evidence Source:</u></p> <p>Strand, V., Baraf, H.S.B., Lavin, P.T., Lim, S., Hosokawa, H. <i>A multicenter, randomized controlled trial comparing a single intra-articular injection of Gel-200, a new cross-linked formulation of hyaluronic acid, to phosphate buffered saline for treatment of osteoarthritis of the knee.</i> <i>Osteoarthritis and Cartilage</i>, volume 20, Issue 5, Pages 350-356, May 2012</p> <p>The HERC draft cites the Sampson publication which considers a 20 to 40 point improvement on a 100 mm VAS scale to be a clinically significant therapy. The HERC draft implies that viscosupplementation studies do not show clinically significant improvements in pain sub-scores. However, in the study referenced above which was conducted for regulatory approval of the product, Gel-One (Gel-200) achieved an average improvement from baseline of 27.8 mm in WOMAC pain score, which amounts to a 39.3% improvement. (This is mentioned in the article as improvement from baseline exceeding 20mm) Studies for some other Hyaluronic Acid (HA) products, also conducted to support regulatory approval, have shown mean improvements of greater than 20 mm.</p>	Strand 2011 is an RCT comparing Gel-200 to saline injection, N=379, primary outcome measure WOMAC pain score (VAS 100 mm) at week 13. Average baseline pain score was 69. While mean improvement from baseline may have been 28 mm in the Gel-200 group, the difference from the control group was at the greatest 8 mms (at 3 and 6 weeks). While the difference was statistically significant, this supports the conclusions of the evidence report that the effect is likely not clinically significant.
	41	<p>The HERC draft concludes that because the RCTs for viscosupplementation did not focus on function and that the studies did not follow patients beyond 3 months, then there is insufficient evidence to understand the impact of viscosupplementation on the eventual recovery of function. However, it may be important to keep in mind that viscosupplementation is a therapy that is administered when other</p>	HTAS understands that pain relief irrespective of functional improvement is an appropriate goal in this population.

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		conservative therapies have failed. It is intended to relieve pain with minimal systemic or local side effects. It may delay eventual arthroplasty, but is not intended to be the final therapy in the continuum of care. Since most insurance coverage policies limit administration of HA injection treatments to once every six months, patients are likely to return for another course of treatment only if their pain was sufficiently relieved to experience some benefit over that six month period.	
	42	Zimmer would like to challenge HERC to justify why the committee has arrived at a different conclusion regarding coverage for viscosupplementation than that of the Washington state HTA clinical committee, which used the same clinical evidence. This therapy is widely covered by both private and public insurers. The HERC draft does not cite any unique or conclusive evidence that would contradict the rationale for coverage by virtually all payers across the country. Zimmer strongly encourages HERC to reconsider its non-coverage guidance proposal for viscosupplementation. Oregon residents will be denied a viable and widely used therapy alternative based on a rationale that is unique to HERC.	See comment #24.
DePuy Mitek, Inc. Raynham, MA	43	Thank you for the opportunity to provide comments on the Oregon HERC's recently developed draft coverage guidance entitled <i>Viscosupplementation for Osteoarthritis of the Knee</i> . We strongly believe that the clinical evidence supports the listing of viscosupplementation with hyaluronic acid (HA) as a covered benefit for the treatment of pain associated with osteoarthritis (OA) of the knee. A summary of the clinical evidence supporting the use of viscosupplementation with HA in OA of the knee, and ORTHOVISC® specifically, is provided below.	Thank you for taking the time to comment.
	44	Role in Therapy It is important that clinicians have access to the widest possible range of therapies for treatment of OA. Nonsurgical treatment options have limitations, NSAIDs cause cardiovascular and gastrointestinal complications. Intra-articular (IA) injections of corticosteroids often provide short term pain relief, but are known to potentially cause long-term cartilage damage. For patients who have not obtained sufficient pain relief from such therapies, joint replacement surgery may be considered, which is associated with morbidity and cost. HA is an intra-articular therapy for OA of the knee in patients who have not had an adequate response to conservative treatment or simple analgesics, who are seeking a longer duration of pain relief compared to IA steroid injections, and who may wish to delay or avoid surgery.	Thank you for your comment. The statement concerning corticosteroids causing long-term cartilage damage is not supported by the evidence.
