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Type of Submission – Check all that apply:
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document.
Please provide any clarifying information for the policy below:

**CPB 0406 – Tinnitus Treatments**

This CPB has been revised to state that the following are considered experimental and investigational for the management of members with tinnitus: (i) acoustic coordinated reset neuromodulation, and (ii) microvascular decompression of the cochlea-vestibular nerve.

**Name of Authorized Individual (Please type or print):**
Chandra A. Kee, MD

**Signature of Authorized Individual:**
[Signature]
Tinnitus Treatments

Number: 0406

(Replaces CPB 478)

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

I. Aetna considers transcutaneous electrical nerve stimulation (TENS) medically necessary durable medical equipment (DME) for members with severe tinnitus when all of the following criteria are met:

A. Medically correctable causes of tinnitus have been ruled out, and
B. Member has experienced severe tinnitus for more than 6 months, and
C. Member has tried and failed conservative tinnitus treatments, including counseling and reassurance, dietary modifications, and drug therapy.

Note: More than 10 TENS sessions per year are not considered medically necessary for the treatment of tinnitus because of a lack of evidence that more frequent TENS treatments provides additional clinically significant benefits for this condition.
II. Aetna considers tinnitus instruments (e.g., maskers, hearing aids, or combination of maskers and hearing aids) experimental and investigational for the management of members with tinnitus because the effectiveness of these instruments has not been demonstrated in randomized controlled studies with large sample size and long-term follow-up evaluation.

**Note:** Tinnitus instruments such as maskers and hearing aids are approved by the Food and Drug Administration (FDA) and are classified as Class III devices; however, tinnitus masking is not approved for coverage by the Centers for Medicare & Medicaid Services (CMS).

III. Aetna considers the following interventions experimental and investigational for the management of members with tinnitus (not an all-inclusive list):

- Acoustic coordinated reset neuromodulation
- Acupuncture (see CPB 0135 - Acupuncture (../100_199/0135.html))
- Antioxidant therapy (e.g., alpha-lipoic acid, Ginkgo biloba, papaverine, vitamin C and vitamin E)
- Audiotherapy (e.g., acoustic stimulation and auditory perceptual training)
- Botulinum toxin (see CPB 113 - Botulinum Toxin)
- Cochlear implants
- Competitive kinesthetic interaction therapy (KKIT)
- Deep brain stimulation
- Ear canal magnets
- Electromagnetic stimulation
- Hyperbaric oxygen therapy (See CPB 0172 - Hyperbaric Oxygen Therapy (HBOT) (../100_199/0172.html))
- Intra-tympanic administration of corticosteroids
- Intravenous lidocaine
- Intravenous mexiletine
- Melatonin (alone or in combination with sulodexide)
- Microvascular decompression of the cochlea-vestibular nerve
- Music therapy
- Neuromonics Tinnitus Treatment/Neuromonics Oasis device
- Noise/sound generators
For biofeedback for tinnitus, see CPB 0132 - Biofeedback
(../100_199/0132.html).

See also CPB 0238 - Chronic Vertigo (../200_299/0238.html); CPB 0469 - Transcranial Magnetic Stimulation and Cranial Electrical Stimulation (0469.html); and CPB 0514 - Meniere's Disease Surgery (../500_599/0514.html).

Background
Tinnitus is defined as the aberrant perception of noise or sound without any external stimulation, and may be described as buzzing, hissing, ringing, roaring or whistling. It may be unilateral or bilateral and has equal prevalence in women and men and is most prevalent between the ages of 40 and 70. Occasionally, tinnitus can also occur in children. Periodic bouts of mild, high-pitched tinnitus lasting for several minutes are common in normal-hearing individuals. Severe and persistent tinnitus can interfere with sleep and the ability to concentrate, causing great psychological distress. In extreme cases, patients with severe chronic tinnitus may consider suicide. Tinnitus can be classified into 2 types: (i) subjective tinnitus, and (ii) objective tinnitus.

Subjective tinnitus, which is more common, is audible only to the patient. It may arise from some types of electrophysiological disturbance anywhere in the auditory system -- the external ear canal, tympanic membrane, ossicles, cochlea, auditory nerve, brainstem or cerebral cortex. The underlying causes of subjective tinnitus include otological (presbycusis, noise-induced hearing loss, Meniere's disease, or chronic otitis media), metabolic (diabetes, thyroid diseases, hyperlipidemia, or zinc...
deficiency/vitamin deficiency), pharmacological (aspirin compounds, non-steroidal anti-inflammatory drugs, caffeine, nicotine, aminoglycosides, or antidepressants), neurological (whiplash, skull fracture/closed head trauma, multiple sclerosis, or following meningitis), psychological (depression or anxiety), as well as infectious and neoplastic (syphilis, acoustic neuroma, autoimmune diseases, or acquired immune deficiency syndrome) disorders.

Objective tinnitus, the less common type of tinnitus, usually refers to noises that can be heard by an examiner. The physician must put his/her ear against the patient's ear or use a stethoscope against the patient's external auditory canal. Objective tinnitus usually has a vascular (arteriovenous malformations/shunts, arterial bruits, hypertension, arteriosclerosis, venous hums, or aneurysms) or mechanical (Eutaschian tube dysfunction, temporomandibular joint disease, palatal myoclonus, or idiopathic stapedal muscle spasm) origin (Schuler and Schleuring, 1994; Seidman and Jacobson, 1996).

Although there is no cure for tinnitus, treatments are designed to provide relief of symptoms. The management of patients with tinnitus often depends on the severity of the condition. If the patient's activities of daily living are not affected by tinnitus, treatment options include counseling, reassurance, and/or behavioral and dietary modifications (avoidance of excessive noise, nicotine, salt, and caffeine). All medications should also be evaluated to eliminate ototoxic drugs. Currently, the medications for patients with severe tinnitus include amitriptyline (Elavil), alprazolam (Xanax), diazepam (Valium), and clonazepam (Klonopin); however, none of these drugs has been approved by the U.S. Food and Drug Administration for the specific treatment of tinnitus. The American Academy of Otolaryngology - Head and Neck Surgery Foundation’s clinical practice guideline on “Tinnitus” (2014) stated that clinicians should not routinely recommend anti-depressants, anti-convulsants, and anxiolytics for a primary indication of treating persistent, bothersome tinnitus.

Biofeedback is a technique in which a person learns to gain
control over unconscious bodily functions, such as the triggers that cause tinnitus. May include stress reduction and relaxation exercises to help the person change their reaction to the condition.

Cognitive behavioral therapy (CBT) attempts to teach coping strategies or distraction skills and relaxation techniques so that the psychological response to the condition may be altered.

Botulinum toxin injections (BTX) controls muscle spasms by temporarily weakening or paralyzing nerves.

**Electrical Stimulation**

Another therapeutic modality is electrical stimulation (ES). Electrical stimulation may include placing electrodes directly on the bony cochlea or the round window niche (one of two openings that connect the inner ear to the middle ear), or anywhere in the vicinity of the ear. The exact mechanism by which electrical stimulation is proposed to reduce tinnitus is unclear.

In a review on tinnitus, Siedman and Jacobson (1996) indicated that ES is a possible treatment modality for patients with severe tinnitus. Hatton et al (1960) reported that only anodal (positive electrode) stimulation produced the suppressive effect. In general, ES is provided through electrodes in the vicinity of the ear. The exact mechanism(s) by which ES suppresses/reduces tinnitus is unclear. However, it has been postulated that positive electrical currents produce a hyperpolarization of nerve fibers, which inhibit and reduce spontaneous discharge rates (Portmann et al, 1983).

Hatton et al (1960) observed that the intensity of tinnitus was reduced in 15 (45.5 %) of 33 patients with ES. Chouard et al (1981) reported that 30 (47 %) of 64 patients achieved success (as determined by reduced intensity that lasted for a few days to more than 1 week) following electrotherapy. None of the 12 patients who received placebo stimulation attained relief. The authors stated that if a patient failed to achieve improvement
after 2 to 3 sessions, it is unlikely that this form of therapy will be successful.

Engelberg and Bauer (1985) performed two experiments to examine the effects of transcutaneous electrical stimulation (TENS) on tinnitus. Experiment 1 had 10 subjects (18 ears) and improvement (defined as either a complete remission or a decrease in the frequency of tinnitus) was seen in 6 of them with tinnitus being eliminated in 3 ears. Experiment 2 employed a single-blind study design with 20 patients (experimental group, n = 10, 17 ears; control group, n = 10, 15 ears). It was found that 9 of 10 patients with 15 (88.2 %) of 17 ears reported improvement following stimulation. These changes lasted from 20 minutes to at least 6 months. On the other hand, only 1 patient (1 ear) in the control group improved (a 13 % decrease in frequency of tinnitus).

Steenerson and Cronin (1996) reported their findings of 246 patients with severe tinnitus of various etiologies treated with ES (a total of 6 to 10 sessions). One hundred and thirty patients (53 %) reported significant benefit (an improvement of at least 2 points in a 1 to 10 subjective rating scale) with 32 patients (13 %) having complete suppression of their tinnitus. At 3-month follow-up, 72 % had continuous benefit.

In a subsequent report, Steenereson and Cronin (1999) reported their findings in 500 patients with tinnitus who were treated with probe electrical stimulation. The authors reported that 53 % of patients showed decreases in their tinnitus as measured by a subjective rating scale. At 3-month follow-up, 72 % had no loss of benefit.

Rahko and Kotti (1997) treated 26 patients with transcutaneous nervous stimulation (TNS) for tinnitus. Except for 3 normal hearing patients, all had cochlear hearing losses. The authors found that tinnitus disappeared in none of the patients, but diminished in 7 patients, versus diminution of tinnitus in 3 in 24 nontreated controls.

In a study that evaluated the effects of psychological factors on
the outcome of TENS for patients with chronic tinnitus (n = 27), Collet and associates (1987) found that the 15 patients (55.6 %) who did not improve showed higher pre-treatment scores of depression, psychasthenia, and schizophrenia. These findings indicated that patients having psychiatric problems such as those mentioned above are unlikely to benefit from treatment.

According to available literature, transcutaneous electrical stimulation for tinnitus is contraindicated in persons with the following conditions:

- Persons taking medications for other diseases/conditions known to have a side effect of tinnitus, such as aspirin, Vasotec (enalapril maleate), etc.; or
- Persons with active ear disease; or
- Persons with cardiac pacemakers, implanted stapes prostheses or other implanted devices, which may be affected by electrical signals; or
- Persons with psychiatric problems such as schizophrenia, depression, hysteria, or hypochondria; or
- Women who are pregnant.

**Masking Instruments**

Tinnitus masking instruments such as maskers, hearing aids, and tinnitus devices (combination of hearing aid and tinnitus masker) have been used for alleviating symptoms associated with tinnitus. However, the effectiveness of these instruments for treating tinnitus has not been established. These devices are all worn behind, or in either the same or opposite ear affected by tinnitus. Tinnitus maskers generate a grossly broad-band high-energy noise, which most patients find an excessive noise intrusion that is unacceptable and intolerable.

