Title: Transtympanic Micropressure Applications as a Treatment of Meniere's Disease

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<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
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<tr>
<td>• With Meniere disease</td>
<td>• Micropressure therapy</td>
<td>• Standard care</td>
<td>• Symptoms</td>
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<td>• Functional outcomes</td>
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DESCRIPTION
Meniere's disease is an idiopathic disorder of the inner ear characterized by episodes of vertigo, fluctuating hearing loss, tinnitus, and ear pressure. The vertigo attacks 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's 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's 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 is continued for as long as patients find themselves in a period of attacks of vertigo.

Regulatory Status
In 1999, the Meniett® device (Medtronic, Minneapolis, MN) was cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process specifically as a symptomatic treatment of Meniere's disease. The device is currently available through Meniette AG.

POLICY
Transtympanic micropressure applications as a treatment of Meniere's disease are considered experimental / investigational.

RATIONALE
This evidence review has been updated periodically using the MEDLINE database. The most recent literature review was performed through December 2, 2015.

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 U.S. Food and Drug Administration (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.1-8 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.

A 2015 Cochrane review on positive pressure therapy for Meniere disease included 5 double-blind, placebo-controlled RCTs (total N=265 patients).9 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.10 The 3 trials with low risk of bias are described next.

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.11 All patients underwent tympanostomy, and patients were additionally randomly assigned to a sham device or a Meniett device. Outcomes were assessed using symptom report cards that focused on the severity and frequency of vertigo. Vertigo was assessed on a scale from 1 to 4, and a score of 2 or higher was considered definitive vertigo. The total number of days of definitive vertigo for all participants was reported at each month. While an analysis of variance (ANOVA) showed that, 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, 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 study was limited by a number of methodologic issues related to the data analysis. In particular, repeated-measures ANOVA, which was the primary statistical method used to analyze these data, assumes normal distribution, equal variances and covariances, and equal variances over time (compound symmetry or the so-called sphericity assumption); whether these assumptions were met is unclear from the report. There were a number of "outlier" patients. These outliers would result in the data not being "normally distributed" and also could be influential in the marginally significant p values noted in the study. It is unclear that the "interim power analysis" performed was preplanned or that the trial was intended as an adaptive group sequential design. Whether consideration was given to protecting the type I error rate is also unclear. Given these concerns, results from this trial do not allow 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.11,12 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 micropressure 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. It was also limited by the relatively short (4-month) follow-up period.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in January 2016 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 randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Five RCTs of positive pressure therapy have been reported, with 4 trials specifically investigating the Meniett device. Systematic reviews of these trials found that micropressure therapy does not result in a greater improvement in vertigo than placebo. The evidence is sufficient to determine qualitatively that the technology is unlikely to improve the net health outcome.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. In response to requests, input was received through 1 physician specialty society (2 reviewers) and 2 academic medical centers while this policy was under review in 2008. Clinical input was
mixed regarding whether this treatment would be considered investigational, as adopted in the policy in 2008.

**Practice Guidelines and Position Statements**

**American Academy of Otolaryngology–Head and Neck Surgery**

In 2012, the American Academy of Otolaryngology–Head and Neck Surgery updated its position statement on the use of transtympanic micropressure: “We find that there is convincing and well-controlled medical evidence to support the use of micropressure therapy (such as the Meniett device) in certain cases of Meniere disease. Micropressure therapy is best used as a second level therapy when medical treatment has failed. The device represents a largely non-surgical therapy that should be available as one of the many treatments for Meniere’s disease.”[^15] No supporting evidence was provided.

**National Institute for Clinical Excellence**

In 2012, guidance from the U.K.’s National Institute for Clinical Excellence concluded that “[c]urrent evidence on the safety of micropressure therapy for refractory Ménière’s disease is inadequate in quantity. There is some evidence of efficacy, but it is based on limited numbers of patients. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.”[^16]

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**CODING**

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

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<tr>
<td>E2120</td>
<td>Pulse generator system for tympanic treatment of inner ear endolymphatic fluid</td>
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- HCPCS code E2120, pulse generator system for tympanic treatment of inner ear endolymphatic fluid, describes the Meniett device.
- Use of the Meniett device requires a prior tympanostomy procedure, a novel indication for this common procedure.

**REVISIONS**

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<td>08-12-2011</td>
<td>Policy added to the bcbsks.com web site.</td>
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<tr>
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REFERENCES