Washington State Health Care Authority

Peripheral nerve ablation for the treatment of limb pain

Draft report – Public comment and response

December 10, 2018

Health Technology Assessment Program (HTA)
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Peripheral nerve ablation for the treatment of limb pain Draft Report

Public Comment and Response

Provided by:

Center for Evidence-based Policy
Oregon Health & Science University

December 10, 2018

Responses to public comments on draft report

The Center for Evidence-based Policy is an independent vendor contracted to produce evidence assessment reports for the Washington Health Technology Assessment (HTA) program. For transparency, all comments received during the public comment period are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

Public comments were received from these individuals and organizations:

- Timothy P. Maus, MD, President, Spine Intervention Society
- Diane F. Weaver, BS, MS, Sr. Manager, Health Policy & Health Economics, Avanos, Inc.
- Greg A. Brown, MD, PhD
- David P. Green, MD, Medical Director, Molina Healthcare of Washington

Specific responses pertaining to comments are shown in **Table 1.**

The full text of all public comments and included references and attachments follows the tables.

Table 1. Responses to comments on draft report for peripheral nerve ablation for the treatment of limb pain

Comments	Response
Commenter: Timothy P. Maus, MD, President, Spine Intervention Society	
Specific comments:	
The Spine Intervention Society, a multi-specialty association of over 2,800 physicians dedicated to the development and promotion of the highest standards for the practice of interventional procedures in the diagnosis and treatment of spine pain, would like to take this opportunity to comment on the Washington State Health Care Authority Health Technology Assessment Program's draft report Peripheral Nerve Ablation for Limb Pain. The Society's membership includes many of the clinicians and academicians whose published literature provides the seminal references upon which the practice of evidence-informed interventional spine care, as well as interventional pain management for musculoskeletal care, is based. Our organization has a strong record of working to eliminate fraudulent, unproven, and inappropriate procedures. At the same time, we are equally committed to assuring that appropriate, effective, and responsible treatments are preserved so that patients do not have to suffer or undergo more invasive and often unnecessary surgical procedures.	Thank you for the comment.
We would specifically like to comment in support of the efficacy and effectiveness of radiofrequency ablation (RFA) of peripheral nerves to treat pain associated with knee osteoarthritis (OA). Current evidence shows that for patients suffering with chronic knee pain (≥ 3 months) due to knee OA and/or after total knee arthroplasty not improved with standard conservative management, RFA of the corresponding genicular nerves is an effective, non-surgical treatment that will improve patient's function and quality of life. Patients treated with RFA experience decreased dependence on oral pain medications, reduced physical therapy utilization, and many are spared future costly and unnecessary surgical interventions. Choi *et al*, in a 2010 double-blinded, randomized controlled trial (RCT) investigated the efficacy of thermal RFA in patients greater than 50 years old with persistent arthritic knee pain (≥ 3 months) not improved with physical therapy, oral analgesics, and intra-articular knee injections (either corticosteroid or hyaluronic acid) [1]. Nineteen patients who had positive diagnostic, fluoroscopically-guided genicular nerve blocks underwent subsequent standard, thermal RFA. The patients in this group reported significant decreased joint pain on the Visual Analog scale (VAS) and Oxford knee scores at 1-, 3-, and 6-month follow-up intervals compared with 19 patients with similar demographics and knee OA severity, who underwent the sham procedure. Similar results were found in a 2016 RCT by Qudsi-Sinclair *et al*; however, this study assessed the effectiveness of RFA in a population of patients with continued knee pain at least 6 months after knee replacement [2]. Prior to RFA, patients underwent fluoroscopically-guided genicular nerve blocks with lidocaine. Of the 28 patients included in the study, 14 were randomized to thermal RFA and 14 to therapeutic peripheral nerve injection with corticosteroid. Both groups' pain and function improved, with decreased use of pain medications at months 3 and 6, with similar results approaching 1 year for both groups. Besides some localized post-injection discomfort, no major adverse events were noted with the above studies.	The RCTs mentioned are included in the report. The observational study by Iannaccone et al. is included in the report. The observational study by Pineda et al. was excluded from the review because it did not present data on safety outcomes, as observational studies were included only for harms.

