

# gammaCore for cluster headache

Medtech innovation briefing

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## Summary

- The **technology** described in this briefing is gammaCore. It is used as a daily preventative measure for cluster headache and can be used to treat pain during a headache.
- The **innovative aspects** compared with other vagus nerve stimulators is that gammaCore is applied to the surface of the neck rather than surgically implanted.
- The **intended place in therapy** would be as well as standard care, most likely where standard treatments for cluster headache are ineffective, not tolerated or contraindicated. It would be prescribed by neurologists who provide specialist headache services.
- The **main points from the evidence** summarised in this briefing are from 5 studies: 3 randomised controlled trials, 1 open-label randomised trial and 1 cohort study including a total of 465 people. They show that use of gammaCore alongside standard care may be more effective than standard care only in treating cluster headaches.
- **Key uncertainties** around the evidence and technology are that people with episodic and chronic cluster headaches respond differently to treatment with gammaCore. The optimal use of gammaCore in the different populations is unclear.
- The **cost** of gammaCore treatment is £625 for 93 days (exclusive of VAT). The **resource impact** would be more than standard care, except where it replaces current treatments.

## The technology

gammaCore (electroCore) is a handheld, patient-controlled, non-invasive vagus nerve stimulator

used for preventing and treating cluster headaches. The device is applied to the neck to deliver a small electric current for 2 minutes at a time. The aim is to modify pain signals by stimulating the vagus nerve through the skin of the neck. gammaCore can be used daily to help prevent cluster headache or when the person feels a cluster headache beginning. The device is small and portable and, after brief training, can be used anywhere that is convenient.

## *Innovations*

gammaCore differs from other vagus nerve stimulators in being applied to the skin of the neck rather than implanted by a surgical procedure.

## *Current care pathway*

NICE interventional procedures guidance on [transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine](#) recommends that the procedure should only be used with special arrangements for clinical governance, consent and audit or research. Current evidence on the safety of the procedure raised no concerns but the evidence on efficacy was limited in quantity and quality.

NICE's clinical guideline on [headache](#) states that oxygen or triptans should be used for acute treatment of cluster headache. It also recommends that verapamil is prescribed for long-term prophylaxis and that electrocardiogram monitoring may be necessary. Anticonvulsants may also be prescribed. The use of verapamil and anticonvulsants for cluster headache is outside their marketing authorisation.

Specialist commentators have stated that many people with cluster headache do not get enough pain relief from current treatment options, which are often limited by side effects and contraindications.

## *Population, setting and intended user*

gammaCore is intended for use by people with cluster headache for whom standard treatment has been unsuccessful or in people who cannot have other prescribed treatments. If used, it is most likely to be an option before more invasive options or treatment with lithium are considered. Around 66,000 people in the UK experience cluster headache. The company estimate that in about 5% of people with cluster headache, standard care will not work or be unsuitable.

gammaCore is most likely to be started by neurologists in tertiary centres who specialise in

headache management. People using gammaCore will need brief training. This is provided by the company at no extra cost. Once trained, people with cluster headache can use gammaCore in any setting.

## Costs

### Technology costs

The gammaCore device, conductive gel consumables, and first 93-day activation card are initially provided free of charge. This allows the effectiveness of the treatment in individual users to be assessed before further treatment is bought. If the trial is successful, further treatment (through new activation cards) costs £625 for 93 days (exclusive of VAT).

### Costs of standard care

Standard care for people with cluster headache includes triptan doses (either as a nasal spray or subcutaneous injection) twice daily to prevent cluster headache and the use of oxygen at home to treat pain during a cluster headache.

**Table 1 Cost of standard care to treat cluster headache**

Description	Cost	Additional information
Triptan therapy used twice daily, various options available. Costs given for cheapest and most expensive options.	Zolmitriptan 5-mg nasal spray: £36.50. Sumatriptan 6-mg subcutaneous injections: £40.41 per injection.	Costs from British national formulary (accessed September 2018).
Average monthly cost of oxygen therapy in the home (used with triptan prescription).	£100 (approximately).	Costs provided by company. This cost is likely to vary depending on use.

### Resource consequences

Using gammaCore would add costs to standard care except in cases where it replaced current treatments. There are no published data to determine how likely this is. The extra costs may be

offset if it reduced the number or dose of prescribed medicines, or avoided the need for more invasive treatment options.

gammaCore is currently being used in around 20 NHS organisations throughout the UK.

People prescribed gammaCore to treat cluster headache will need brief training which can be given by the company or by specialist clinicians. No changes to the way current services are organised and delivered are expected to be needed.

## Regulatory information

gammaCore is a CE marked class IIa medical device.

No medical device alerts for this technology have been identified. The instructions for use for gammaCore state that it should not be operated with wet hands.

## Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

People with cluster headache are likely to be described as disabled because it is a chronic condition which is likely to last longer than 1 year. This technology avoids invasive treatments, or use of unlicensed medications with potentially serious side effects. Self-administration of treatment with gammaCore needs manual dexterity and the ability to follow instructions. gammaCore cannot be used by people with cochlear implants or pacemakers and has not been used in people who are pregnant, lactating or aged under 18 years.

## Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence

for this briefing was selected is available on request by contacting [mibs@nice.org.uk](mailto:mibs@nice.org.uk).

## *Published evidence*

5 studies are summarised in this briefing, including a total of 465 people.

The evidence for gammaCore comprises 3 randomised controlled trials (2 of which compare gammaCore with a sham device); 1 open-label randomised study and a cohort study done in the UK.

Table 2 summarises the clinical evidence as well as its strengths and limitations.

## *Overall assessment of the evidence*

The studies included in table 2 examine the use of gammaCore as a prophylactic treatment for preventing cluster headache and for treating acute pain after the onset of a cluster headache. Several of the studies also separate cohorts into those that have been diagnosed with chronic cluster headache and people diagnosed with episodic cluster headache. The studies recruited relatively large populations given the prevalence of cluster headache. The study design and comparator selection were generalisable to NHS standard practice. The studies suggest that gammaCore is only effective in chronic cluster headache when used as a preventative measure. In episodic cluster headache it is only effective when used as a treatment for acute pain.

### **Table 2 Summary of selected studies**

<u>Goadsby et al. (2018)</u>	
Study size, design and location	102 people with cluster headache (30 episodic and 72 chronic). Randomised, double-blind sham-controlled study. Location: UK, Netherlands, Germany, Denmark.
Intervention and comparator(s)	gammaCore (used as a treatment for acute pain) and sham device, both arms also had standard care.

Key outcomes	The primary efficacy end point was the proportion of all treated attacks that achieved pain-free status within 15 minutes after starting treatment, without rescue treatment. For the total cohort, there was no significant difference between gammaCore (14%) and the sham device (12%), however, in the episodic cluster headache group gammaCore was statistically significantly superior to sham (48% versus 6%, $p=0.01$ ). No significant differences were seen in the chronic cluster headache group.
Strengths and limitations	Sham-controlled study. The study was sponsored by the company.
<u>Gaul et al. (2017)</u>	
Study size, design and location	97 people with chronic cluster headache. Randomised controlled trial. Location: Germany, Belgium.
Intervention and comparator(s)	gammaCore (used as preventative and acute treatment) plus standard care versus standard care only.
Key outcomes	gammaCore was used 6 times daily to prevent cluster headache. Use of gammaCore in addition to standard care led to a statistically significant reduction in cluster headaches compared with standard care alone ( $p<0.05$ ). Frequency of headaches reduced by 40% in the gammaCore group compared with standard care and frequency increase of 1% in the standard care only group.
Strengths and limitations	Randomised controlled trial. The study was funded by the company.
<u>Gaul et al. (2015)</u>	
Study size, design and location	97 people with cluster headache. Open-label randomised study. Location: UK, Belgium, Germany and Sweden.
Intervention and comparator(s)	gammaCore (used as preventative and acute treatment) and standard care (medication).

Key outcomes	People in the standard care plus gammaCore arm (n=45) had a significantly greater reduction in the number of cluster headaches per week versus people in the medication only arm (n=48; 5.9 versus 2.1, respectively). People in the gammaCore arm had a mean therapeutic gain of 3.9 fewer attacks per week (95% CI 0.5–7.2; p=0.02). Response rates were also seen in the gammaCore arm (40% [18/45]) versus people in the control arm (8.3% [4/48]; p<0.001). No serious treatment-related adverse events happened.
Strengths and limitations	Prospective, randomly allocated trial. The study was company sponsored, including having company representatives as co-authors and company sponsored editorial support. The authors stated that gammaCore did not work as an acute treatment.
<u>Silberstein et al. (2016)</u>	
Study size, design and location	150 people with either episodic or chronic cluster headache. Randomised controlled trial using a sham device as control followed by an open-label phase. Location: US.
Intervention and comparator(s)	gammaCore referred to as nVNS (used as a treatment for acute pain) and sham device.
Key outcomes	The intention-to-treat population comprised 133 subjects: 60 nVNS-treated (eCH, n=38; cCH, n=22) and 73 sham treated (eCH, n=47; cCH, n=26). The response rate was not significantly different (versus sham) for the total population (response was achieved in 26.7% of nVNS-treated subjects and 15.1% of sham-treated subjects [p=0.1]). Response rates were significantly higher for gammaCore in the eCH cohort (nVNS, 34.2%; sham, 10.6%; p=0.008) but not the cCH cohort (nVNS, 13.6%; sham, 23.1%; p=0.48). No serious adverse events happened.
Strengths and limitations	Randomised controlled trial. The study was company sponsored, including having company representatives as co-authors and company sponsored editorial support.
<u>Nesbitt et al. (2015)</u>	