The goal of hearing aids is to bring in more sounds from the person’s surroundings, thus naturally covering the tinnitus and making it less noticeable. Some hearing aids may exist as a combination hearing aid and a broadband noise generator or masking device for tinnitus relief. An example of a combination hearing aid includes, but may not be limited to, the Phonak
hearing aid combined with the Phonak tinnitus balance.

Masking devices are similar in appearance to hearing aids; however, they do not amplify sounds, but instead produce constant low-level white noise, intended to provide a distraction from the internal tinnitus. Masking may also be accomplished by using or enhancing background noise with tabletop sound machines, etc. Examples of masking devices include, but may not be limited to, the following: Levo tinnitus symptoms masking systems; Neuromonics tinnitus treatment; Phonak tinnitus balance; Refuge tinnitus masker; Serenade tinnitus treatment; The Inhibitor; The Jump C TRT; and Unitron tinnitus masker.

A review of 69 randomized clinical trials of therapies for tinnitus (Dobie, 1999) concluded that no treatment (pharmacotherapy, psychotherapy, and various non-drug treatments including masking) could yet be considered established in terms of providing reproducible long-term benefits, in excess of placebo effects.

A systematic review of the evidence for tinnitus treatments by BMJ Clinical Evidence concluded that tinnitus masking devices and hearing aids are of "unknown effectiveness" (Savage et al, 2011).

The Centers for Medicare and Medicaid Services (CMS, 2006) has concluded: “Tinnitus masking is considered an experimental therapy at this time because of a lack of controlled clinical trials demonstrating effectiveness and the unstudied possibility of serious toxicity in the form of noise induced hearing loss.”

In a Cochrane review, Hobson et al (2010) examined the effects of sound therapy (masking) in the management of tinnitus in adults. Prospective, randomized controlled trials recruiting adults with persistent, distressing, subjective tinnitus of any etiology in which the management strategy included maskers, noise-generating device and/or hearing aids, used either as the sole management tool or in combination with other strategies, including counselling were included in this review. A total of 6 trials (553 subjects) were
included in this review. Studies were varied in design, with significant heterogeneity in the evaluation of subjective tinnitus perception, with different scores, scales, tests and questionnaires as well as variance in the outcome measures used to assess the improvement in tinnitus sensation/quality of life. This precluded meta-analysis of the data. There was no long-term follow-up. These researchers assessed the risk of bias as medium in 3 and high in 3 studies. No side effects or significant morbidity were reported from the use of sound-creating devices. The authors concluded that the limited data from the included studies failed to show strong evidence of the efficacy of sound therapy in tinnitus management. The absence of conclusive evidence should not be interpreted as evidence of lack of effectiveness. The lack of quality research in this area, in addition to the common use of combined approaches (hearing therapy plus counselling) in the management of tinnitus are, in part, responsible for the lack of conclusive evidence.

**Ear Canal Magnets and Electromagnetic Stimulation**

A systematic evidence review published in BMJ Clinical Evidence (Savage, et al., 2009; Savage, et al., 2011) concluded that the effectiveness of ear canal magnets and electromagnetic stimulation for tinnitus are unknown.

The systematic evidence review identified two small randomized, controlled clinical trials comparing electromagnetic stimulation to placebo. The first trial (n = 58) found that 15 minutes per day of electromagnetic stimulation significantly increased the proportion of people who had subjective improvements in tinnitus compared to placebo after one week (citing Roland et al, 1993). Based upon subjective responses assessed by a 4-point questionnaire, 14 of 31 subjects assigned to electromagnetic stimulation improved compared to 2 of 23 subjects assigned to placebo (p = 0.0013). The systematic review noted that 4 subjects withdrew from the trial, and that the analysis was not by intention to treat. A second randomized controlled clinical trial (n = 20) used a crossover design and did not report results before the crossover (citing Dobie et al, 1986). The crossover trial found similar effects between electromagnetic stimulation and a
placebo device in reducing tinnitus severity. Severity, measured on a scale of 0-7, was reported as less severe in 2 of 20 subjects with the active device versus three of 20 subjects with a placebo device.

The systematic evidence review found one randomized controlled clinical trial (n = 49) that found similar effects between a simple ear-canal magnet and placebo (similar unmagnetized material) in tinnitus symptoms after 4 weeks' treatment (citing Coles et al, 1991). Symptom improvement was reported in 7 of 26 persons with the magnet compared to 4 of 23 persons with placebo.

Tinnitus Retraining Therapy

Tinnitus retraining therapy (TRT) is a neurophysiological approach centering on behavioral retraining of the associations induced by perception of tinnitus. TRT uses a combination of low-level broad-band noise along with counseling to achieve the habituation of tinnitus. The goal is to become unaware of the tinnitus unless it is consciously focused on and to remain unbothered by it, even when aware of it.

TRT uses devices similar to tinnitus maskers. These devices, known as white noise generators, produce white noise, and are used over a period of several months to help patients in their habituation of tinnitus. Measurement of the tinnitus match is performed after an audiogram. The patient is asked to identify which of the tones of the audiometer match the tone of the ringing of his or her tinnitus. Examples of measures quantified include pitch, loudness and minimal masking level of the tinnitus. As mentioned, these parameters are then used for tinnitus retraining and for selecting devices, which can produce “white noise” to counterbalance and reduce or eliminate the tinnitus. There are several factors that influence the frequency spectrum of the perceived noise such that the perception of white noise from a white noise generator is unlikely. These factors include (i) the actual spectrum of the emitted noise, (ii) the ear canal resonance of the patient, and (iii) the hearing sensitivity of the patient. Furthermore, a study stated that methodological limitations of the research published to date preclude any claims
about the efficacy of TRT at the present time (Wilson et al, 1998). A technology assessment prepared for the Wessex Institute for Health Research and Development (Leal and Milne, 1998) concluded that the available case series are inadequate, owing to problems of methodology, and that there is no evidence to suggest that TRT is effective in the treatment of debilitating tinnitus in adult patients.

Kroener-Herwig et al (2000) stated that there is no published study evaluating TRT using a randomized group design even though this is the only design able to give valid information on the empirical status of a therapy. They concluded that the praise of TRT as the most promising therapy for chronic tinnitus can only be regarded as premature, and the claim of its effectiveness by its advocates await scientific corroboration. Randomized, controlled clinical studies that include no-treatment and placebo groups are needed to ascertain the effectiveness of TRT in the management of patients with tinnitus.

An assessment by the Washington Department of Labor and Industries Office of the Medical Director (Wang, 2004) concluded that “[d]ue to the lack of prospective trials with comparison groups, the efficacy of TRT for subjective tinnitus has not been established. Therefore, TRT is considered investigational and controversial.”

A systematic review of the evidence for tinnitus treatments by BMJ Clinical Evidence concluded that tinnitus training therapy is of "unknown effectiveness" (Savage et al, 2011).

Hiller and Haerkotter (2005) reported that noise generators had benefit in persons with tinnitus. However, post-hoc analysis revealed benefits in a subgroup of tinnitus patients with hyperacusis. They stated that this finding would need to be replicated in a prospective well-controlled study to evaluate sound generators in hyperacusis.

Transcranial Magnetic Stimulation

Repetitive transcranial magnetic stimulation (rTMS) treatment
Tinnitus Treatments

consists of low-level electrical stimulation emitted from an
electrostimulator device placed on the earlobes or behind the
ears.

Clinical, neurophysiological and neuroimaging data suggest that
chronic tinnitus resembles neuropsychiatric syndromes
characterized by focal brain activation. Low-frequency repetitive
transcranial magnetic stimulation (rTMS) has been proposed as a
method in treating brain hyperexcitability disorders by reducing
cortical excitability. Kleinjung et al (2005) examined the effects of
rTMS on patients with chronic tinnitus (n = 14). Increased
metabolic activation in the auditory cortex was verified in all
patients. After 5 days of rTMS, a highly significant improvement of
the tinnitus score was found whereas the sham treatment did not
show any significant changes. The treatment outcome after 6
months still demonstrated significant reduction of tinnitus score.
The authors concluded that these preliminary results showed that
neuro-navigated rTMS offers new possibilities in the
understanding and treatment of chronic tinnitus. The findings of
this study need to be verified by further investigation with larger
sample size and long follow-up.

Pridmore et al (2006) examined the literature and considered the
potential for TMS as a treatment for patients with tinnitus. These
researchers noted that a small number of studies have suggested
that TMS may be effective in the treatment of tinnitus. There is a
good theoretical basis and early research evidence suggesting
that TMS may have treatment potential in tinnitus. Moreover,
they stated that further, larger studies are necessary to ascertain
the effectiveness of this approach.

In a randomized, placebo-controlled (sham stimulation)
cross-over pilot study, Smith et al (2007) evaluated the
effectiveness of neuro-navigated rTMS and its effects on
attentional deficits and cortical asymmetry in 4 patients with
chronic tinnitus using objective and subjective measures and
employing an optimization technique refined in their laboratory.
Patients received 5 consecutive days of active, low-frequency
rTMS or sham treatment (using a 45-degree coil-tilt method)
before crossing over. Subjective tinnitus was assessed at baseline,
after each treatment, and 4 weeks later. Positron emission
 tomography/computed tomography (PET/CT) scans were
 obtained at baseline and immediately after active treatment to
 examine change in cortical asymmetry. Attentional vigilance was
 assessed at baseline and after each treatment using a simple
 reaction time test. All patients had a response to active (but not
 sham) rTMS, as indicated by their best tinnitus ratings; however,
tinnitus returned in all patients by 4 weeks after active treatment.
All patients had reduced cortical activity visualized on PET
immediately after active rTMS. Mean reaction time improved (p <
0.05) after active but not sham rTMS. The authors concluded that
rTMS is a promising treatment modality that can transiently
diminish tinnitus in some individuals, but more studies are
needed to determine the optimal techniques needed to achieve a
lasting response. It is unclear if the improved reaction times were
caused by tinnitus reduction or a general effect of rTMS. PET/CT
scans immediately after treatment suggest that improvement
may be related to reduction of cortical asymmetry associated
with tinnitus.

Khedr et al (2008) compared the effect of different frequencies of
rTMS (1 Hz, 10 Hz, 25 Hz and sham (occipital, 1 Hz)), given daily
over the left temporo-parietal cortex for 2 weeks, on 66 patients
with chronic tinnitus randomly divided into four treatment
groups. Patients were assessed using the Tinnitus Handicap
Inventory (THI), self-ratings of symptoms and audiometric
measures of residual inhibition before, immediately after 2
weeks' treatment and monthly thereafter for 4 consecutive
months. There were no significant differences in basal measures
between the four groups of patients. A 2-factor ANOVA revealed a
significant "rTMS" x "time" interaction for all measures. This
was because real rTMS produced greater improvement than
sham. However, there was no significant difference between the
responses to different frequencies of rTMS. The response to rTMS
depended on the duration of tinnitus: patients who had tinnitus
for the longest period of time were the least likely to respond to
treatment. The authors concluded that daily sessions of rTMS
over the temporo-parietal cortex may be a useful potential
treatment for tinnitus.
In a pilot study, Lee and colleagues (2008) examined the effectiveness of rTMS in veterans with debilitating tinnitus. A total of 8 patients received 5 consecutive days of rTMS (0.5 Hz, 20 minutes) to the left temporo-parietal area. Outcome was measured by means of THI before sessions 1 and 3 and after session 5. Patient 1’s THI decreased from 40 to 34 to 26, patient 4 reported a subjective improvement, patient 8 withdrew, and the remaining 5 patients reported no improvement. Side effects included temporary soreness, restlessness, and photophobia. The authors concluded that with these current parameters, rTMS did not improve tinnitus in veterans.