Comments	Response
Commenter: Timothy P. Maus, MD, President, Spine Intervention Society	
Specific comments:	
The 2018 trial by Davis *et al* is the largest study and was also the first to employ cooled radiofrequency ablation (CRFA) [3]. Patients meeting inclusion criteria had at least grade 2 Kellgren–Lawrence radiographic OA, refractory knee pain of ≥6 month duration, pain of at least 6 of 10 on a Numeric Rating Scale (NRS), an Oxford Knee Score (OKS) of at least 35, and at least 50% improvement with genicular nerve blocks. The 151 patients who met the inclusion criteria were randomized to receive either CRFA or intra-articular steroid (IAS) injection. CRFA was performed under fluoroscopic guidance with 17-gauge introducers at 60°C for 150 seconds. The primary outcome measure was the percentage of patients achieving at least 50% pain reduction at 6 month follow-up as measured by the NRS. Secondary outcome measures included function measured on OKS, patient's overall perception of the treatment, and analgesic usage. Pain relief with CRFA was superior to that obtained with IAS at all time periods, and at 6 month follow-up, 74% of the CRFA group had at least 50% relief compared with just 16% of the IAS group. Function and global perception were also superior in the CRFA cohort, although there was no statistically significant difference between the groups in terms of oral opioid use. The longer duration of relief noted in this study, compared with duration of relief reported for traditional RFA, provides evidence for the theoretical increased benefit of CRFA -- namely the creation of larger lesions to reduce the technical failure rate of the procedure (i.e., failure to effectively ablate the target nerves). The most recent 2018 RCT by El-Hakeim *et al* compared RFA to conservative management consisting of oral acetaminophen, diclofenac, and physical therapy, as needed [4]. Sixty patients with grade 3 or 4 Kellgren–Lawrence OA were randomized to receive either RFA or conservative treatment. RFA was accomplished with three 90 seconds cycles at 90°C per site, which is a substantially longer duration of RFA than that employed by any other RCT. Patients were evaluated at baseline, 2 weeks, 3 months, and 6 months. Results showed statistically significant, superior pain relief with RFA at all follow-up intervals. Function, as assessed by the WOMAC Index, was improved in both groups at 6 months, but was superior with RFA. Lastly, patient satisfaction as measured on a Likert scale was significantly higher at 3- and 6-month follow-up in the RFA group. However, the study is limited by the failure to select patients based on response to diagnostic blocks and the absence of patient blinding. The 2017 RCT by McCormick *et al* also employed CRFA, but the study was designed to determine the predictive value of prognostic nerve blocks, not to compare RFA to other modalities [5]. Fifty-four patients with chronic knee pain due to OA received CRFA. The study included patients between 30 and 80 years of age, with >6 months of refractory knee pain, NRS pain score of at least four, and at least grade 2 radiographic OA. Prior to RFA, the 32 patients in the nerve block group received prognostic blocks, of which 29 had positive blocks and proceeded to RFA. Notably, only three of 32 (9.3%) patients had a negative block, defined as <50% pain relief. Twenty-five patients were randomized to the nonnerve block RFA group. Follow-up was conducted at 1, 3, and 6 months, but the primary outcome measure was attainment of at least 50% pain relief at the 6-month mark. Results showed significant improvements in both groups at 6 months, with 58.6% of the nerve block group and 64% of the non-nerve block group achieving at least 50%	