	45	Evidence Supporting Use of HA for OA of the Knee There is consistent evidence in the medical literature demonstrating that HA is safe and results in lower mean pain scores and improves mean function scores for up to six months. This evidence comes from four systematic reviews looking at the efficacy of HA (Bellamy 2006, Samson 2007, Hayes 2010, Bannuru 2011), one comparing hylan with HA (Reichenbach 2007), and one comparing HA with	All but Bannuru 2011 were included in the WA HTA evidence review.

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		corticosteroids (Bannuru 2009).	
	46	In the draft coverage guidance from Oregon’s HERC, only two evidence sources are cited (Hayes in 2010 and Samson 2007 review). The 2006 Cochrane Review (Bellamy) and Hayes 2010 reviews had positive conclusions regarding the overall efficacy of HAs. The Cochrane report reviewed 76 trials, and is one of the most comprehensive reviews to date and examined multiple HA products for effects thru 52 weeks. In assessing the pooled effect size in comparison to placebo, the reduction in pain was significant and physical function also improved. HAs also demonstrated superior reduction in pain at 8 weeks over corticosteroids and continued to be significant up to 14 weeks.	Hayes 2010 is the WA HTA report, and includes Bellamy, Samson and 3 other SRs. In Bellamy, the mean effect measure difference at 8-12 weeks was 13mm VAS
	47	Samson et al reviewed 42 trials (N=5,843) which generally showed positive effects of HAs on pain and function scores compared to placebo. However, the authors cited considerable uncertainty of the results due to variable trial quality, potential publication bias, and unclear clinical significance of the changes reported. Nonetheless that the minimal clinically important threshold of 20 mm or 40 percent reduction in VAS pain from baseline proposed by Samson, has been successfully met by several of the large published HA studies.	While this threshold has been met for the HA group compared to baseline, when the mean difference from placebo injection is considered, it has not been met.
	48	Meta-analysis by Bannuru (2011) inferred that HAs are efficacious by 4 weeks, reaches peak effectiveness at 8 weeks and exerts a residual detectable effect at 24 weeks. The peak effect size (ES) for HAs of 0.46 is greater than published effects from other OA analgesics (acetaminophen ES = 0.13; NSAIDs ES = 0.29 COX-2 inhibitors ES = 0.44). An ES above 0.20 is considered to be clinically relevant on an individual patient basis in chronic pain conditions such as knee OA. This pooled analysis looking at post-administration trajectory of effect confirms that the magnitude of effect of HA exceeds a minimally clinically significant threshold.	Bannuru 2011 included 54 trials, 53 of which were funded or had involvement from industry. Authors calculated effect sizes using Bayesian random effects model.
	49	Hayes (2010) reported two studies with patients who improved ≥ 20 mm on a 100 mm scale where the results favored HA over placebo. Note that >20 mm improvement was defined as clinically meaningful by the IMMPACT collaborative group. Overall, the different conclusions reached in the systematic reviews were due to differences in methodology (i.e., dissimilar sets of RCTs, differences in selection criteria).	Citations not provided. However, in the WA HTA report, there is mention on page 17 of 2 trials that report > 20 mm improvement, but both were compared to “conventional treatment”, not placebo.
	50	We strongly encourage the Oregon HERC to <i>broaden</i> the evidence base to include the systematic reviews cited above, similar to the evidence-based approach recently published by Washington State HTA of Viscosupplementations.	HTAS has utilized the WA HTA report as their evidence source.