Kleinjung et al (2008) stated that a growing number of studies demonstrate reduction of tinnitus after repeated sessions of low-frequency rTMS and indicate that rTMS might represent a new promising approach for the treatment of tinnitus. Single sessions of high-frequency rTMS over the temporal cortex have been successful in reducing the intensity of tinnitus during the time of stimulation and could be predictive for treatment outcome of chronic epidural stimulation using implanted electrodes. Because most available studies have been performed with small sample sizes and show only moderate effect sizes and high inter-individual variability of treatment effects, further development of the technique is needed before it can be recommended for use in clinical routine. Both patient-related (e.g., hearing loss, tinnitus duration, age) and stimulation-related (e.g., stimulation site, stimulation protocols) factors seem to influence treatment outcome; however, their exact impact still remains to be clarified.

In a Cochrane review, Meng et al (2011) evaluated the safety and effectiveness of rTMS versus placebo in patients with tinnitus. These investigators searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was May 24, 2011. Randomized controlled trials of rTMS versus sham rTMS were selected for this analysis. Two review authors reviewed the titles, abstracts and
keywords of all records retrieved; 3 review authors independently collected and extracted data, and assessed the risk of bias of the trials. A total of 5 trials comprising of 233 participants met inclusion criteria. Each study described the use of a different rTMS device that delivered different waveforms at different frequencies. All 5 trials were relatively small studies but generally they demonstrated a low-risk of bias. When considering the impact of tinnitus on patients' quality of life, the results of only 1 study demonstrated a statistically significant improvement in THI scores at 4 months follow-up (defined as a "partial improvement" by the study authors (THI reduction of 21% to 80%)) when low-frequency rTMS was compared with a sham control treatment. However, no statistically significant improvement was demonstrated by another 2 studies that considered rTMS at the same frequency. Furthermore, this single positive finding should be taken in the context of the many different variables which were recorded at many different points in time by the study authors. In accordance with the authors' pre-specified subgroup analysis, they extracted the data from 1 study to consider the differential effectiveness between "lower" low-frequency rTMS (1 Hz) and "higher" low-frequency rTMS (10 Hz, 25 Hz). In doing this they were able to demonstrate a statistically significant difference between rTMS employing a frequency of 1 Hz and the sham group when considering tinnitus severity and disability after 4 months follow-up ("partial" improvement). However, no statistically significant difference was demonstrated between 10 Hz and 25 Hz rTMS, and the sham control group, when considering the severity and disability of tinnitus at 4 months follow-up. When considering tinnitus loudness in patients undergoing rTMS these investigators were able to demonstrate a statistically significant reduction in tinnitus loudness when the results of 2 studies were pooled (risk ratio 4.17, 95% confidence interval [CI]: 1.30 to 13.40). However, this finding was based on 2 small trials and consequently the confidence interval was particularly wide. No serious adverse effects were reported in any of the trials. The authors concluded that there is very limited support for the use of low-frequency rTMS for the treatment of patients with tinnitus. When considering the impact of tinnitus on patients' quality of life, support is from a single study with a low-risk of bias based on a single outcome measure at a single
point in time. When considering the impact on tinnitus loudness, this is based on the analysis of pooled data with a large confidence interval. Studies suggested that rTMS is a safe treatment for tinnitus in the short-term, however there were insufficient data to provide any support for the safety of this treatment in the long-term. The authors stated that more prospective, randomized, placebo-controlled, double-blind studies with large sample sizes are needed to confirm the effectiveness of rTMS for tinnitus patients. Furthermore, uniform, validated, tinnitus-specific questionnaires as well as measurement scales should be used in future studies.

Plewnia et al (2012) examined if 4 weeks of bilateral rTMS to the temporal or temporo-parietal cortex is effective and safe in the treatment of chronic tinnitus. In this controlled 3-armed trial, a total 48 patients with chronic tinnitus were treated with 4 weeks (20 sessions) of bilateral continuous theta burst stimulation (cTBS). They were randomized to stimulation above the temporal cortex, the temporo-parietal cortex, or as sham condition behind the mastoid. Patients were masked for the stimulation condition. Tinnitus severity was assessed after 2 and primarily 4 weeks of treatment and at 3 months follow-up with the tinnitus questionnaire and by a tinnitus change score. Audiologic safety was monitored by pure-tone and speech audiometry after 2 and 4 weeks of cTBS. Tinnitus severity was slightly reduced from baseline by a mean (SD) 2.6 (8.2) after sham, 2.4 (8.0) after temporo-parietal, 2.2 (8.3) after temporal treatment of 16 patients each, but there was no significant difference between sham treatments and temporal (CI: -5.4 to +6.7) or temporo-parietal cTBS (CI: -5.9 to +6.3) or real cTBS (CI: -7 to +5.1). Patients' global evaluation of tinnitus change after treatment did not indicate any effects. Audiologic measures were unaffected by treatment. The authors concluded that treating chronic tinnitus for 4 weeks by applying cTBS to the temporal or temporo-parietal cortex of both hemispheres appears to be safe but not more effective than sham stimulation.

In a review on “Repetitive transcranial magnetic stimulation as a treatment for chronic tinnitus”, Theodoroff and Folmer (2013) concluded that “Although optimism for the clinical use of rTMS as
an effective treatment for tinnitus remains high among many researchers, clinicians, and patients, several key questions and procedural issues remain unresolved. Suggestions for improving rTMS research protocols are described and discussed”.

The American Academy of Otolaryngology - Head and Neck Surgery Foundation’s clinical practice guideline on “Tinnitus” (2014) stated that clinicians should not recommend transcranial magnetic stimulation (TMS) for the treatment of patients with persistent, bothersome tinnitus.

**Transcranial Electrical Neuromodulation**

Claes et al (2014) stated there is evidence that neuroplastic changes in both neural pathways are involved in the generation and maintaining of tinnitus. Neuromodulation has been suggested to interfere with these neuroplastic alterations. In this study these researchers compared the effect of 2 upcoming forms of transcranial electrical neuromodulation: (i) alternating current stimulation (tACS) and (ii) random noise stimulation (tRNS), both applied on the auditory cortex. A database with 228 patients with chronic tinnitus who underwent non-invasive neuromodulation was retrospectively analyzed. The results of this study showed that a single session of tRNS induced a significant suppressive effect on tinnitus loudness and distress, in contrast to tACS. Multiple sessions of tRNS augmented the suppressive effect on tinnitus loudness but have no effect on tinnitus distress. The authors concluded that the findings of this preliminary study showed a possibly beneficial effect of tRNS on tinnitus and can be a motivation for future randomized placebo-controlled clinical studies with auditory tRNS for tinnitus. They stated that auditory alpha-modulated tACS does not seem to be contributing to the treatment of tinnitus.

Joos et al (2015) noted that recently tRNS applied over the auditory cortex induced a more pronounced effect on tinnitus loudness than transcranial direct current and alternating current stimulation. These investigators performed tRNS over the temporo-parietal cortex in 154 patients with non-pulsatile tinnitus. A total of 119 patients received low-frequency tRNS
(lf-tRNS), 19 high-frequency tRNS (hf-tRNS) and 16 whole frequency spectrum tRNS (wf-tRNS). The effect was evaluated by using the numeric rating scale loudness and distress pre- and post-stimulation. This study revealed a significant reduction in tinnitus loudness when lf-tRNS and hf-tRNS were applied as well as a reduction in tinnitus-related distress with lf-tRNS. Moreover, these researchers observed a significantly more pronounced reduction in loudness and distress in pure tone (PT) tinnitus compared to narrow band noise (NBN) tinnitus when hf-tRNS was applied, a difference that could not be obtained with lf-tRNS. The authors concluded that based on these results, tRNS might be a promising treatment option for non-pulsatile tinnitus; however, they cannot yet provide a clear mechanistic explanation for the different results obtained with different types of stimulation, i.e., lf-tRNS, hf-tRNS and wf-tRNS, or with different types of tinnitus, i.e., PT and NBN tinnitus.

Transmeatal Laser Irradiation

With transmeatal laser irradiation, a low-level laser irradiation applied through the external acoustic meatus of the affected ear. The treatment takes place once a week for six minutes over a four week period or more.

In a prospective, randomized, double-blinded, controlled study, Nakashima et al (2002) assessed the effectiveness of 60-mW laser irradiation in the treatment of tinnitus. A total of 68 ears in 45 patients with disabling unilateral or bilateral tinnitus were included in this trial. The active or placebo laser treatment was administered transmeatally once a week for 6 minutes. Laser irradiation was performed four times during a 4-week period. A questionnaire was administered to evaluate the loudness, duration, quality, and annoyance of tinnitus before and after irradiation. The loudness and pitch match for tinnitus were obtained, and distortion product otoacoustic emissions were also examined. No significant difference was observed between the active and placebo laser groups with regard to outcome of loudness, duration, quality, and annoyance of tinnitus. In 1 patient who received active laser treatment, acute hearing deterioration occurred after the third irradiation. These
investigators concluded that transmeatal low-power laser irradiation with 60 mW is ineffective for the treatment of tinnitus.

Tauber et al (2003) presented their findings of a feasibility study on the use of a laser application system in patients with chronic cochlear tinnitus and sensorineural hearing loss (n = 35). The laser TCL-system, consisting of 4 diode lasers (lambda = 635 to 830 nm) was developed on the basis of dosimetric data from a former light-dosimetric study. The chronic symptoms persisted after standard therapeutic procedures for at least 6 months, while retrocochlear or middle-ear pathologies have been ruled out. The patients were randomised and received 5 single-diode laser treatments (lambda = 635 nm, 7.8 mW cw, n = 17 and lambda = 830 nm, 20 mW cw, n = 18) with a space irradiation of 4 J/cm^2 site of maximal cochlear injury. For evaluation of laser-induced effects complete otolaryngological examinations with audiometry, tinnitus masking and matching, and a tinnitus-self-assessment were performed before, during, and after the laser-irradiation. The first clinical use of the TCL-system has been well-tolerated without side-effects and produced no observable damage to the external, middle or inner ear. Changes of tinnitus loudness and tinnitus matching have been described. After a follow-up period of 6 months, tinnitus loudness was attenuated in 13 of 35 irradiated patients, while 2 of 35 patients reported their tinnitus as totally absent. Hearing threshold levels and middle ear function remained unchanged. These researchers stated that further investigations by large double-blind placebo-controlled studies are mandatory for clinical evaluation of the presented TCL-system and its therapeutic effectiveness in acute and chronic cochlear dysfunction.

A systematic review of randomized controlled clinical trials of low-powered laser treatments for tinnitus found no statistically significant difference between laser and placebo (Meehan et al, 2004).