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Specific comments:	
relief at 6 months. There were no significant differences between groups in terms of pain and function at any of the time periods. Prospective observational evidence outside of RCTs can also be used to demonstrate the effectiveness of a procedure. In fact, when the outcomes of well-performed, prospective trials demonstrate dramatic and sustainable results that are reproducible across studies, one could argue that the need to demonstrate that the effects of the procedure are not due to placebo effects alone are seriously minimized. One such prospective cohort study published by Iannaccone *et al* presents results of 31 patients treated with genicular RFA [6]. The patients were assessed at both 3 and 6 months after RFA. At 3 months the average pain relief was 67% improvement from baseline and at 6 months those that received pain relief at 3 months continued to have durable pain relief of 95%. Another study by Pineda *et al* in 2017 presented evidence that RFA of the genicular nerves significantly reduced perceived pain and disability in the majority of participants, without adverse events [7]. This single-center, prospective, observational study included patients with grade 3 to 4 arthrosis suffering from intractable knee pain of at least 6 months and scoring 5 or more on the visual analog scale (VAS). The proportion of participants with improvement of at least 50% in pretreatment VAS scores at 1, 6, and 12 months following intervention were 88% (22/25), 64% (16/25), and 32% (8/25), respectively. Due to the robust nature of the evidence, RFA of the genicular nerves is a valuable treatment for patients suffering from chronic knee pain and for patients with residual pain after total knee arthroplasty. Further, the procedure is indicated and may be the only option for patients that are not surgical candidates or who choose not to have surgical treatment. Acknowledging the strength and quality of the evidence in support of the safety and effectiveness of genicular nerve RFA, the American Medical Association's Current Procedural Terminology (CPT®) Editorial Panel has approved a Category I code that will go into effect on January 1, 2020.	
We hope that this information, as well as any dialogue and collaboration between the Washington State Health Care Authority's Health Technology Assessment Program and the Spine Intervention Society, will lead to the establishment of a reasonable coverage policy that will eliminate inappropriate utilization while preserving access in appropriately selected patients. We offer our ongoing input and expertise in this matter.	Thank you for the comment.
References: 1. Choi WJ, Hwang SJ, Song JG, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: a double-blind randomized controlled trial. Pain 2011;152:481–487. 2. Qudsi-Sinclair S, Borrás-Rubio E, Abellan-Guillén JF, Padilla del Rey ML, Ruiz-Merino G. A comparison of genicular nerve treatment using either radiofrequency or analgesic block with corticosteroid for pain after a total knee arthroplasty: a double-blind, randomized clinical study. Pain Pract 2017;17(5):578–588.	See above responses.

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Specific comments:	
3. Davis T, Loudermilk E, Depalma M, et al. Prospective, multicenter, randomized, crossover clinical trial comparing the safety and effectiveness of cooled radiofrequency ablation with corticosteroid injection in the management of knee pain from osteoarthritis. Reg Anesth Pain Med 2018;43(1):84–91. 4. El-Hakeim EH, Elawamy A, Kamel EZ, et al. Fluoroscopic guided radiofrequency of genicular nerves for pain alleviation in chronic knee osteoarthritis: a single-blind randomized controlled trial. Pain Physician 2018;21(2):169–177. 5. McCormick ZL, Reddy R, Korn M, et al. A prospective randomized trial of prognostic genicular nerve blocks to determine the predictive value for the outcome of cooled radiofrequency ablation for chronic knee pain due to osteoarthritis. Pain Med 2018;19(8):1628-1638. 6. Iannaccone F, Dixon S, Kaufman A. A review of long-term pain relief after genicular nerve radiofrequency ablation in chronic knee osteoarthritis. Pain Physician 2017;20:E437-44. 7. Pineda S, Vanlinthout L, et al. Analgesic effect and functional improvement caused by radiofrequency treatment of genicular nerves in patients with advanced osteoarthritis of the knee until 1 year following treatment. Reg Anesth Pain Med 2017;42:62-68.	

Comments	Response
Commenter: Diane F. Weaver, BS, MS, Sr. Manager, Health Policy & Health Economics, Avanos, Inc.	
Specific comments:	
Avanos, in their commitment to provide next generation innovative and evidence-based healthcare solutions, thanks the Health Technology Assessment program for the opportunity to comment on the October 26, 2018 Draft evidence report entitled *Peripheral nerve ablation for the treatment of limb pain* and provide clarity on the evidence-base supporting the quality and cost-effectiveness of Radiofrequency (RF) ablation in the treatment of chronic knee pain secondary to osteoarthritis (OA). The Health Technology Assessment Program (HTA) of the Washington State Health Care Authority is to be commended in their efforts to assist health care decision makers, clinicians, patients, and policy makers in making evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Knee osteoarthritis (OA) is reported to be the most common type of arthritis with a prevalence that is expected to increase as life expectancy and obesity rises. Approximately 13% of women and 10% of men 60 years and older have symptomatic knee OA while the prevalence rises to as high as 40% in those older than 70 years of age.[1] As a world-wide leader of technology, Avanos is committed to delivering advanced technologies to address important unmet medical needs, including non-surgical and non-opioid based treatments for chronic pain.	Thank you for the comment.