	51	<i>Evidence Supporting the Use of ORTHOVISC® for OA of the Knee</i> ORTHOVISC® is an effective treatment for reducing pain in patients with knee OA. Evidence from two clinical studies have shown significant improvements in mild to moderate pain for up to 6 months following treatment with three or four ORTHOVISC® injections (Brandt 2001, Neustadt 2005). It is important to note that ORTHOVISC® gained FDA clearance on the basis of <i>responder rate</i> , rather than	Both studies were published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies

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		mean VAS pain score. Responder rate is defined as the percentage of patients that experience significant pain relief from a therapy, as opposed to the mean pain score experienced by the entire study population of responders and non- responders. Responder rate is a true indicator of patient benefit whereas mean population VAS scores tend to mask the effects on individual patients. Clinical data show that over 65.4% of patients responded to ORTHOVISC® and had significant, long term pain relief. ORTHOVISC® also has an excellent safety profile compared to the potential safety issues with NSAIDs and steroid injections.	are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	52	<i>HTAs and Guidelines</i> A number of HTAs (i.e., Washington State Healthcare Authority, Veterans Administration), clinical guidelines (i.e., Osteoarthritis Research Society International) Medicare Administrative Contractor and health plan policies (i.e., Trailblazer, Regence Blue Cross Blue Shield Inc., United Health Group Inc.) have supported the use of viscosupplementation for OA of the knee. Most recently (2010), using some of the same source documents as cited in the <i>draft</i> Oregon coverage decision, the Washington State Health Care Authority committee concluded that there is sufficient evidence to cover viscosupplementation with HAs for OA of the knee.	HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies. HTAS has utilized the WA HTA report as their evidence source, but reached different conclusions.
	53	In conclusion, we strongly believe that the clinical evidence cited above supports the listing of viscosupplementation with HAs, especially ORTHOVISC®, as a covered benefit for the treatment of pain associated with OA of the knee. If you have any questions about the information included in this letter or require additional information, please contact us.	See comment #24.
Bioventus, LLC Durham, NC	54	We are writing to respond to your May 21 decision to recommend non coverage of viscosupplements for patients with osteoarthritic knee pain. We appreciate the opportunity to provide commentary on this draft recommendation to the Health Evidence Review Commission (HERC) and respectfully request reconsideration of this decision. We understand Oregon State's concern around the cost of healthcare and the desire to find ways to reduce expenditures by seeking reductions in utilization of certain therapies. We believe, however, that the decision to discontinue access to viscosupplements will have the consequence of eliminating an important physician treatment tool, result in a reduction of the quality of care available to the residents of Oregon and may actually contribute to a <u>rise</u> in the cost of treating knee OA pain. We offer the following comments supporting this position.	Thank you for taking the time to comment.
	55	<i>Burden of Illness and Prevalence</i> Osteoarthritis (OA) is a progressive disorder of the joints caused by gradual loss of cartilage. This manifests itself as pain, swelling and loss of function for the patient. Contributing factors include	The HTAS is aware of the natural history and burden of disease of OA of the knee.

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		<p>advancing age, trauma to the knee, and obesity.</p> <p>Arthritis is among the leading causes of disability in the US and osteoarthritis (OA) is the most common type of arthritis. Knee OA, is the most frequent form of lower extremity OA.</p>	
	56	<p>There are few options for treating knee OA and the associated pain before prior to expensive knee replacement. Typically patients will self-treat with OTC pain medications in the early stages of the disease before seeking help from a medical professional.</p> <p>Medical professionals have but a few conservative treatment options that include NSAIDs and corticosteroid injections to help maintain the patient before moving to the more radical and expensive option of total knee replacement (TKR). It is widely recognized that there is a gap in the OA treatment paradigm between conservative therapies and joint replacement that high-dose NSAID therapy and intra-articular corticosteroids <u>cannot fill alone</u>. Viscosupplements are needed to complete the knee OA treatment armamentarium.</p>	The HTAS agrees that additional treatment options for OA of the knee are desirable, but providing an option that is not clinically significantly superior to placebo is not helpful.
