Transtympanic Micropressure Applications as a Treatment of Meniere Disease

Policy # 00505
Original Effective Date: 06/20/2016
Current Effective Date: 06/21/2017

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Based on review on available data, the Company considers the use of transtympanic micropressure applications as a treatment of Meniere disease to be investigational.*

Background/Overview
Meniere disease is an idiopathic disorder of the inner ear characterized by episodes of vertigo, fluctuating hearing loss, tinnitus, and ear pressure. Conservative therapy includes a low sodium diet and diuretics to reduce fluid accumulation (ie, hydrops) and pharmacologic therapy to reduce vestibular symptoms. Transtympanic pressure treatment has been proposed as an alternative treatment for Meniere disease. This treatment involves use of a handheld device (eg, Meniett) that delivers air pressure pulses to the ear.

Vertigo attacks in Meniere disease are often unpredictable and incapacitating and may prevent activities of daily living. Therapy is symptomatic in nature and does not address the underlying pathophysiology. Although the pathophysiology of Meniere disease is not precisely known, it is thought to be related to a disturbance in the pressure/volume relationship of the endolymph within the inner ear. Conservative therapy includes a low sodium diet and diuretics to reduce fluid accumulation (ie, hydrops) and pharmacologic therapy to reduce vestibular symptoms. Persons who do not respond to these conservative measures may receive gentamicin drops in the ear, as a technique of chemical labyrinthectomy to ablate vestibular function on the affected side. No therapy is available to restore hearing loss.

There has been interest in developing a more physiologic approach to treatment by applying local transtympanic pressure treatment to restore the underlying fluid homeostasis. Researchers have noted that symptoms of Meniere disease improve with fluctuations in ambient pressure, and patients with acute vertigo have been successfully treated in hypobaric chambers. It is hypothesized that the application of low-frequency, low-amplitude pressure pulse to the middle ear functions to evacuate endolymphatic fluids from the inner ear, thus relieving vertigo. Transtympanic micropressure treatment for Meniere disease involves use of a handheld air pressure generator (Meniett) that delivers intermittent complex pressure pulses. For this device to be used, a conventional ventilation tube is surgically placed in the eardrum. Patients then place an ear-cuff in the external ear canal and treat themselves for 3 minutes, 3 times daily. Treatment continues for as long as patients have vertigo attacks.

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FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
In 1999, the Meniett device (Medtronic, Xomed, Jacksonville, FL) was cleared for marketing by the FDA through the 510(k) process specifically as a symptomatic treatment of Meniere disease.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source
Assessment of efficacy for a therapeutic intervention involves a determination of whether the intervention improves health outcomes compared to available alternatives. The optimal study design for this purpose is a randomized controlled trial (RCT) that compares the therapeutic intervention with existing alternative treatments, uses a placebo control, and includes clinically relevant measures of health outcomes.

The data submitted to the FDA as part of the FDA-approval process consisted of a case series of 20 patients. Other case series have also been published in the peer-reviewed literature, some reporting 2- to 4-year outcomes in patients who had failed medical therapy. These case series are inadequate to form conclusions due to the lack of a control group, and they will not be discussed further in this review. The remaining literature review will focus on RCTs and systematic reviews of RCTs that have been published.

Systematic Reviews
A 2015 Cochrane review on positive pressure therapy for Meniere disease included 5 double-blind, placebo-controlled RCTs (total N=265 patients). Three of the studies were considered to be at low risk of bias, 1 was at unclear risk, and 1 study was at high risk of bias. Results on the primary outcome measure, control of vertigo, could not be pooled due to heterogeneity in measurement, but most trials showed no significant difference in vertigo between Meniette therapy and placebo. This review supports the conclusion that there is no evidence that positive pressure therapy is effective for the treatment of Meniere disease, and that there is some evidence that hearing is impaired with this treatment. Another systematic review, which included 4 of the same RCTs that specifically used the Meniett device, also found no significant difference between low pressure therapy and placebo for the frequency of vertigo. The 3 trials with low risk of bias are described next.

Randomized Controlled Trials
RCTs Included in the 2015 Cochrane Review
In 2004, Gates et al. reported the 4-month results of a randomized, multi-institutional study that enrolled 67 patients with active unilateral Meniere disease refractory to a 3-month trial of medical management. All patients underwent tympanostomy, and patients were additionally randomly assigned to a sham device or a Meniett device. Over the entire 4-month trial, there was a significant difference in the total number of episodes of vertigo in the treatment group compared with the control group. However, the difference between the groups was most apparent at 1 month, while at 4 months the treatment effect had disappeared almost entirely. Similarly, overall, there was a significant decrease in the frequency of vertigo in the treatment group, but again this difference was most apparent at the 1-month interval and almost...
disappeared at 4 months. This trial was limited by a number of methodologic issues related to the data analysis, and results from this trial do not permit drawing conclusions about the impact of this device on patient outcomes.