<table>
<tr><th>Comments</th><th>Response</th></tr>
<tr><td colspan="2">Commenter: Diane F. Weaver, BS, MS, Sr. Manager, Health Policy & Health Economics, Avanos, Inc.</td></tr>
<tr><td>Specific comments:</td><td></td></tr>
<tr><td>Literature Review
The HTA has clearly conducted a robust literature search and detailed review. While we realize the current body of evidence published to date does not achieve the HTA's high level of standards in the support of the efficacy of peripheral nerve ablation in the limb, the evidence is not entirely without merit. The HTA assessment of literature pertaining to RF as "low quality" and excluding studies without comparators has limited the dissemination of evidence related to "real world use" which is particularly deleterious to FDA cleared technologies, such as COOLIEF*.</td><td>Thank you for the comment.</td></tr>
<tr><td>Avanos would specifically like to comment on the evidence presented by Davis et al (2017) who conducted a prospective, randomized, open-label, multicenter clinical study with a pragmatic parallel-group design to compare cooled RF ablation with intraarticular steroid (IAS) injection. The strength of this un-blinded clinical trial is that it represents real world usage. In addition, the study was powered as a non-inferiority evaluation and took into consideration multiple comparisons as accounted for with an adjusted α. The findings indicate that cooled RF ablation for genicular nerve ablation is superior to a single corticosteroid injection in osteoarthritic subjects for managing knee pain, and the authors concluded that cooled RF ablation is an effective long term therapeutic option for managing pain and improving physical function and quality of life for patients with painful knee OA when compared with IAS injection.

The following table addresses the Davis study concerns presented by the HTA of high Risk of Bias:
<table>
<tr><th>Concern/ Limitation</th><th>Rationale</th></tr>
<tr><td>Design Bias</td><td>The study was intentionally designed to be consistent with current practice and was developed in conjunction with the FDA to specifically assess against the 510(K) labeling and indications for use (K163461). The endpoint of 6 months is consistent with the purpose of the study to establish a duration of effect for COOLIEF* RF as part of those discussions. While it is true that a single steroid injection is not expected to provide relief for that long, statistical significance between groups was achieved at all follow up time points (1, 3, and 6 months).</td></tr>
<tr><td>Consultant Bias</td><td>The Avanos COOLIEF* system represents newer, next generation technology and is currently building market share. As a relatively complex device, there is a current limitation on the number and availability of physicians who have the experience, training and familiarity with application of the device from both the technical and procedural perspectives. The number of current users who have this experience with the product who also have the operational capacity to manage formalized clinical research is small. The majority of the physicians that consult on the behalf of Avanos are utilized in a training capacity to support other physicians in learning the technology/procedures at cadaver workshops. Several also assisted the Steering Committee in execution of the trial.</td></tr>
</table></td><td>These comments have been taken into consideration in writing the final report. The additional information on randomization allowed this study to have its risk of bias rating changed from high to moderate. Limitations identified in the report, including outcome assessment, losses to follow up, appropriateness of comparator, and financial conflicts of interest remain. The overall quality of evidence, according to the GRADE methodology specified in the report, remains at very low for pain and function outcomes of cooled RFA. This is because of the remaining moderate risk of bias, indirectness, and imprecision factors.</td></tr>
</table>

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Enrollment Bias	This was mitigated by weekly evaluations of all site screening lots to assure that no subjects were excluded based on investigator bias.	
Outcome Bias	The outcome measures in this study (NRS, Oxford, GPE) were self-administered by the subjects and not based on the opinions of the investigator, thus minimizing potential for bias related to the outcome. Additional safeguards included the use of outside/independent monitor, Data Management and Statistical teams.	
Treatment Group Attrition	This was a pragmatic trial conducted primarily at independent, non-institution, outpatient pain management centers. The nature of this patient population is somewhat transient as evidenced throughout the trial. Participation in clinical trials is also an 'at will' arrangement and therefore patients can withdraw at any time for any reason. Most were lost to follow up or withdrew consent limiting ability to understand exact rationale. Adverse Events were closely monitored, and patients were followed until resolution and/or a clinically stable state was achieved, and no patient withdrew as a result of an Adverse Event. Additionally, 68 patients returned to provide data at the 6-month time point from the Treatment Group, which represents the largest dataset reported in the literature to date at this time point for any radiofrequency procedure utilized for Osteoarthritis of the knee.	
Random-ization	It was an oversight to not discuss the randomization process in more detail. The process was as follows: Randomly generated treatment assignments (1:1 randomization) were proactively prepared by the study statistician using a computerized randomization program and were provided to the site in sealed envelopes. The randomization envelopes were maintained in a secure location at the site with access limited to authorized study personnel only. Randomization envelopes were sequentially numbered. At the time of randomization, the site was instructed to always use the envelope with the lowest available number to maintain the sequential ordering of randomization. Envelopes were opened one at a time and only when it was confirmed that a patient met the eligibility criteria and had completed all the protocol required tasks. Only one randomization envelope was used per subject. Opened randomization envelopes were maintained with the appropriate subject's source documentation. The independent monitors confirmed that the randomization process was being appropriately followed and documentation was being maintained as appropriate. No deviations to the randomization process was identified during the trial.	
Allocation Concealment	This was an open label trial; therefore, the randomization treatment received was known to all involved. As the treatments are quite varied in their application, the only way to apply a	