	57	<p><u>Viscosupplementation</u></p> <p>Viscosupplementation provides an important FDA-approved treatment for patients with OA of the knee. It is the <u>only</u> available intra-articular analgesic for OA treatment, and the only device that is essentially free off systemic adverse events and drug interactions. It is a <u>critically important option</u> for patients with GI or CV comorbidities for whom chronic NSAID administration is contraindicated, and for patients who are not good candidates for (TKR). The safety and effectiveness of viscosupplements is <u>not however, limited to this patient population</u>.</p>	HTAS disagrees that viscosupplementation is free of systemic AE. While most AE are minor and local, serious AE can occur, including sepsis of the joint, which clearly has systemic consequences.
	58	<p><u>Effectiveness of Viscosupplements</u></p> <p>A recently published Cochrane Systematic Review of viscosupplementation for the treatment of OA of the knee³. Identified 76 randomized controlled trials (RCTs) for analysis. This meta-analysis, supported the superiority of viscosupplement products over saline placebo, and concluded that the RCT literature provides evidence of <u>efficacy</u>. The analyses suggest that viscosupplements are comparable in efficacy to systemic forms of active (drug) intervention, with fewer systemic adverse events. The authors conclude that the analyses support the use of viscosupplement products in the treatment of knee OA.</p>	The Cochrane review is one of five meta-analyses that were included in the evidence source, with others reaching a different conclusion.
	59	<p>In virtually <u>all</u> clinical trials, regardless of patient type or inclusion criteria, patients treated with viscosupplements consistently demonstrated significant improvements in pain or function from <u>baseline</u>.</p>	HTAS disagrees with this statement, as evidenced by the WA HTA review.
	60	<p><u>SUPARTZ Effectiveness</u></p> <p>The approval of SUPARTZ was based on five randomized, double-blind, saline-controlled multicenter trials, and an integrated analysis (n==1155) of thee primary patient data from these five RCTs.⁴. The SUPARTZ efficacy studies utilized a five-injection treatment regimen. In 2006 a label change was approved that modified the directions for use to include the statement “some patients may respond to</p>	Thank you for this information about your product.

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		3 injections.....”. ⁵ This statement is based on several trials, one of which is included in the SUPARTZ labeling that compared 3-injection and 5-injection treatment regimens, and found the mean response comparable. Thus although FDA labeling allows physicians the flexibility of administering up to 5 SUPARTZ injections when required, although a 3-injection course of treatment with SUPARTZ has demonstrated effectiveness similar to products restricted to a 3-inj regimen. This flexibility allows physicians to decide when more than 3 injections are required.	
	61	<u>Safety of Viscosupplements</u> Intra-articular viscosupplements are an extremely safe treatment for OA knee pain. Although on the US market since 1997, there has never been reported a patient fatality attributed to its’ use. Moreover, because it is a locally acting device, has no known drug interactions, and is free of systemic side effects common to NSAIDs and intra-articular corticosteroid injections ^{7,8} .	See comment #57.
	62	The primary adverse event associated with viscosupplements, are local reactions, which are usually transient and self-resolving. Examples include arthralgia, local joint pain and swelling, inflammation, injection site pain, and local erythema.	Thank you, the HTAS is aware of the AE profile of viscosupplementation.
	63	Overall IA-HA offers significant safety advantages over systemic OA treatments and corticosteroid injections	HTAS does not agree that viscosupplementation has a significantly different safety profile from intra-articular steroid injection.