In 2006, Gates et al reported 2-year, open-label, follow-up from the 2004 randomized trial. At the end of the randomized phase of the study, 61 of 67 patients from both the control and active treatment arms were treated with the Meniett device; 3 were subsequently lost to follow-up or excluded due to concurrent health problems. Vertigo episodes were reported on a daily symptom diary (44 patients) or by a structured telephone interview (17 patients). Of the 58 patients followed for 2 years, 14 (24%) dropped out to seek alternative surgical treatment, 5 (9%) showed little or no improvement, and 39 (67%) reported being in remission or substantially improved. Patients who went into remission had an 80% probability of remaining in remission for the 2 years. This assessment is limited, however, by the lack of a control group followed over the same period.

A 2005 multicenter, double-blind, placebo-controlled trial of 63 patients compared micro pressure devices with ventilation tubes and sham pressure devices. This trial reported an improvement in functionality (American Academy of Otolaryngology–Head and Neck Surgery criteria) and a trend (p=0.09) toward a reduction in episodes of vertigo for the active treatment group compared with controls. The frequency of attacks decreased from 10.5 to 4.0 in the placebo group and from 9.6 to 1.9 in the active group. There were no changes in secondary outcome measures (patient's perception of tinnitus, aural pressure, hearing). In addition to a marginal improvement in efficacy over ventilation tubes with sham pressure, this study was limited by a high dropout rate (37%), lack of intention-to-treat analysis, and short (2-month) monitoring period.

In 2012, Gurkov et al reported a randomized double-blind sham-controlled trial with the Meniett device. After a 4-week baseline period, 74 patients underwent ventilation tube placement and were monitored for another 4 weeks. Patients were then randomized to 16 weeks of active or sham treatment (5 minutes, 3 times daily). The primary outcomes were subjective vertigo score, number of definitive vertigo days, and number of sick days as recorded on a daily log over the last 4 weeks of treatment. Sixty-eight (92%) patients completed the study. The cumulative vertigo score decreased by 6.5 in the active group and by 1.19 in the sham group (p=0.048). The number of vertigo days decreased by 2.42 in the active treatment group and by 0.42 in the sham group (p=0.102), and the number of sick days decreased by 2.32 in the active treatment group and increased by 0.58 days in the sham group (p=0.041). There was no significant difference between groups in the vertigo-free days, activity score, hearing level, or slow phase velocity. This study showed a modest improvement in 2 of 5 subjective measures, but not in objective outcome measures, with the Meniett device.

RCTs Subsequent to the 2015 Cochrane Review

Russo et al reported on an industry-sponsored, multicenter, double-blind RCT of the Meniett device in 2017.15 A total of 129 patients with Meniere disease not controlled by medical treatment were withdrawn from any vertigo treatment and received placement of a transtympanic tube. Patients (n=97 [75%]) who continued to have symptoms (≥2 vertigo episodes during a 6-week period) after placement of a transtympanic tube were randomized to an active or sham device for 6 weeks, and then were followed for
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an additional 6 weeks. The number of vertigo episodes during the baseline period did not differ significantly between groups (p=0.07). The trial was powered to detect a 30% difference in vertigo episodes compared to the sham group. Per protocol analysis showed a significant decrease in vertigo episodes in both groups (see Table 1), but no between-group difference (p=0.11), suggesting a possible effect of the transtympanic tube. Vertigo-related quality of life also did not differ between groups.

Table 1. Number of Vertigo Episodes

<table>
<thead>
<tr>
<th>Treatment Arms</th>
<th>Before Treatment (SEM)</th>
<th>During Treatment (SEM)</th>
<th>After Treatment (SEM)</th>
</tr>
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<tbody>
<tr>
<td>Active</td>
<td>3.2 (0.4)</td>
<td>2.5 (NR)¹</td>
<td>1.5 (0.02)²</td>
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<tr>
<td>Sham</td>
<td>4.3 (0.6)</td>
<td>2.6 (0.05)²</td>
<td>1.8 (0.8)³</td>
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NR: not reported.
¹ p<0.005 vs during treatment.
² p<0.05 vs baseline.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in January 2017 did not identify any ongoing or unpublished trials that would likely influence this review.

Summary of Evidence
The evidence for micropressure therapy in individuals who have Meniere disease includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Six RCTs of positive pressure therapy have been reported, with 5 trials specifically investigating the Meniett device. A systematic reviews of 5 of these trials found that micropressure therapy does not result in a greater reduction in vertigo than placebo. The evidence is insufficient to determine that the technology is likely to improve the net health outcome, therefore transtympanic micropressure applications as a treatment of Meniere disease is considered investigational.

References
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Policy History
Original Effective Date: 06/20/2016
Current Effective Date: 06/21/2017
06/02/2016 Medical Policy Committee review
06/20/2016 Medical Policy Implementation Committee approval. New Policy.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
06/01/2017 Medical Policy Committee review
06/21/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 06/2018

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<tr>
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<tr>
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<td>A4638, E2120</td>
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| ICD-10 Diagnosis | H81.01-H81.09 |

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A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

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