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	blind would have been to add additional needle sticks to patients (3 for the Steroid Group and 1 for the COOLIEF* group), adding undue risk of infection, soft tissue damage, etc. It should also be noted that Choi, et al 2011 had previously conducted a trial describing the anticipated Sham effect from the radiofrequency procedure, therefore; it was determined that the additional risk to incorporate the blind was unwarranted, so it was not undertaken.	
Publication Process	As this was an industry sponsored study, the sponsor owns the data as well as the ultimate decision to publish. However, the sponsor maintained an administrative role in creation and submission of the manuscript at the guidance of a steering committee, specifically created to manage this process for this research. The Steering Committee was created utilizing several of the investigators in the trial (as consultants) to make decisions about content, publication target, timing, language, etc.	
Steroid Utilization	Standard of care for this routine procedure was not dictated in the protocol, nor was it attempted to limit physician preference of medications, other than being consistent with dose utilized. The instructions from the protocol state: *Subjects randomized to corticosteroid injection will be placed in a supine position and the knee will be prepared in a sterile fashion. A topical anesthetic (such as ethyl chloride spray) will be applied immediately prior to injection for subject comfort and an appropriately sized needle per the institution's standard practice will be placed into the suprapatellar pouch.* ***A solution with the dose equivalent to 40mg DepoMedrol will be injected into the joint space.*** Across the study, Depo-Medrol, Kenalog (triamcinolone), and betamethasone were used in 70%, 18%, and 12% of treatments, respectively.'	
This clarification of the Davis study and provision of additional information to specifically address the concerns related to limitations and risk of bias serves to prompt the HTA to reconsider its downgrading of the study two levels for risk of bias and one level for indirectness (lack of longer-term outcomes) to reclassify the quality of evidence from a score of one to a score of three or four.		
The HTA has also acknowledged numerous studies (9 specifically for the knee to be completed between 2018 and 2021) in progress which will provide additional evidence of peripheral nerve ablation as a treatment of limb pain. Of significance, RF has been used for more than 75 years[2] with a safety profile supported by long term and wide spread clinical use across diverse therapeutic areas such as neurology, cardiology, and oncology and is currently used to successfully relieve pain generating from the facet joints of the cervical, thoracic and lumbar spine, as well as the sacroiliac, knee and hip joints, and the intervertebral discs.[3]		Thank you for the comment. This report was designed to examine the evidence for effectiveness, safety, and cost-effectiveness for peripheral nerve procedures. We did not identify major safety concerns, and this conclusion is reinforced by this comment.
Selected Payer Coverage Determinations Importantly, RF ablation is considered medically necessary as evidenced by wide spread third-party reimbursement for the treatment of cervical, thoracic and		We have added the relevant Medicare LCD to the report. No geographically relevant new commercial payer coverage changes for