Study size, design and location	19 people, 11 with chronic cluster headache and 8 with episodic cluster headache. Drug therapy was unsuitable for 7 people in the study. Open-label observational cohort study (audit). Location: UK and Republic of Ireland.
Intervention and comparator(s)	gammaCore for both prophylactic and acute use.
Key outcomes	15 patients reported an improvement; 4 reported no change. 47% of cluster headaches were aborted within an average of 11±1 minutes of using gammaCore. Ten patients reduced their acute use of high-flow oxygen by 55% with 9 reducing triptan use by 48%. Prophylactic use of gammaCore resulted in a substantial reduction in estimated mean attack frequency from 4.5/24 hours to 2.6/24 hours (p<0.0005).
Strengths and limitations	Small audit study. The study was supported by a grant from the company.
Abbreviations: cCH: chronic cluster headache, CI: confidence interval, eCH: episodic cluster headache, nVNS: non-invasive vagus nerve stimulation	

## Recent and ongoing studies

No ongoing or in-development trials were identified.

## Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 4 specialists were familiar with or had used this technology before.

## Level of innovation

All 4 specialists agreed that gammaCore was innovative. The specialists stated that gammaCore is different to other treatments for cluster headache. The specialists noted that gammaCore has no known side effects and needs no clinical monitoring, unlike the medications used to treat cluster



headache. The specialists noted that gammaCore is the only nerve stimulator for cluster headache that does not need to be surgically implanted.

### *Potential patient impact*

Three specialists stated that gammaCore is likely to be beneficial to people with cluster headache because it has no known side effects and can be used as many times a day as needed. This means that there is potential for gammaCore to be a treatment option for people with cluster headache for whom current treatments are not effective or tolerable. One specialist noted that gammaCore had the potential to reduce the amount of medication needed to treat cluster headache. Two specialists noted that gammaCore was effective in about 50% of people with cluster headache based on their clinical practice. The specialists stated that use of gammaCore has led to life changing improvements for some people, allowing them to return to work and normal activities. The specialists noted that there is a high risk of suicide for people with cluster headache and that many of these patients have significant unmet needs.

The specialists stated that gammaCore was easy to teach and use and people with cluster headache had good compliance with the treatment when using it at home every day. One specialist noted that although gammaCore needs conductive gel to be used many people find this mode of administration preferable to self-injecting or oxygen therapy. One specialist noted that gammaCore was portable and easy to use on the go.

The specialists agreed that gammaCore could be used by anyone with cluster headache but would be particularly beneficial for those people in whom current treatments are not tolerated or are contraindicated. For example, people for whom triptans, high-flow oxygen and verapamil are ineffective or people with cardiovascular disease.

### *Potential system impact*

All 4 specialists agreed that gammaCore had the potential to save money through the NHS by reducing the cost of treating cluster headache. The specialists noted that people with cluster headache for whom gammaCore is successful are likely to have fewer future complications and disabilities because of their condition. This is likely to reduce the need for expensive drug and oxygen therapy (and monitoring thereof), A&E visits, hospital admissions and a reduced need for invasive surgical procedures. Two specialists noted that if people with cluster headache are able to use gammaCore at home to control their symptoms then the workload on headache specialists in the NHS will decrease. One specialist stated that there could be an increase in the workload of headache specialists if the introduction of gammaCore encourages more people to seek treatment.

## General comments

Specialist commentators advise that cluster headache affects 1:1,000 population and around 5% of these people will not have enough symptom control with standard care. The specialists noted that once trained to use gammaCore, most people will not need any further assistance. However, it should be noted that a moderate level of dexterity is needed to use the device. The specialist commentators noted that the evidence for gammaCore showed positive outcomes in line with their clinical experience and was of high quality, particularly in comparison to the quality of research done in cluster headache in general. However, all specialists noted that further real world data would help to address questions on how long the treatment is effective for, how to best select patients and the economic effect on the NHS.

## Patient organisation comments

The Migraine Trust noted that people with cluster headache experience significant unmet need and that their condition may go undiagnosed. Cluster headache has a huge effect on a person's life which may affect their ability to work or do normal activities. People with cluster headache may feel socially stigmatised and may be viewed as unreliable by others (for example employers) who do not understand the debilitating effects of cluster headache. They note that their members who are using gammaCore find it to be much easier to use than current options of treatment. The Migraine Trust notes that although they do not expect gammaCore to work for everyone, it is a safe and cheap option that can be tried.

## Specialist commentators

The following clinicians contributed to this briefing:

- Dr Nicholas Silver, consultant neurologist, The Walton Centre, has received payment for advisory roles and principal/chief investigator fees from electroCore since 2015. Has also taken payment from other companies working in treatment of headache disorders.
- Nicola Giffin, consultant neurologist, Royal United Hospital NHS trust, did not declare any interests.
- Manjit Matharu, consultant neurologist, UCL Institute of Neurology and The National Hospital for Neurology and Neurosurgery, centre provided a headache course for GPs that was part funded by electroCore in 2015–16.
- Dr M S Chong, Consultant Neurologist, Pain Management Centre, National Hospital for

- Neurology and Neurosurgery, did not declare any interests.

Representatives from the following patient organisations contributed to this briefing:

- The Migraine Trust.

## Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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