Gungor et al (2008) assessed the effectiveness of laser irradiation in the treatment of chronic tinnitus. This study included 66 ears in 45 patients with chronic unilateral or bilateral tinnitus. A 5 mW laser with a wavelength of 650 nm, or placebo laser, was applied
transmeatally for 15 minutes, once-daily for a week. A questionnaire was administered which asked patients to score their symptoms on a 5-point scale, before and 2 weeks after laser irradiation. A decrease of 1 scale point, regarding the loudness, duration and degree of annoyance of tinnitus, was deemed as improvement. The loudness, duration and degree of annoyance of tinnitus were improved, respectively, in up to 48.8, 57.7 and 55.5 % of the patients in the active laser group. No significant improvement was observed in the placebo laser group. The authors concluded that transmeatal, low power (5 mW) laser irradiation was found to be useful for the treatment of chronic tinnitus. The findings of this study need to be validated by larger studies with longer follow-up.

Noble (2008) stated that the various forms of treatment for tinnitus that have been tested in properly controlled trials can be classified as pharmacological, acoustic-physical, and psychological. In clinical trials, no pharmacological agent has been shown to have lasting effect on the presence or severity of tinnitus, although there are promising signs in an animal model. Acoustic devices do not seem to influence tinnitus, although appropriately fitted hearing aids may slightly reduce its prominence. Of physical treatments, cortical implantation may hold some promise of being effective for tinnitus suppression in selected cases. There was no mention on the use of laser.

In a prospective, randomized double-blind study, Teggi et al (2009) examined the effectiveness of low-level laser therapy on 60 outpatients with tinnitus presenting sensori-neural hearing loss in the affected ear. They were randomly divided into two groups: (i) one group received active laser therapy 20 mins a day for 3 months with a 650-nm, 5-mW soft laser (group L), and (ii) the second group received a dummy device which duplicated all aspects of active laser therapy except for the activation of the laser beam (group C). One subject in both groups dropped out due to an increase in tinnitus loudness. Two more patients in each group ceased to comply with the protocol due to familiar problems. The THI was considered the main outcome measure; no statistical difference was detected between the two groups in the THI total score (p = 0.97), and its functional (p = 0.89),
emotional (p = 0.89) and catastrophic (p = 0.89) sub-scales. Moreover, a visual analog scale for self-perceived loudness of the tinnitus showed no difference between the groups (p = 0.69).

Regarding psycho-acoustic parameters, the minimum masking level showed no difference (p = 0.42), while loudness expressed in sensation level exhibited lower values in group L (p = 0.0127). Group L subjects also presented a decreased rate of hyperacusis (p = 0.02). No changes were detected in the audiometric threshold in both groups. The authors concluded that soft laser therapy demonstrated no efficacy as a therapeutic measure for tinnitus.

In a prospective, double-blinded, randomized, placebo-controlled trial, Ngao et al (2014) examined the effectiveness of transmeatal low-power laser stimulation (TLLS) in treating tinnitus. Patients with persistent subjective tinnitus as their main symptom were recruited into the study from the out-patient clinics. The recruited patients were randomized into the experimental group or TLLS+ group (patients in this group were prescribed to use TLLS at 5 mW at 650 nM wavelength for 20 mins daily and oral betahistine 24 mg twice-daily for a total of 10 weeks) and the control group or TLLS- group (patients in this group were prescribed with a placebo device to use and oral betahistine 24 mg twice-daily for 10 weeks). All patients were required to answer 2 sets of questionnaires: (i) the THI and (ii) visual analogue scale (VAS) symptoms rating scales, before starting the treatment and at the end of the 10-week treatment period. The total score of the THI questionnaire was further graded into 5 grades, grade 1 being mild and grade 5 being catastrophic.

Wilcoxon-signed ranks test and Mann-Whitney test were used to compare and analyze the THI and VAS scores before and after treatment for each group. Changes with p value of < 0.05 were considered as statistically significant. Chi-square test was used to analyze the change of parameters in categorical forms (to compare between TLLS+ and TLLS-). Changes with p value of < 1.5 were considered as statistically significant. A total of 43 patients successfully and diligently completed their treatment. It was noted that using any condition of the device, TLLS+ or TLLS-, patient's tinnitus symptoms improved in terms of THI scores (TLLS+, p value = 0.038; TLLS-, p value = 0.001) or VAS scores with
a change of at least one grade (TLLS+, p value = 0.007; TLLS-, p value = 0.002) at p value <0.05 significant level. In contrast when TLLS+ group was compared with TLLS- group, no statistically significant result was obtained. In term of VAS scores, there seemed to be no statistically significant improvement in patients' annoyance, sleep disruption, depression, concentration and tinnitus loudness and pitch heard between the two groups. They stated that transmeatal low-power laser stimulation did not demonstrate significant efficacy as a therapeutic measure in treating tinnitus.

In a prospective, double-blind, placebo-controlled study, Dehkordi et al (2015) examined the effect of low-dose laser therapy on chronic cochlear tinnitus. The study population was made up of 66 patients -- 33 who received active laser treatment (case group) and 33 who received inactive dummy treatment (control group). Patients in the laser group received 5 mV with a wavelength of 650 nm for 20 minutes a day, 5 days a week, for 4 weeks. The controls followed the same schedule, but they were "treated" with an inactive device. The degree of tinnitus was evaluated before and after treatment in each group in 3 ways: (i) the TSI, (ii) a subjective 10-point self-assessment scale for tinnitus loudness, and (iii) the Tinnitus Evaluation Test (TET). At study's end, these researchers found no statistically significant differences between the case and control groups in the number of patients who experienced a reduction in TSI values (p = 0.589) or a reduction in subjective self-assessment scores (p = 0.475). In addition, these investigators did not find any significant reductions in the loudness (p = 0.665) and frequency (p = 0.396) of tinnitus as determined by the TET. The authors concluded that 5-mV laser therapy with a wavelength of 650 nm is no better than placebo for improving hearing thresholds overall or for treating tinnitus with regard to age, sex, environmental noise level, and the duration of tinnitus.

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy has been proposed as a treatment for tinnitus that often accompanies sensorineural hearing loss. A patient is placed in a specially designed chamber as the pressure
in the chamber is increased and 100% oxygen is breathed.

In a Cochrane review on the use of hyperbaric oxygen therapy (HBOT) for the treatment of idiopathic sudden sensorineural hearing loss (ISSHL) and tinnitus, Bennett et al (2005) stated that HBOT improved hearing, but the clinical significance of the level of improvement is unclear. Routine application of HBOT to patients with ISSHL is not justified by this review. These investigators noted that more research is needed.

A systematic evidence review of tinnitus treatments by BMJ Clinical Evidence concluded that hyperbaric oxygen is of "unknown effectiveness" (Savage et al 2009).

**Competitive kinesthetic interaction therapy (KKIT)**

Competitive kinesthetic interaction therapy (KKIT) is adapted physiotherapy using expressive movements of body language. Different groups of muscles in the hand, arm, leg, foot and body, from the feet up to the face, are activated, which purportedly guides the patient into a situation of peaceful resting, reduction of tension and finally into relaxation. This scheme was adapted from a rehabilitation program for treating pain. There is a lack of reliable evidence for KKIT for treatment of tinnitus.

**Sequential Phase Shift Sound Cancellation Treatment**

Sequential phase shift sound cancellation is a novel treatment for predominant-tone tinnitus. It entails the use of a phase-shift sound cancellation protocol in which a patient’s tinnitus is first identified as to frequency and amplitude. Then, a signal, 6 degrees out-of-phase with the identified tinnitus signal, is fed sequentially (6 degrees, 12 degrees, etc.) into the patient’s headphones for 30 seconds each for 30 minutes, or until 360 degrees is achieved. Available evidence on the effectiveness of this approach has mainly been in abstract forms (Noik, 2005; Choy and Kaminow, 2005; Lipman et al, 2006). The only published full-length paper on this subject is by Lipman and Lipman (2007) who assessed phase shift treatment for predominant tone tinnitus in a prospective, single-blinded, cross-over study. A total
of 61 patients participated in 2 weeks of control and 2 weeks of phase shift treatment. Outcome measures included frequency and intensity matching, pre- and post-treatment tinnitus handicap inventory (THI) scores, and patient diaries. Initial volume comparisons showed a strong relationship between treatment and decrease in tinnitus intensity, with 57% of patients achieving successful treatment. Thirty-seven percent decreased by one THI grade, 5% by two. Utilizing patient diaries, 42% of patients reported periods of complete residual inhibition (CRI) ranging from 1 hour to 7 days (average of 2 days). No periods of CRI were reported in control weeks. The authors concluded that phase shift treatment significantly benefited the majority of patients. These findings suggested that this device may be a valuable tool. They noted that further long-term studies with home therapy are needed.

In a double-blind, cross-over, randomized-controlled trial, Heijneman et al (2012) compared the effectiveness of the treatment of tinnitus with a phase-shifting pure tone to that of the same tone treatment without phase shifting. A total of 22 patients with predominantly tonal tinnitus underwent both intervention and control treatments. Each treatment consisted of three 30-minute sessions in 1 week. The control treatment was identical to the intervention treatment, except that the stimulus was a pure tone without phase shifting. Questionnaires, tinnitus loudness match, and annoyance and loudness ratings were used to measure treatment effects. Pure-tone treatment and phase-shift treatment had no significant effect on tinnitus according to questionnaires (Tinnitus Handicap Index, Tinnitus Reaction Questionnaire, Hospital Anxiety and Depression Scale, and Maastricht Questionnaire), audiological matching procedures, and loudness and annoyance ratings of tinnitus. Furthermore, phase-shift treatment showed no additional significant improvement in comparison with pure-tone treatment. Changes in questionnaire scores due to pure-tone and the phase-shift treatment were correlated. The authors concluded that on average across the group, both treatments failed to demonstrate a significant effect. Both treatments were beneficial for some patients. However, a positive effect was not demonstrated that could be attributed to the periodic shifting of
the phase of the stimulus tone.

Thus, there is currently insufficient evidence to support the use of sequential phase shift sound cancellation treatment for tinnitus.