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lumbar facet pain. For example, treatment of facet pain in these anatomies are covered by Aetna; Cigna; United HealthCare; HCSC (BCBS OK, TX, NM, MT, IL); Humana, and a majority of Medicare LCDs. Relative to limb pain, Noridian Healthcare Solutions, LLC published an LCD entitled NERVE BLOCKADE for Treatment of Chronic Pain and Neuropathy (L35456) with an effective date of 10/01/2017. The LCD includes coverage for therapies that induce longer lasting or permanent blockade, including thermal (not pulsed) radiofrequency for pain, and lists the following ICD 10 diagnoses codes in support of medical necessity: M25.561 Pain in right knee and M25.562 Pain in left knee.	peripheral nerve ablation were identified. Policies for coverage in other clinical areas are not relevant to this review.
Clinical Practice Guidelines The HTA did not identify any clinical practice guidelines recommending the use of nerve ablation procedures. Positive society support for radiofrequency ablation procedures would typically not be garnered from surgical societies, as they are not "surgical" procedures, as researched by the HTA. Nor would the technology be endorsed by the American Physical Therapy Association as application of this technology is not within their scope of practice. Rather, ablative techniques are heavily utilized and endorsed by professional nerve and pain management societies both stateside and abroad, such as ASRA (American Society of Regional Anesthesiologists), Spine Intervention Society (SIS), ESRA (European Society of Regional Anesthesia), etc. In fact, the American Society of Regional Anesthesia dedicated an entire plenary session of its November 2018 Annual Pain Medicine meeting to the use of these interventions in patients with osteoarthritis. (https://www.asra.com/content/documents/program-faculty_pm18.pdf). To make evidence-based decisions related to RF therapy, it is critical for health care decision makers, clinicians, patients, and policy makers to appreciate that cooled radiofrequency procedures are classified as thermal ablative procedures, and not cryoablation, in which extreme cold is used to denervate tissue. Furthermore, studies have validated that cooled radiofrequency reaches ablative temperatures at or above 80°C/176°F in tissues adjacent to the probe tip similar to ablative temperatures with conventional radiofrequency procedures.[4] The following professional societies endorse radiofrequency ablation procedures: • "We would specifically like to support any efforts to appropriately classify cooled radiofrequency neurotomy procedures as thermal ablative procedures. Cooled RF should not be confused with cryoablation. While the name may be misleading, the procedure achieves thermal denervation or ablation of nerve tissue. Studies have validated that cooled radiofrequency reaches ablative temperatures at or above 80°C/176°F in tissues adjacent to the probe tip similar to ablative temperatures with conventional radiofrequency procedures." John MacVicar, MB, ChB, President, Spine Intervention Society. • "Based on the review of the literature, RFA has demonstrated clinical benefit in the treatment of chronic knee pain. Given the current opioid epidemic it is irresponsible to place these patients on opioids when treatment options such as RFA can be used for chronic pain." Asokumar Buvanendran, MD, President, American Society of Regional Anesthesia and Pain Medicine.	The report included a wide search for clinical practice guidelines in multiple databases. We did not identify clinical practice guidelines from the mentioned organizations. Endorsement statements from society leaders are not considered clinical practice guidelines. Conference presentations, posters, and abstracts were not eligible for inclusion.

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Specific comments:	
Safety and Cost Effectiveness Peripheral nerve ablation was selected as a technology of interest because of high concerns for safety and efficacy of the procedure and medium to high concern for cost. The clinical data demonstrate that radiofrequency procedures in general and specifically the COOLIEF* Cooled RF probe do not present safety or effectiveness issues related to the proposed indication for use. Of significance related to safety and efficacy, the COOLIEF* Cooled RF Probe is the only RF modality with FDA clearance specifically for the creation of radiofrequency lesions of the genicular nerves for patients suffering from osteoarthritic knee pain. Furthermore, the 510(k) Summary includes pertinent information related to evidence of efficacy and effectiveness; the lack of safety or effectiveness concerns; and a clearly defined target population and anatomical site to support efficacy/effectiveness outcomes and prevent harm.	We identified no major safety concerns regarding this device.
While the committee's searches did not retrieve any studies that reported economic outcomes including cost effectiveness, please acknowledge the results of a poster presentation of the 2018 World Congress on Regional Anesthesia & Pain Medicine[5] which demonstrated: • Cooled RF ablation (CRFA) resulted in greater quality-adjusted life-year (QALY) gains at 6 and 12 months compared to IAS • Incremental cost-effectiveness ratios (ICERs) at 6 and 12 months were US$ 12,696 and US$ 5,047 per QALY for all CRFA patients in trial • 12-month analysis, 1st line CRFA was dominate (cost saving) compared to 2nd line CRFA (patients who crossed over at 6 months)	Thank you for the comment. This review required full-text studies for inclusion. Poster presentations often contain limited methodological information and data, making full assessment of them not possible.
Summary It is a challenging task to evaluate emerging technology for adaptation to public health policy. However, now more than ever it now becomes critical to support technology that addresses *H.R. 6, the Opioid Addiction Action Plan Act* specifically as it relates to Sec. 6112 directing Medicare and MA prescription drug plan sponsors to annually disclose information to enrollees about the risks of prolonged opioid use, as well as coverage for nonpharmacological therapies, devices and non-opioid medications. From 1999-2014 more than 165,000 persons died from overdose related to opioid pain medication in the US.[6] Peripheral nerve ablation, specifically cooled radiofrequency, is among the key emerging advanced technologies offering a minimally invasive treatment of pain that supports H.R. 6 in combatting the nation's opioid crisis. It is also critical to look holistically at the burden and overall cost of disease—not just the cost of the interventions. The HTA can be commended for acknowledging the broad societal impact of chronic musculoskeletal pain. However, a more thorough analysis of real-world evidence as it continues to emerge with advancing technology would provide a more complete assessment in meeting the unmet medical need for non-surgical and non-opioid pain relief treatment. We appreciate your efforts and consideration of these comments as part of your re-assessment of the technology. Thank you for the opportunity to comment!	Thank you for the comment.