	64	<u>SUPARTZ Safety Profile</u> The safety of SUPARTZ was evaluated by an integrated analysis of the Intent-to-Treat (ITT) population from five, randomized, double-blind, saline-controlled multicenter trials. The most common adverse events occurring in SUPARTZ-treated patients were arthralgia, defined as joint pain with no evidence of inflammation, arthropathy/arthrosis/arthritis, defined as joint pain with evidence of inflammation, back pain, pain (non-specific), injection site reaction, headache, and injection site pain. There were no statistically significant differences in the incidence rates of these adverse events between the saline control group and the SUPARTZ group. ⁴	Thank you for this information.
	65	<u>Other Treatment Options</u> <u>NSAIDs</u> Although NSAIDs are generally considered effective for OA pain, concerns about patient safety and high cost are important considerations. According to the AHRQ publication, <i>Managing Osteoarthritis</i> , nonsteroidal anti-inflammatory drugs were considered the medications of choice for osteoarthritis pain until research showed that they affect joint cartilage metabolism, have greater risk of toxicity than acetaminophen, can cause upper gastrointestinal bleeding, and may cause or aggravate peptic ulcer disease. ¹¹⁴ AHRQ research further showed that NSAIDs provided only a modest decrease in osteoarthritis pain and little improvement in function, and their association with ulcers, bleeding, and	HTAS is aware of the limitations and adverse events of NSAIDs.

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		perforation caused a four- to five-fold increase in hospitalizations due to gastrointestinal complications. ¹⁴	
	66	<u>Corticosteroids</u> Corticosteroids are <u>not</u> indicated for the treatment of pain whereas viscosupplements <u>are specifically</u> indicated to relieve pain associated with knee OA. A recent meta-analysis comparing intra-articular HA and corticosteroids concluded that although corticosteroids provide better short term relief, HA provides more sustained benefits (2-4 weeks compared to 3-6 months). ¹⁵ <i>Comments truncated, as word limit exceeded.</i>	See comment #48 regarding the Bannuru SR.
Patient/Citizen Aloha, OR	67	I am responding to the HERC DRAFTED coverage guidance that states Viscosupplementation should NOT be covered for the treatment of pain associated with Osteoarthritis (OA) of the knee. I served a vigorous career as a firefighter while maintaining an athletic lifestyle including basketball and tennis leagues. I began having pain in my knees 10 years ago and had to quit playing basketball. I tried taking ibuprophen, but the relief was always so temporary while having adverse reactions to it involving high protein in my kidneys. I continued tennis since it had less of a vertical impact on my knees. Within this last year the pain became so constant that I had to quit playing tennis as well. After multiple DR visits I finally met with an Orthopedic surgeon and he performed a Bi-Lateral knee scope with debridement including meniscus and beginning stages of Osteoarthritis of both knees. 8-10 weeks following the surgery, I received a Synvisc 1 injection in each knee. I am still active and on my feet daily. It has been approx 8 weeks since my injections and my pain has subsided progressively. I believe that the viscosupplement has played a vital and affective role in my pain relief and DO NOT agree with what you are proposing in not covering this procedure. I ask you, "What would be my alternative?" Should I have a \$40K total knee to relieve my pain from Osteoarthritis? \$80K for both knees? How about I continue conservative care such as a \$160.00 knee injection in the recommended series by ALL of the viscosupplement companies. What you are suggesting in taking away conservative care COMPLETELY CONTRADICTS GOVERNOR KITZHABER and his conservative & preventative treatment initiative. Why on earth would you turn down an inexpensive knee injection when the alternative is a \$40,000.00 option???	Thank you for taking the time to share your experience with this disease and treatment. HTAS is aware of the limited treatment options available to patients with OA of the knee, and is glad that you experienced a positive outcome. However, HTAS as a policy making body makes decisions based on the best available evidence, and does not believe offering a treatment that does not provide any clinically meaningful improvement in pain or function is helpful.
	68	I truly hope that you will give my agruement an honest evaluation and see that with my personal evidence of relief, and the costly alternative to the knee injection, you have made a grave error in drafting this NO COVERAGE GUIDANCE of viscosupplements. I invite your response either by email or phone call.	See comment #67.