**Neuromonics Tinnitus Treatment**

The Neuromonics Tinnitus Treatment (NTT) combines the use of acoustic stimulation with a structured program of counseling and support by a clinician specifically trained in tinnitus rehabilitation. The acoustic component has been designed to provide stimulation to auditory pathways deprived by hearing loss, engage with the limbic system, and allow intermittent, momentary tinnitus perception within a pleasant and relaxing stimulus, thereby facilitating desensitization to the tinnitus signal. Davis and colleagues (2007) examined the effectiveness of NTT, when enhanced with various modifications since previously reported trials and tested the relative clinical effectiveness of two variations of the approach. In the first, intermittent tinnitus perception was facilitated throughout treatment via the use of a stimulus in which intensity peaks allowed the subjects' tinnitus perception to be completely covered up, whereas in the intensity troughs their tinnitus was briefly discernible. In the second, subjects experienced little tinnitus perception while listening to the treatment for the first 2 months, then experienced intermittent perception. A total of 35 subjects with a predominantly moderate-to-severe level of tinnitus-related distress before treatment were randomly allocated into one of two treatment groups, corresponding to the 2 stage-based variations of the NTT. Subjects were provided with a high-fidelity personal sound player with earphones and an acoustic stimulus that had been spectrally modified according to their individual audiometric profile. They were instructed to use the acoustic stimulus for at least 2 hours per day, particularly at those times when their tinnitus was usually disturbing. Each group had equal amounts of clinician time for education, monitoring, and support. At 2, 4, 6, and 12 months after commencing treatment, both groups displayed clinically and statistically significant improvements in tinnitus distress, awareness, and minimum masking levels as well as loudness discomfort levels.
Improvements increased with time over the first 6 months of therapy, at which time 91% of all subjects across the 2 groups reported an improvement in tinnitus disturbance (as measured by the Tinnitus Reaction Questionnaire) of at least 40%, with a mean improvement of 65%. Furthermore, 80% of subjects at 6 months reported a level of tinnitus disturbance that was no longer clinically significant. There was some indication of a more consistent benefit over 12 months for the group that was provided initially with a high level of tinnitus interaction; however, inter-group differences were not statistically significant. A relation between reported treatment usage (hours per day) and clinical outcomes was observed, suggesting that a "dosage effect" may apply with the stimulus provided. The authors concluded that this study found that the NNT provides rapid and profound improvements to the severity of tinnitus symptoms and their effect on the subject's quality of life. This was a consistent effect, provided by a treatment that subjects reported as being pleasant to use. Both of the stage-based variations of the treatment that were tested in this study were shown to be successful in achieving these outcomes.

Davis and associates (2008) conducted another clinical study on the effectiveness of NTT. This treatment approach is provided as part of a structured rehabilitation program. In this study, patients who received the customized stimulus (NTT group) reported significantly greater and more consistent alleviation of tinnitus symptoms than did patients who participated in a counseling and support program with and without delivery of a broad-band noise stimulus (Noise + Counseling group and Counseling-Only group, respectively). After 6 months of treatment, 86% of the NTT patients met the minimum criterion for clinical success, defined as an alleviation of tinnitus disturbance of at least 40% (as judged by the Tinnitus Reaction Questionnaire score). By contrast, only 47% and 23% of the Noise + Counseling and Counseling-Only groups, respectively, reported a successful result according to this criterion. Mean improvements in tinnitus disturbance scores in the NNT, Noise+Counseling, and Counseling-Only groups were 66%, 22%, and 15%, respectively. The differences between the NTT group and the control groups were statistically significant. Significant differences were observed in other clinical outcomes.
Patient reports of user acceptability were more consistently positive in the NTT group. It is unclear whether they were overlapping of patients in these two studies.

The major drawbacks of these two studies were (i) small numbers of subjects, and (ii) short-term follow-up (not exceeding 12 months). Moreover, it is unclear whether they were overlapping of patients in these two studies. These findings need to be validated by further investigation.

Auditory Perceptual Training

Hoare et al (2010) stated that auditory perceptual training affects neural plasticity and so represents a potential strategy for tinnitus management. These investigators assessed the effects of auditory perceptual training on tinnitus perception and/or its intrusiveness via a systematic review of published literature. An electronic database search using the keywords 'tinnitus and learning' or "tinnitus and training" was conducted, updated by a hand search. The 10 studies identified were reviewed independently by 2 reviewers, data were extracted, study quality was assessed according to a number of specific criteria and the information was synthesised using a narrative approach. Nine out of the 10 studies reported some significant change in either self-reported or psychoacoustic outcome measures after auditory training. However, all studies were quality rated as providing low or moderate levels of evidence for an effect. The authors identified a need for appropriately randomized and controlled studies that will generate high-quality unbiased and generalisable evidence to ascertain if auditory perceptual training has a clinically relevant effect on tinnitus.

Intra-Tympanic Administration of Corticosteroids

Dodson and Sismanis (2004) reviewed the evidence regarding intra-tympanic treatment for tinnitus and provided the following comments: (i) lidocaine, although effective in decreasing tinnitus, has been largely abandoned because of its severe side-effect profile and need for inpatient administration, (ii) corticosteroids have been associated with few if any side effects, (iii) the good
results reported in the literature with intra-tympanic steroids for treating tinnitus of various causes should be viewed with caution, because most are retrospective and uncontrolled studies, (iv) some Meniere’s disease patients with tinnitus may experience tinnitus improvement following intra-tympanic steroids. This treatment may be considered in such patients, especially for those with good hearing, (v) gentamicin is effective in eliminating or reducing tinnitus in a significant number of patients with Meniere’s disease and may be considered especially for those with non-serviceable hearing, (vi) further prospective, randomized, controlled studies to evaluate the effect of intra-tympanic perfusion for the treatment of tinnitus are warranted.

In a randomized, prospective, single-blind study, Araújo and colleagues (2005) tested the effectiveness of intra-tympanic dexamethasone injections as a treatment for severe disabling cochlear tinnitus. A total of 36 patients with severe disabling tinnitus predominantly of cochlear origin were randomly assigned to receive intra-tympanic injections of a dexamethasone solution or isotonic saline solution. Under topical anesthesia and after randomization, 36 patients received 0.5 ml intra-tympanic injections once per week for 4 weeks of either a 4 mg/ml dexamethasone solution or saline solution. Five patients were excluded from analysis because they did not complete the treatment or did not return for follow-up. Main outcome measure was improvement of tinnitus measured with a VAS. The 2 groups were similar in age, sex, tinnitus laterality, measurement of tinnitus intensity on the VAS, and main otologic diagnosis. These researchers considered a 2-point improvement on the VAS to be significant. Twenty-nine percent of the ears in the saline group and 33 % of the ears in the dexamethasone group showed significant improvement immediately after completion of treatment. These measurements were not significantly different from each other. Follow-up varied from 13 to 31 months, and the patients with improved tinnitus returned to the initial measurements over time. The authors concluded that there was no advantage in intra-tympanic injections of dexamethasone over saline solution in the treatment of severe, disabling tinnitus. Both solutions produced a placebo-like improvement.
In a prospective, randomized, placebo-controlled, single-blinded study, Topak et al (2009) examined if intra-tympanically injected methylprednisolone is effective in treating subjective tinnitus refractory to medical treatment. A total of 70 adult patients with subjective tinnitus of cochlear origin were randomly assigned to receive intra-tympanic injection of either methylprednisolone or saline solution. The treatment protocol comprised 3 intra-tympanic injections, 1 per week for 3 weeks. Improvement in tinnitus severity was measured by a self-rated tinnitus loudness scale and by the tinnitus severity index, at baseline and 2 weeks after the last injection. Data for 59 patients were available for analysis. There was no significant difference between the 2 treatment groups regarding age, sex, pure tone average, pre-treatment tinnitus intensity, tinnitus laterality or tinnitus duration. There was a significant post-treatment improvement in self-rated tinnitus loudness scale results in both groups. No significant post-treatment changes in the tinnitus severity index individual and total scores were observed in either group. The most frequently encountered side effects were pain during injection, vertigo, a burning sensation around the ear and in the throat, and a bitter taste. A burning sensation and bitter taste were observed more often in the methylprednisolone group compared with the placebo group. The authors concluded that these findings indicated that intra-tympanic methylprednisolone has no benefit, compared with placebo, for the treatment of subjective tinnitus of cochlear origin refractory to medical treatment.

In a Cochrane review, Phillips and Westerberg (2011) assessed the effectiveness of intra-tympanic steroids on the frequency and severity of attacks of vertigo, on chronic symptoms such as tinnitus, imbalance and hearing loss, and on the progression of these symptoms in patients with definite Meniere’s disease or syndrome, as defined by the AAO-HNS Committee. These investigators searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ISTRP and additional sources for published and unpublished trials. The date of the most recent search was January 13, 2011.
Randomized controlled trials of intra-tympanic dexamethasone versus placebo in patients with Meniere's disease were selected for this analysis. Two authors independently assessed trial risk of bias and extracted data. They contacted study authors for further information where possible. A single trial containing 22 patients, with a low-risk of bias was included. This trial found that after 24 months, compared with placebo, the use of intra-tympanic dexamethasone demonstrated a statistically significant improvement in vertigo as defined by a respective improvement in functional level (90% versus 42%), class (82% versus 57%), change in Dizziness Handicap Inventory scores (60.4 versus 41.3) and mean vertigo subjective improvement (90% versus 57%). The treatment regime described by the authors involved daily injections of dexamethasone solution 4 mg/ml for 5 consecutive days. These results were clinically significant. No complications were reported. The authors concluded that these findings of a single trial provide limited evidence to support the effectiveness of intra-tympanic steroids in patients with Meniere's disease. This trial demonstrated a statistically and clinically significant improvement of the frequency and severity of vertigo measured 24 months after the treatment was administered. It is important to note that there were a few aspects of the study that the authors were unable to clarify with the study authors.

The American Academy of Otolaryngology - Head and Neck Surgery Foundation’s clinical practice guideline on “Tinnitus” (2014) stated that clinicians should not routinely recommend intra-tympanic medications for a primary indication of treating persistent, bothersome tinnitus.

In a prospective, randomized, placebo-controlled, double-blinded, multi-center study, Lee and colleagues (2017) examined the effectiveness of intra-tympanic dexamethasone injection (ITDI) in acute tinnitus of presumed cochlear origin. Between August 2013 and December 2015, a total of 54 patients with unilateral tinnitus were enrolled at 4 different centers. Patients were assigned either to an ITDI (n = 27) or an intra-tympanic normal saline injection (ITNI; n = 27) group through block randomization. Intra-tympanic injections were administered 4 times over 2 weeks. At 4 weeks after initial injection, these
researchers analyzed the improvement rates of tinnitus using the THI and VAS for loudness, awareness, and annoyance. They defined improvement as the reduction of more than 7 points or of more than 20% in the final THI score compared to the initial THI score. The initial mean hearing thresholds and VAS and THI scores of the 2 groups did not differ significantly. At 4 weeks after initial injection, the mean VAS and THI scores of both groups had significantly reduced. However, the improvement rate did not differ significantly between the groups (ITDI, 51.9%; ITNI, 59.3%). The authors concluded that these findings indicated that ITDI might not be more effective than ITNI for the treatment of acute unilateral tinnitus; thus, ITDI should not be considered as the main treatment for patients presenting with acute tinnitus as the primary symptom.

Deep Brain Stimulation

In a case series with chart review, Shi et al (2009) reported deep brain stimulation (DBS) effects in patients with tinnitus. A total of 7 patients implanted with deep brain stimulation (DBS) systems for movement disorders who also reported having tinnitus were interviewed about their tinnitus conditions. Four were available for testing in a specialized tinnitus clinic with their DBS systems turned off or on. Testing included matching of self-rated and psychoacoustically measured tinnitus loudness to measure the impact of DBS on tinnitus; 3 of the 7 patients reported reduced tinnitus loudness when DBS was turned on. Of the 4 patients tested in the clinic, results indicated that DBS of the ventralis intermedius nucleus of the thalamus caused decreases in tinnitus loudness in 2 patients with relatively prolonged residual inhibition. The authors concluded that these results suggested that DBS of non-auditory thalamus structures may provide tinnitus relief for some patients. This preliminary findings needs to be validated by well-designed studies.