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Commenter: Diane F. Weaver, BS, MS, Sr. Manager, Health Policy & Health Economics, Avanos, Inc.	
Specific comments:	
References: 1. Hsu H, Siwiec RM. Osteoarthritis, Knee. [Updated 2018 Jun 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507884/. Accessed October 2, 2018. 2. https://www.medscape.com/viewarticle/718292_2 3. Stelzer W. MD, Use of Radiofrequency Lateral Branch Neurotomy for the Treatment of Sacroiliac Joint-Mediated Low Back Pain: A Large Case Series. Pain Medicine, 2013 Jan (1) 29-35 4. Ball RD. The science of conventional and water-cooled monopolar lumbar radiofrequency rhizsotomy: an electrical engineering point of view. Pain Physician. 2014;17(2): E175-211 5. Desai, M., Bently, A., Buckland, A., Cooled Radiofrequency Ablation of the Genicular Nerves for Chronic Pain Due to Osteoarthritis of the Knee: A Cost-Effectiveness Analysis Based on Trial Data. International Spine Pain and Performance Center, George Washington University, Washington, DC., USA: Mtech Access, Oxfordshire, UK. Presented at the 2018 World Congress on Regional Anesthesia & Pain Medicine • April 19-21, 2018 • New York City, USA 6. CDC. Multiple cause of death data on CDC WONDER. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. http://wonder.cdc.gov/mcd.html	Thank you for the comment. All citations that were potentially relevant for inclusion have been evaluated for inclusion into report. See Table 1 of the report methods section for a detailed list of inclusion and exclusion criteria and Appendix I for a list of excluded studies and the reasons for exclusion.
Additional study submitted: Jamison DE, Cohen SP. Radiofrequency techniques to treat chronic knee pain: a comprehensive review of anatomy, effectiveness, treatment parameters, and patient selection. J Pain Res. 2018;11:1879-1888. doi: 10.2147/jpr.s144633.	This study was evaluated and was included for background, but did not have evidence for inclusion into results.

Comments	Response
Commenter: Greg A. Brown, MD, PhD	
Specific comments:	
The preliminary report is incomplete. The HTCC decision tool requires the consideration of appropriate subgroups. Knee osteoarthritis patients are an important subgroup of knee pain patients and there are 9 randomized controlled trials assessing the effectiveness of RF nerve ablation with appropriate comparators. The final report needs a specific subgroup analysis of RF nerve ablation as a treatment for knee osteoarthritis with appropriate comparators. <u>Knee Nerve Ablation RCTs</u> RFA vs Intra-Articular Corticosteroids Davis[1] Sari[2] Yuan[3] RFA vs Hyaluronic acid	The authorizing language for the Washington HTA program requires that the committee "consider any unique impact the health technology has on specific populations based on factors like sex, age, ethnicity, race, or disability, as identified in the technology assessment." All of the RCTs included for evidence of efficacy of nerve ablation for knee pain involved populations with osteoarthritis of the knee. The study populations were similar in terms of identified characteristics such as age, sex, and race. None of these RCTs presented analyses by any of these population characteristics.

