Northern Treatment Advisory Group

Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	4th September 2018 (updated 25th February 2020 & 8th June 2021)
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered a re-appraisal of **Non-invasive transcutaneous vagus nerve stimulation (nVNS) for treatment of cluster headache and migraine.** **gammaCore (electroCore LLC)** is the only available handheld device; it is the size of a mobile phone to provide non-invasive transcutaneous vagus nerve stimulation (nVNS).
Recommendation	**The Northern (NHS) Treatment Advisory Group recommends the use of non-invasive transcutaneous vagus nerve stimulation (gammaCore) for the treatment of cluster headache.** The group agreed that there is an unmet clinical need in the management of chronic cluster headache and that gammaCore may offer a further treatment option in these patients when verapamil and topiramate have failed, and before trialling lithium and implanted devices such as occipital nerve stimulation or referral for invasive brain stimulation. This NTAG recommendation supports the NICE Medical technologies guidance [MTG46] December 2019 which supports the case for adopting gammaCore to treat cluster headache in the NHS. Treatment with gammaCore should only continue for people whose symptoms reduce in the first 3 months. **The Northern (NHS) Treatment Advisory Group <u>does not</u> recommend the use of non-invasive transcutaneous vagus nerve stimulation for the treatment of migraine.** The group were concerned about the limited evidence of efficacy and cost effectiveness for migraine and agreed with the NICE IP guidance that further research is required**.**
Clinical evidence summary	The Prevention and Acute Treatment of Chronic Cluster Headache (PREVA) trial was an open-label RCT which compared the gammaCore device plus individualised standard care to standard care alone. The nVNS group had greater reductions in cluster headache frequency than standard care alone (-5.9 vs. -2.1 attacks/week) and were more likely to reduce attack frequency by at least half (40% vs. 8.3%). Quality of life and headache impact scores were significantly improved. However the trial is limited by its open-label design and short duration. Sham devices, as used in other trials, had not yet been developed when this trial was conducted. Another RCT for acute treatment of cluster headache found no difference in cluster headache pain intensity when nVNS was compared to sham nVNS. A subgroup analysis suggested there may be a significant benefit in patients with episodic, but not chronic, cluster headache. Some limitations of the trial were that the sham nVNS device did not cause localised muscle contraction at the application site in the same way as the active device. This may have led to

Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

	accidental unblinding, and in fact the authors noted that "a considerable proportion of patients correctly guessed their treatment allocation" after one treatment. This may have introduced bias. One double-blind sham-controlled RCT assessed nVNS for treatment and prophylaxis of migraine. The trial found no difference between groups in the mean number of monthly headache days. Several smaller, non-randomised studies have been conducted for both indications, but add little to the available evidence on effectiveness. Limitations of the randomised trials, such as incomplete blinding and short duration, mean that their results should be interpreted with caution.
Safety	Treatment with nVNS appears safe and well-tolerated. The longest-term safety data come from a very small (n=19) 52-week cohort study in patients with cluster headache. There are theoretical safety concerns due to the diverse functions of the vagus nerve, but experience with implanted devices suggests no excess of adverse events.
Patient Perspective	Non-invasive transcutaneous stimulation of the vagus nerve (nVNS) is a newer treatment modality which aims to treat headache disorders while avoiding the need for an implanted device. If used for acute treatment patients will need to carry their gammaCore device with them at all times. While the device is not large or heavy, this may be a nuisance for some. Either prophylactic or acute use may necessitate the use of the device in public for some patients, depending on usual daily activities. This may reduce adherence due to practical considerations or feelings of awkwardness or embarrassment. These factors will vary with the individual patient. Given that cluster headache and migraine can have a substantial impact on quality of life, many may find these inconveniences perfectly acceptable. Most however will prefer oral tablet therapies.
Cost analysis summary	A German cost-effectiveness analysis suggests that this is cost-effective in cluster headache patients but no UK analyses are available. Drug costs are lower in the UK than those quoted in the analysis, which may alter the cost-effectiveness.
Financial impact	The prevalence for cluster headache is 0.2% whereas Migraine is much more common than cluster headache, with a prevalence of around 18% in women and 6% in men. Treatment with gammaCore costs around £210 per patient per month (ex VAT) As of 1st April 2021 this technology is now commissioned by CCG from providers through the MedTech Funding Mandate policy 2021/22 for use in the management of chronic headache. The gammaCore device is normally delivered to the patient's home. There is not expected to be any financial impact in the management of migraine as nVNS is not recommended.