Cheung and Larson (2010) reported that that application of DBS therapy to a locus of caudate neurons (area LC) can decrease or increase tinnitus loudness perception. The DBS lead traversed through or was adjacent to area LC in 6 Parkinson's disease and essential tremor subjects with concomitant tinnitus who
underwent implantation of the subthalamic or ventral intermediate nucleus. In 5 subjects where the DBS lead tip traversed area LC, tinnitus loudness in both ears was suppressed to a nadir of level 2 or lower on a 0 to 10 rating scale. In 1 subject where the DBS lead was outside area LC, tinnitus was not modulated. In 3 subjects with pre-operative and post-operative audiograms, hearing thresholds were unchanged by area LC stimulation. Neuromodulation of area LC may be interrupting perceptual integration of phantom sensations generated in the central auditory system. The authors stated that this new, basal ganglia-based approach to tinnitus modulation warrants further investigation and may be ultimately refined to treat patients with refractory symptoms.

**Vagal Nerve Stimulation**

Schnupp (2011) stated that recent observations linking the vagus nerve to plasticity in the central nervous system could pave the way to new treatments for tinnitus, one of the most common and intractable disorders of the auditory system. Furthermore, an UpToDate review on "Treatments for tinnitus" (Dinces, 2012) does not mention the use of vagal nerve stimulation as a therapeutic option.

**Cochlear Implant**

A cochlear implant is a surgically implanted electronic device that can provide improved speech and hearing communication abilities for people who have severe to profound hearing loss in both ears. Purportedly, the device may help tinnitus by masking with ambient sound or by suppression when electrical stimulation is sent through the auditory nerve.

Tao and Chen (2012) evaluated the effects of cochlear implantation (CI) on ipsilateral tinnitus. With standard assessment table and standard testing program, 48 post-lingual hearing-impaired adults aged 18 to 62 years (mean age at implantation: 35.0) were operated at 5 clinical centers from June 2009 to March 2010. There were 23 males (47.9 %) and 25 females (52.1 %). These researchers evaluated the pre- and
post-implantation degrees of tinnitus, performed free sound field audiometry and scored speech perception during different periods. Secondary analyses were conducted to examine the correlation between the effects of implantation on tinnitus and hearing or speech perception rehabilitation. Before implantation, there were 16 cases with ipsilateral tinnitus and 32 cases without tinnitus. After implantation, among 16 cases, the outcomes were recovery (n = 6), tinnitus suppression (n = 1) and no change in symptoms (n = 9). The total effective rate was 43.8 %. Among another 32 cases without pre-operative tinnitus, 2 cases developed tinnitus after implantation. The effects of CI on tinnitus were negatively correlated with the course of tinnitus. There was no more correlation with other factors. The authors concluded that CIs have significant therapeutic effects on tinnitus in 43.8 % of implant users. Better efficacies are correlated with a shorter course of tinnitus. However, they stated that tinnitus suppression using electrical stimulation via CI for deafness needs to be further evaluated.

Tavora-Vieira et al (2013) examined the effectiveness of CI in patients with unilateral deafness with and without tinnitus. A total of 9 post-lingually deafened subjects with unilateral hearing loss, with and without tinnitus ipsilaterally, and functional hearing in the contralateral ear were implanted with a standard electrode. Speech perception in noise was tested using the Bamford-Kowal-Bench presented at 65 dB SPL. The Speech, Spatial, and Qualities (SSQ) of Hearing Scale was used to evaluate the subjective perception of hearing outcomes, and the Tinnitus Reaction Questionnaire assessed the effect on tinnitus. All patients were implanted with the Med-El Flex soft electrode, Innsbruck, Austria. They were regularly wearing the speech processor and found it beneficial in improving their ability to hear, particularly in noise. Decrease of tinnitus perception and an improvement of sound localization sounds were also reported by these patients. The authors concluded that in this case series, CI was successful for all 9 patients, with improvement of speech recognition in noise, self-perceived improvement of hearing, and for tinnitus control. Moreover, they stated that several factors such as deafness duration, age of deafness onset, the presence of residual hearing, patient motivation, and the rehabilitation
intensity need to be further investigated in order to understand their impact on performance after implantation. (It is unclear how many of the 9 patients had tinnitus)

In a review on “Cochlear implantation for single-sided deafness: The outcomes. An evidence-based approach”, Vlastarakos et al (2014) reviewed the current evidence on the effectiveness of CI as a treatment modality for SSD, and/or unilateral tinnitus. Systematic literature review in Medline and other database sources was conducted along with critical analysis of pooled data. The study selection includes prospective and retrospective comparative studies, case series and case reports. The total number of analyzed studies was 17. A total of 108 patients with SSD have been implanted; 66 patients due to problems associated with SSD, and 42 primarily because of debilitating tinnitus. Cochlear implantation in SSD leads to improved sound localization performance and speech perception in noise from the ipsilateral side with an angle of coverage up to (but not including) 90° to the front, when noise is present in the contralateral quartile (Strength of recommendation B). Speech and spatial hearing also subjectively improve following the insertion of a CI (Strength of recommendation B); this was not the case regarding the quality of hearing. Tinnitus improvement was also reported following implant placement (Strength of recommendation B); however, patients need to be advised that the suppression is mainly successful when the implant is activated. The overall quality of the available evidence supports a wider use of CI in SSD following appropriate selection and counseling (overall strength of recommendation B). It remains to be seen if the long-term follow-up of large number of patients in well conducted high quality studies will confirm the above mentioned results.

Blasco and Redleaf (2014) noted that in recent years, otologists have begun to place cochlear implants into non-functioning ears after sudden unilateral hearing loss. Patients in these trials demonstrated differing degrees of hearing loss in the un-implanted ear. Few studies have examined the role of implantation in patients with normal hearing in the un-implanted ear. These researchers reviewed the available literature to understand if this practice benefits these patients in terms of
Tinnitus, sound localization, and speech understanding. Medline, Embase, and Cochrane databases were searched for publications from database inception to June 1, 2013, without restriction of language. A search of multiple medical databases was performed to identify articles reporting cases series of CI for unilateral hearing loss. Subjects were included for analysis only if the course of hearing loss was acute and rapidly progressive, if the loss was severe to profound, and if the contralateral ear had normal hearing. A total of 9 appropriate articles were identified, in which 36 patients met the inclusion criteria. Three meta-analyses were performed: of tinnitus (22 patients); of the lowest signal-to-noise ratio, which still allowed 50 % sentence understanding (16 patients); and of sentence understanding at a fixed signal-to-noise ratio (12 patients). They found that measures of tinnitus reduction and decreased signal-to-noise ratios to still allow 50 % speech discrimination were statistically significantly reduced. Systematic review of subjective changes of tinnitus in 27 patients, speech understanding in 16 patients, and sound localization in 16 patients found 96 %, 100 %, and 87 % improvements, respectively. The authors concluded that CI in unilateral sudden hearing loss with a normal functioning contralateral ear might prove to be an effective therapy. Tinnitus is reduced as is the signal-to-noise ratio, which still allows 50 % speech discrimination. All patients felt that they localized sound better, and most felt that they understood speech better. They stated that further studies should be conducted to compare the success of hearing rehabilitation of CI and traditional modalities such as contralateral routing of signal and bone-anchored hearing aids.

Furthermore, an August 2013 Agency for Healthcare Research and Quality’s comparative effectiveness review on “Evaluation and treatment of tinnitus” (Pichora-Fuller et al, 2013) indicated that the use of cochlear implants for tinnitus and single-sided deafness is a very recent off-label indication, and indicated insufficient evidence for the use of this and other sound therapies for tinnitus.

**Acupuncture**
Acupuncture is the technique of inserting and manipulating very fine needles into the skin to stimulate specific anatomic points in the body for therapeutic purposes.

Liu and colleagues (2016) performed a systematic review and meta-analysis of all available randomized controlled trials (RCTs) using acupuncture to treat tinnitus. A total of 5 electronic databases, in both English and Chinese, were searched. All studies in this review and meta-analysis included parallel RCTs of tinnitus patients, which compared subjects receiving acupuncture (or its other forms, such as electro-acupuncture) to subjects receiving no treatment, sham treatment, drugs or basic medical therapy. Data from the articles were validated and extracted using a predefined data extraction form. Nearly all of Chinese studies reported positive results, while most of English studies reported negative results. Analysis of the combined data found that the acupuncture treatments appeared to provide some advantages over conventional therapies for tinnitus. It had difference in acupuncture points and sessions between Chinese studies and English studies. Methodological flaws were also found in many of the RCTs, especially in Chinese studies. The authors concluded that the findings of this review suggested that acupuncture therapy may offer subjective benefit to some tinnitus patients. They noted that acupuncture points and sessions used in Chinese studies may be more appropriate, however, these studies have many methodological flaws and risk bias, which prevented them making a definitive conclusion.

He et al (2016) examined the effect of electro-acupuncture for alleviating the symptoms of subjective tinnitus. These researchers performed literature searches in 3 English and 4 Chinese databases (PubMed, EMBASE, Cochrane Library, CNKI, Wanfang Chinese Digital Periodical and Conference Database, VIP, and ChiCTR). The date of the most recent search was June 1, 2014. Randomized controlled trials or quasi-RCTs were included. The titles, abstracts, and keywords of all records were reviewed by 2 authors independently; the data were collected and extracted by 3 authors. The risk of bias in the trials was assessed in accordance with the Cochrane Handbook, version 5.1.0. (http://www.handbook.cochrane.org). A total of 89 studies were
retrieved; after discarding 84 articles, 5 studies with 322 subjects were identified. Assessment of the methodological quality of the studies identified weaknesses in all 5 studies. All studies were judged as having a high risk of selection and performance bias. The attrition bias was high in 4 studies. Incompleteness bias was low in all studies. Reporting bias was unclear in all studies.

Because of the limited number of trials included and the various types of interventions and outcomes, these researchers were unable to conduct pooled analyses. The authors concluded that due to the poor methodological quality of the primary studies and the small sample sizes, no convincing evidence that electro-acupuncture is beneficial for treating tinnitus could be found.

There is an urgent need for more high-quality trials with large sample sizes for the investigation of electro-acupuncture treatment for tinnitus.

In a RCT, Laureano and associates (2016) examined the effect of acupuncture on brain perfusion using ethyl cysteinate dimer single-photon emission computed tomography (99mTc-ECD SPECT) in patients with tinnitus. This randomized, single-blind, sham-control study examined patients (18 to 60 years old) with normal hearing and CIT. A total of 57 subjects were randomly assigned to true (n = 30) or sham (n = 27) acupuncture (ACP); 99mTc-ECD SPECT examinations were performed before and after 12 twice-weekly ACP sessions. Secondary outcomes included changes in the THI, VAS, Hamilton Anxiety Scale (HAS) and Beck Depression Inventory (BDI). Imaging data were analyzed using Statistical Parametric Mapping (SPM8) software. Regression models were used to examine secondary outcomes via 2 paradigms: intention-to-treat (ITT; where multiple imputations were conducted because of study attrition) and complete cases. No between-group brain perfusion differences were observed. However, a significant improvement in THI scores was observed at the end of true ACP treatment for all domains (all p values < 0.01) except the catastrophic scale. The authors concluded that ACP might reduce the effects of tinnitus on daily life; however, additional studies should be conducted to verify the effects of ACP on the neural architecture and brain function of tinnitus patients.
The American Academy of Otolaryngology - Head and Neck Surgery Foundation’s clinical practice guideline on “Tinnitus” (2014) stated that no recommendation can be made regarding the effect of acupuncture in patients with persistent bothersome tinnitus.