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Specific comments:	
Ray[4] RFA vs PRP and HA injections Shen[5] RFA vs Paracetamol and Diclofenac El-Hakeim[6] RFA vs Sham Choi[7] RFA vs Intra-Articular Erythropoietin or Prolotherapy (dextrose) Rahimzadeh[8] RFA vs Analgesic Nerve Block Qudsi-Sinclair[9]	One study (Qudsi-Sinclair et al.) was somewhat different in that it enrolled only people who had persistent pain after knee replacement. It represented the only identifiable subgroup among the included studies and is discussed in the subgroup findings for Key Question 3. Thank you for the bibliography of studies included in another review that is in process. The inclusion criteria of that review and the WA HTA review differ. However, there was a high degree of overlap on the studies pertaining to knee osteoarthritis treatment that were included in our review. In response to this comment, we included the RCT by Ray et al. It was not identified in our searches because the journal (*Indian Journal of Pain*) is not indexed in MEDLINE or any of the sources for the Cochrane Controlled Trials Register. We had previously excluded the RCTs by Yuan et al. and Rahimzadeh et al. (intra-articular pRF rather than defined nerve target) and Shen et al. (no description of RF technique given to determine eligibility). The other references named are included in the review.
References: 1. Davis T, Loudermilk E, DePalma M, et al. Prospective, Multicenter, Randomized, Crossover Clinical Trial Comparing the Safety and Effectiveness of Cooled Radiofrequency Ablation With Corticosteroid Injection in the Management of Knee Pain From Osteoarthritis. *Regional anesthesia and pain medicine.* 2018;43(1):84-91. 2. Sari S, Aydin ON, Turan Y, Ozlulerden P, Efe U, Kurt Omurlu I. Which one is more effective for the clinical treatment of chronic pain in knee osteoarthritis: radiofrequency neurotomy of the genicular nerves or intra-articular injection? *International journal of rheumatic diseases.* 2018;21(10):1772-1778. 3. Yuan Y, Shen W, Han Q, et al. Clinical Observation of Pulsed Radiofrequency in Treatment of Knee Osteoarthritis. *Int J Exp Med.* 2016;9(10):20050-20055. 4. Ray D, Goswami S, Dasgupta SR, Ray S, Basu S. Intra-Articular Hyaluronic Acid Injection versus FR Ablation of Genicular Nerve for Knee Osteoarthritis Pain: A Randomized, Open-Label, Clinical Trial. *Indian Journal of Pain.* 2018;32(1):36-39. 5. Shen WS, Xu XQ, Zhai NN, Zhou ZS, Shao J, Yu YH. Radiofrequency Thermocoagulation in Relieving Refractory Pain of Knee Osteoarthritis. *American journal of therapeutics.* 2017;24(6):e693-e700.	See response above.

Comments	Response
Commenter: Greg A. Brown, MD, PhD	
Specific comments:	
6. El-Hakeim EH, Elawamy A, Kamel EZ, et al. Fluoroscopic Guided Radiofrequency of Genicular Nerves for Pain Alleviation in Chronic Knee Osteoarthritis: A Single-Blind Randomized Controlled Trial. *Pain physician.* 2018;21(2):169-177. 7. Choi WJ, Hwang SJ, Song JG, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: a double-blind randomized controlled trial. *Pain.* 2011;152(3):481-487. 8. Rahimzadeh P, Imani F, Faiz SH, Entezary SR, Nasiri AA, Ziaeefard M. Investigation the efficacy of intra-articular prolotherapy with erythropoietin and dextrose and intra-articular pulsed radiofrequency on pain level reduction and range of motion improvement in primary osteoarthritis of knee. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences.* 2014;19(8):696-702. 9. Qudsi-Sinclair S, Borras-Rubio E, Abellan-Guillen JF, Padilla Del Rey ML, Ruiz-Merino G. A Comparison of Genicular Nerve Treatment Using Either Radiofrequency or Analgesic Block with Corticosteroid for Pain after a Total Knee Arthroplasty: A Double-Blind, Randomized Clinical Study. *Pain practice : the official journal of World Institute of Pain.* 2017;17(5):578-588.	

Comments	Response
Commenter: David P. Green, MD, Medical Director, Molina Healthcare of Washington	
Specific comments:	
I wanted to submit a few comments for this upcoming review. I appreciate that this topic is being addressed because the number of requests for these procedures has been increasing. There is currently little in the way of guidance as to medical necessity. It seems likely from the draft report that these injections and subsequent RFAs will not be covered. 1) Requests for these procedures will be difficult to sort out in the prior auth process because they have non-specific CPT codes: 64450 and 64640. One way to identify them may be based on the submitted diagnosis codes. 2) The cost of doing a prior auth review is very similar to the reimbursement rates for 64450 and 64640.	Thank you for the comment. This relates to implementation of coverage rather than the evidence about the procedures.