**Lidocaine**

Kallio et al (2008) stated that intravenous (IV) lidocaine has been used to ameliorate tinnitus, but in general its effect has been limited. The longer acting local anesthetic ropivacaine may be more effective. These investigators compared ropivacaine with lidocaine for the treatment of tinnitus. A total of 19 randomized, double-blind, cross-over study patients suffering from chronic tinnitus were given a 30-min IV infusion of ropivacaine or lidocaine 1.5 mg/kg at an interval of 2 to 3 months. The intensity of tinnitus was evaluated on THI scale and on the VAS. Plasma ropivacaine and lidocaine concentrations were determined. In both treatments, the infusion decreased the VAS score significantly. At the end of infusion, a greater than or equal to 50 % reduction in VAS score was observed in 5 patients by ropivacaine and in 1 patient by lidocaine, but this effect was sustained for 1 hour only in 3 patients. However, the THI scores did not differ significantly within or between treatments. On the post-infusion day, 3 patients after ropivacaine and 5 after lidocaine treatment had greater than or equal to 30 % improvement in the THI score. Four weeks later, 1 patient after ropivacaine and 2 after lidocaine had a greater than or equal to 30 % reduction in the THI score. One patient developed seizures soon after ropivacaine infusion from which he recovered uneventfully. His plasma concentration of ropivacaine was 1,817 ng/ml. The highest individual ropivacaine and lidocaine concentrations were 3,483 and 1,680 ng/ml, respectively. The authors concluded that temporary clinically significant alleviation of tinnitus was observed only in a few individuals after both IV ropivacaine and lidocaine.

Hahn et al (2008) performed a retrospective study of patients suffering from chronic unilateral or bilateral tinnitus that was previously ineffectively treated by oral drugs [betahistine...
(Betaserc), extract of Ginkgo biloba (EGb 761), tanakan (Tebokan), and cinnarizine-dimenhydrinate (Arlevert), singly or in combination. These researchers divided 150 tinnitus patients (80 men, 70 women) into 7 treatment groups. Treatments consisted of application of intravenous pentoxifylline, lidocaine, or vinpocetine (Cavinton) and combination of these agents with physiotherapy and soft laser. Mean duration (+/- standard deviation) of tinnitus in these patients was 7.4 +/- 6.0 years; their mean age was 55.6 +/- 12.5 years. The aim of the study was to compare treatment modalities and define their effectiveness for tinnitus relief. The most effective treatment was defined as a combination of Cavinton and physiotherapy. The authors found that pure lidocaine infusion therapy was ineffective. None of the treatment modalities had an objective correlate of improvement, though improvement was reported by a VAS.

Also, an UpToDate review on “Treatment of tinnitus” (Dinces, 2014) states that “Historically, lidocaine, either intratympanic or intravenous, has been found in observational studies to be modestly efficacious in reducing symptoms of tinnitus. However, given the adverse effects of intravenous lidocaine that clearly outweigh any small benefits, lidocaine should not be used in the treatment of tinnitus”.

The American Academy of Otolaryngology - Head and Neck Surgery Foundation’s clinical practice guideline on “Tinnitus” (2014) stated that clinicians should not routinely recommend intra-tympanic medications for a primary indication of treating persistent, bothersome tinnitus.

Mexiletine

In a pilot study, Berninger et al (2006) examined the effect of intravenously administered mexiletine on subjective tinnitus and hearing in 6 patients, who initially responded positively to lidocaine. Distinct mexiletine-induced decreases in tinnitus loudness were demonstrated in 3 subjects, as reflected by maximum VAS level reduction of 34 %, 95 %, and 100 %, respectively. One subject reported change in tinnitus pitch, another one showed a slight (18 % on VAS) tinnitus reduction,
and 1 subject disclosed no effect. Side effects were seen only during 1 of 7 infusions. Mexiletine induced shifts in pure-tone threshold, transient evoked oto-acoustic emission, and acoustic reflex threshold, probably reflecting a reversible interference in the function of organ of Corti. The concentration effect relationship remained unclear and no general “therapeutic” level could be identified. The authors concluded that this study confirmed the effect of mexiletine on the auditory function and its potential as a possible therapeutic agent or a model for further development in tinnitus pharmacotherapy.

An UpToDate review on “Treatment of tinnitus” (Dinces, 2014) does not mention the use of mexiletine as a therapeutic option.

**Melatonin**

Miroddi et al (2015) performed a review to summarize, analyze and discuss the evidence provided by clinical studies evaluating effectiveness of melatonin in the cure of tinnitus. Due to the fact that there is no satisfactory treatment for tinnitus, clinical research has explored new therapeutic approaches. A search of PubMed, Medline, Embase, Central and Google Scholar was conducted to find trials published prior March 2014 on melatonin in the treatment of tinnitus. Design of the studies, randomization, allocation concealment procedures and diagnostic instruments (scales for tinnitus evaluation) were critical evaluated. A total of 5 clinical studies were included; 3 of them tested effectiveness of melatonin alone, the remaining 2 along with sulpiride and sulodexide, respectively. Considered clinical trials adopted various experimental designs: single-arm, randomized placebo-controlled and randomized placebo-controlled followed by cross-over. These studies were characterized by several methodological weaknesses. The authors concluded that confirmation of melatonin clinical effectiveness in the treatment of tinnitus cannot be given in the light of the biases observed in the considered evidence. Melatonin seems to improve sleep disturbance linked to tinnitus.

In a retrospective study, Ferrari and colleagues (2015) determined the effectiveness of combined treatment with sulodexide (a
natural glycosaminoglycan with anti-thrombotic, pro-fibrinolytic and vascular anti-inflammatory properties) and melatonin for the treatment of tinnitus. A total of 30 patients with tinnitus were treated with sulodexide (250 LSU BID, in the morning and in the evening) and melatonin (3 mg in the evening before going to sleep) for 80 days. Evaluations were performed comparing different parameters at basal (T0) and after 40 days (T1) and 80 days (T2) of treatment. The results of THI and acufenometry showed a significant improvement of tinnitus after treatment with sulodexide and melatonin. In particular, THI total score was reduced from 37 ± 20 to 27 ± 18 (p < 0.001) and 21 ± 19 (p < 0.001) at T1 and T2, respectively. The percentage of patients with improved symptoms (i.e., reduced score at THI) was 76.7 % at T1 and 90.0 % at T2. Finally a significant improvement was also detected in the tone audiometry test. No side effects were observed during the treatment period. The authors concluded that the combined use of sulodexide and melatonin confirmed to an important and promising therapeutically option in the tinnitus management.

Larsen and Ovesen (2014) performed a literature search on tinnitus guidelines and treatment. The authors stated that anti-depressants, melatonin and cognitive behavioral therapy have no effect on tinnitus, whereas sound generators, hearing aids and tinnitus retraining therapy show some but limited improvement. They stated that national recommendations are needed to ensure a homogenous and optimum offer for all patients.

Miscellaneous Interventions

Zenner and associates (2015) stated that chronic idiopathic tinnitus (CIT) is the most frequent type of tinnitus. A considerable number of treatment strategies are used to treat CIT; however, there is no evidence of effectiveness for many of these interventions. In order to enable scientific evidence-based treatment of CIT, German inter-disciplinary S3 guidelines have recently been constructed for the first time. These investigators presented a short form of these S3 guidelines. The guidelines were constructed based on a meta-analysis of the treatment of
chronic tinnitus performed by the authors. Additionally, a systematic literature search was performed in the PubMed and Cochrane Library databases. Furthermore, a systematic search for international guidelines was performed in Google, as well as in the Guidelines International Network and National Guideline Clearinghouse (USA) database. Evidence was classified according to the Oxford Centre for Evidence-Based Medicine system. According to the guidelines, alongside counselling, manualized structured tinnitus-specific cognitive behavioral therapy (tCBT) with a validated treatment manual is available as evidence-based therapy. In addition, the guidelines recommended concurrent treatment of co-morbidities, including drug-based treatment, where appropriate. Particularly important is treatment of anxiety and depression. Where a psychic or psychiatric co-morbidity is suspected, further diagnosis and treatment should be performed by an appropriately qualified specialist (psychiatrist, neurologist, psychosomatic medicine consultant) or psychological psychotherapist. In cases accompanied by deafness or hearing loss bordering on deafness, cochlear implants may be indicated. The authors concluded that no recommendations can be made for drug-based treatment of CIT, audiotherapy, transcranial magnetic or electrical stimulation, specific forms of acoustic stimulation or music therapy; or such recommendations must remain open due to the lack of available evidence. Moreover, they stated that poly-pragmatic tinnitus treatment with therapeutic strategies for which there is no evidence of effectiveness from controlled studies is to be refused.

Antioxidant Therapy

In a prospective, randomized, double-blinded, placebo-controlled, clinical trial, Polanski et al (2015) evaluated the effects of antioxidant therapy for tinnitus in a group of elderly patients. The sample consisted of 58 subjects aged 60 years or older, with a complaint of tinnitus associated with sensorineural hearing loss. These individuals completed the THI questionnaire before and after 6 months of therapy. The treatment regimens were: Ginkgo biloba dry extract (120 mg/day), alpha-lipoic acid (60 mg/day) + vitamin C (600 mg/day), papaverine hydrochloride (100 mg/day) + vitamin E (400 mg/day), and placebo. There was no statistically
significant difference between THI by degree (p = 0.441) and by score (p = 0.848) before and after treatment. The authors concluded that there was no benefit from the use of antioxidant agents for tinnitus in this sample.

Radiofrequency Lesion of the Superior Cervical Sympathetic Ganglion

Koning et al (2015) examined the effectiveness of radiofrequency lesioning of the superior cervical sympathetic ganglion for patients with tinnitus. This was a retrospective long-term clinical review of patients with tinnitus treated with a blockade of the superior cervical sympathetic ganglion. Subjects were 366 consecutive patients who came to the DC Klinieken in Almere and Amsterdam from January 2010 to January 2014 for consultations on their tinnitus that persisted for 1 month or longer. Data were recorded from patients whose charts were reviewed retrospectively to identify the patients who were treated with a blockade of the superior cervical sympathetic ganglion for tinnitus. An independent observer conducted a long-term follow-up assessment of the therapy by telephone interview. Relief of tinnitus at 7-week follow-up was achieved in 64% of the patients treated with a radiofrequency lesion of the superior cervical sympathetic ganglion after a positive test blockade of this structure. Two years after the treatment, the maintenance of a tinnitus relief occurred in almost 40% of the patients with a follow-up period of 2 years or longer. The authors concluded that radiofrequency lesion of the superior cervical sympathetic ganglion may be a useful alternative for patients with tinnitus not responding to conventional therapy. These preliminary findings need to be validated by well-designed studies.

Vitamin B12 Injections

In a randomized, double-blind, pilot study, Singh et al (2016) examined the role of vitamin B12 in treatment of chronic tinnitus. A total 40 patients were enrolled, of which 20 in Group A (cases) received intramuscular therapy of 1 ml vitamin B12 (2,500 ug) weekly for a period of 6 weeks and Group B (20) patients received placebo isotonic saline intramuscular injection. Subjects were
subjected to vitamin B12 assay and audiometry pre- and post-therapy. Of the total patients of tinnitus, 17 were vitamin B12 deficient (i.e., 42.5 % showed deficiency when the normal levels were considered to be 250 pg/ml). A paired t-test showed that in Group A, patients with vitamin B12 deficiency showed significant improvement in mean tinnitus severity index score and VAS after vitamin B12 therapy. The authors concluded that the findings of this pilot study highlighted the significant prevalence of vitamin B12 deficiency in North Indian population; and improvement in tinnitus severity scores and VAS in cobalamin-deficient patients receiving intramuscular vitamin B12 weekly for 6 weeks further provided a link between cobalamin deficiency and tinnitus thereby is suggestive of a therapeutic role of vitamin B12 in cobalamin-deficient patients of tinnitus. These preliminary findings need to be validated by well-designed studies.

Acoustic Coordinated Reset Neuromodulation

Wegger and colleagues (2017) noted that there are growing technological advances in the development of sound-based methods for the treatment of tinnitus. Most of these methods intend to affect the speculated underlying neurological causes of tinnitus. Acoustic coordinated reset (CR) neuromodulation is a novel method that as of yet seems inadequately reviewed. These investigators evaluated the current evidence on acoustic CR neuromodulation as a method for the treatment of tinnitus and examined if the method can be implemented in daily clinical practice. They performed a systematic literature search in 13 databases in the period from February 1, 2015 to May 1, 2016. Studies regarding acoustic CR neuromodulation as a treatment method for tinnitus were included in the present review. A total of 8 studies were eligible for being reviewed comprising a total of 329 patients. Overall, the evidence level of the published literature was low. The main findings in the included studies were that acoustic CR neuromodulation was safe and well-tolerated and most patients reported reduction of tinnitus symptoms. The neurophysiological basis of the method was claimed to be desynchronization, anti-kindling, and change of abnormal frequency couplings in a widespread tinnitus network comprising both auditory and non/auditory brain areas based on
electroencephalographic (EEG) analyses. The authors concluded that the available evidence is insufficient for clinical implementation of acoustic CR neuromodulation. They stated that the limited level of evidence suggested that acoustic CR neuromodulation may have positive effects on tinnitus symptoms. The authors stated that the preliminary EEG data are compatible with the claim that tinnitus reduction after CR treatment is mediated by a desynchronizing effect; however, a proof for this claim is still lacking.

Microvascular Decompression of the Cochlea-Vestibular Nerve

van den Berge and colleagues (2016) stated that microvascular decompression (MVD) is regarded as a valid treatment modality in neurovascular conflicts (NVCs) causing, for example, trigeminal neuralgia and hemi-facial spasms. An NVC of the cochlea-vestibular nerve might cause tinnitus and/or vertigo; however, general acceptance of MVD for this indication is lacking. These investigators examined the safety, effectiveness, and prognostic factors for success of MVD of the cochlea-vestibular nerve. A systematic review and meta-analysis of individual patient data (IPD) were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Individual Patient Data (PRISMA-IPD) guidelines. By a comprehensive search (conducted in January 2016) in Medline, Embase, and Google Scholar, eligible studies were identified. The collected outcome was a global measurement of improvement of (i) tinnitus, (ii) vertigo, and (iii) tinnitus combined with vertigo. For the meta-analysis, IPD were collected from the papers and/or from the authors; IPD were analyzed with logistic regression analysis while accounting for study clustering. A total of 35 studies (572 patients) were included. The level of evidence provided by these studies was low. In 28% of patients with tinnitus and 32% of patients with vertigo, complete relief following MVD was reported. Patients with both tinnitus and vertigo had complete relief in 62% of cases. In 11% of patients, greater than or equal to 1 complications were reported. Meta-analysis of IPD (165 patients) demonstrated that patients with both tinnitus and vertigo had a higher chance of success (odd ratio [OR] 3.8, 95% CI: 1.45 to 10.10) than patients with tinnitus alone. No other
variables were significantly related to success. The authors concluded that due to low success rates, MVD cannot be considered as a standard treatment method for tinnitus or vertigo. Moreover, a substantial complication rate was found. However, patients with combined symptoms had a higher chance of success. When combined symptoms occur, it is more likely that an NVC is the underlying pathology and MVD might be appropriate. Due to the low level of evidence in the included studies, this conclusion must be taken with caution. They stated that further validation is needed to examine if patients with combined symptoms are indeed better candidates for MVD.

<table>
<thead>
<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</strong></td>
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### CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>64550</td>
<td>Application of surface (transcutaneous) neurostimulator</td>
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</tbody>
</table>

### CPT codes not covered for indications listed in the CPB:

**Competitive kinesthetic interaction therapy (KKIT), radiofrequency lesion of the superior cervical sympathetic ganglion - no specific code:**

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61850</td>
<td>Twist drill or burr hole(s) for implantation of neurostimulator electrodes, cortical</td>
</tr>
<tr>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; first array</td>
</tr>
<tr>
<td>+61864</td>
<td>each additional array (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>61867</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; first array</td>
</tr>
<tr>
<td>+61868</td>
<td>each additional array (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td>61870</td>
<td>Craniectomy for implantation of neurostimulator electrodes, cerebellar; cortical</td>
</tr>
<tr>
<td>61880</td>
<td>Revision or removal of intracranial neurostimulator electrodes</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td>with connection to 2 or more electrode arrays</td>
</tr>
<tr>
<td>61888</td>
<td>Revision or removal of cranial neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td>64568</td>
<td>Incision for implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator</td>
</tr>
<tr>
<td>64569</td>
<td>Revision or replacement of cranial nerve (e.g., vagus nerve) neurostimulator electrode array, including connection to existing pulse generator</td>
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<tr>
<td>69930</td>
<td>Cochlear device implantation, with or without mastoidectomy</td>
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<tr>
<td>90867</td>
<td>Therapeutic repetitive transcranial magnetic stimulation treatment; planning</td>
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<tr>
<td>90868</td>
<td>delivery and management, per session</td>
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<tr>
<td>92590</td>
<td>Hearing aid examination and selection; monaural</td>
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<tr>
<td>92591</td>
<td>binaural</td>
</tr>
<tr>
<td>92601 - 92604</td>
<td>Diagnostic analysis of cochlear implant</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of waveform, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
</tr>
<tr>
<td>95974</td>
<td>Complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, first hour</td>
</tr>
<tr>
<td>95975</td>
<td>Complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, each additional 30 minutes after first hour (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>+95979</td>
<td>each additional 30 minutes after first hour (List separately in addition to code for primary procedure)</td>
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<tr>
<td>97810 - 97814</td>
<td>Acupuncture</td>
</tr>
<tr>
<td>99183</td>
<td>Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session</td>
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**HCPCS codes covered if selection criteria are met:**

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<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>A4595</td>
<td>Electrical stimulator supplies, 2 lead, per month, (e.g. TENS, NMES)</td>
</tr>
<tr>
<td>E0720</td>
<td>Transcutaneous electrical nerve stimulation (TENS) device, two lead, localized stimulation</td>
</tr>
<tr>
<td>E0730</td>
<td>Transcutaneous electrical nerve stimulation (TENS) device, four or more leads, for multiple nerve stimulation</td>
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</table>

**HCPCS codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), nonrechargeable</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
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<tr>
<td>C1778</td>
<td>Lead, neurostimulator (implantable)</td>
</tr>
<tr>
<td>C1816</td>
<td>Receiver and/or transmitter, neurostimulator (implantable)</td>
</tr>
<tr>
<td>C1883</td>
<td>Adaptor/extension, pacing lead or neurostimulator lead (implantable)</td>
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<tr>
<td>G0176</td>
<td>Activity therapy, such as music, dance, art or play therapies not for recreation, related to the care and treatment of patient’s disabling mental health problems, per session (45 minutes or more)</td>
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<tr>
<td>G0277</td>
<td>Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval</td>
</tr>
<tr>
<td>G0295</td>
<td>Electromagnetic therapy, to one or more areas, for wound care other than described in G0329 or for other uses</td>
</tr>
<tr>
<td>J0585</td>
<td>Injection, onabotulinumtoxina, 1 unit</td>
</tr>
<tr>
<td>J0586</td>
<td>Injection, abobotulinumtoxina, 5 units</td>
</tr>
<tr>
<td>J0587</td>
<td>Injection, rimabotulinumtoxinb, 100 units</td>
</tr>
<tr>
<td>J0588</td>
<td>Injection, incobotulinumtoxin a, 1 unit</td>
</tr>
<tr>
<td>J2001</td>
<td>Injection, lidocaine HCl for intravenous infusion, 10 mg -</td>
</tr>
<tr>
<td>J3420</td>
<td>Injection, vitamin b-12 cyanocobalamin, up to 1000 mcg</td>
</tr>
<tr>
<td>L8614</td>
<td>Cochlear implant components</td>
</tr>
<tr>
<td>L8629</td>
<td></td>
</tr>
<tr>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only</td>
</tr>
<tr>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8685</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
</tbody>
</table>
Tinnitus Treatments

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implanted neurostimulator, replacement only</td>
</tr>
<tr>
<td>L8695</td>
<td>External recharging system for battery (external) for use with implantable neurostimulator, replacement only</td>
</tr>
<tr>
<td>V5010 - V5267, V5275, V5298</td>
<td>Hearing aid services and supplies</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>H81.01 - H81.09</td>
<td>Meniere's disease</td>
</tr>
<tr>
<td>H93.11 - H93.19</td>
<td>Tinnitus</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

**Transcutaneous Electrical Nerve Stimulation for Tinnitus:**


**Tinnitus Instruments (Maskers, Hearing Aids):**


**Ear Canal Magnets and Electromagnetic Stimulation:**


4. Dobie RA, Hoberg KE, Rees TS. Electrical tinnitus


Tinnitus Retraining Therapy:


11. Londero A, Peignard P, Malinvaud D, et al. Tinnitus and


Transcranial Magnetic Stimulation:


7. Lee SL, Abraham M, Cacace AT, Silver SM. Repetitive


Transmeatal Laser Irradiation:


5. Gungor A, Dogru S, Cincik H, et al. Effectiveness of


**Hyperbaric Oxygen Therapy:**


**Sequential Phase Shift Sound Cancellation Treatment:**


2. Choy DSJ, Kaminow I. A novel treatment of predominant


Neuromonics Tinnitus Treatment:


Auditory Perceptual Training:


Intra-Tympanic Administration of Corticosteroids:


**Deep Brain Stimulation:**


**Vagal Nerve Stimulation:**


2. Dinces EA. Treatments for tinnitus. UpToDate [online serial]. Waltham, MA: UpToDate; February 2012.

**Miscellaneous Treatments:**


25. Laureano MR, Onishi ET, Bressan RA, et al. The

AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to Aetna Clinical Policy Bulletin Number:

0406 Tinnitus Treatments

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania

revised 06/13/2017