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In response to an enquiry from electroCore Ltd.

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## gammaCore for cluster headache\*

*\*adaptation for NHSScotland of guidance published by National Institute for Health and Care Excellence*

### Recommendations for NHSScotland

- gammaCore should be available for a 3-month trial for people experiencing cluster headaches. Evidence demonstrates that gammaCore can reduce the frequency and intensity of cluster headache attacks and improves quality of life.
- gammaCore is not effective for everyone with cluster headache. Treatment with gammaCore should only continue for people whose symptoms reduce in the first 3 months.
- Cost modelling estimates that, in the first year of treatment, adding gammaCore to standard care is cost saving compared with standard care alone by an average of £450 per person. This estimated cost saving:
  - is based on the first 3-month period of gammaCore use being offered free of charge;
  - largely results from less use of subcutaneous sumatriptan by those who respond to gammaCore treatment.

*The Scottish Health Technology Group (SHTG) recommendation is based on [guidance produced by National Institute for Health and Care Excellence \(NICE\) in 2019](#). The original NICE guidance was modified following an SHTG adaptation process. NHSScotland is required to consider SHTG recommendations.*

## Description of the technology under consideration

gammaCore is a handheld, patient-controlled, non-invasive vagus nerve stimulator used for preventing and treating cluster headaches.

gammaCore was referred to SHTG by the manufacturer, electroCore Ltd. SHTG were asked to consider the guidance produced by the National Institute for Health and Care Excellence (NICE), and whether it could be applied to NHSScotland.

## Why is this important?

The NICE guidance noted the devastating impact that cluster headaches can have on the lives of sufferers and the desperation that can result from ineffective treatment.

## What was our approach?

We undertook an SHTG adaptation process of [guidance produced by NICE](#) in 2019. The European Network for Health Technology Assessment (EUnetHTA) adaptation toolkit was used to assess the relevance, reliability and transferability of the NICE guidance. Key findings from the toolkit are included within the SHTG Adaptation to inform the final recommendations.

As part of the adaptation process, the views, perspectives and experience of topic experts were obtained via two rounds of questioning. The first draft of the SHTG Adaptation was distributed to topic experts, along with a survey. The experts were asked to consider whether the NICE recommendations were appropriate for Scotland and if so, whether they should be adopted with no changes, or adapted to make them more relevant to the NHSScotland context.

Based on the responses received, the draft SHTG Adaptation document was reviewed. A revised draft, along with anonymised responses to the first round of questioning, was sent back to the experts for a second round of questioning. Further changes were made to the draft based on the responses received.

Topic experts' comments are captured within the SHTG Adaptation including a detailed summary from each round of questioning. All experts' comments were available for consideration by SHTG Council to inform the final recommendations.

## What next?

The SHTG Adaptation will be disseminated across NHSScotland health boards to inform the use of gammaCore for cluster headache.

## Considerations for NHSScotland

### Epidemiology and predicted volume

NICE estimates that around 0.1% of the UK population experience cluster headaches. Based on a Scottish population of 5.46 million, this equates to 5,460 people in Scotland. electroCore Ltd., the manufacturer of gammaCore, estimates that for 5% of people experiencing cluster headaches (273 patients in Scotland), standard care does not work or is unsuitable. The NICE guidance states that based upon expert advice, 5% may be an underestimate.

### Organisational issues

The administration of gammaCore has minimal impact on patients' care pathway; gammaCore is self-administered or administered by a carer. The NICE guidance notes that gammaCore requires brief training and some manual dexterity. Training for patients and staff is provided by the manufacturer as a free service. electroCore Ltd. states that training can also be provided by the NHS-based headache team (neurologist or headache nurse), and that no changes to the way current services are organised and delivered should be required.

The clinical experts consulted as part of developing the NICE guidance stated that patients should be reassessed after the first 3 months of treatment to review headache frequency and intensity, with subsequent follow-up at 12 months and every year afterwards. This follow-up schedule fits with normal routine appointments (with the neurologist or a headache nurse) in Scotland (Dr Callum Duncan, Consultant Neurologist, Aberdeen Royal Infirmary, Personal communication, September 2020).

As part of the SHTG adaptation process, Scottish topic experts were asked to identify barriers to the adoption of the NICE recommendations in NHSScotland. Three respondents raised the difficulty in access to specialist headache centres. Two experts noted that an increase in demand for this technology would have to be supported by relevant funding pathways. One expert suggested a need to develop a Scottish clinical care pathway to support centres that may need additional resources or expertise in the management of patients with cluster headaches to support the use of gammaCore. It was also noted that there are strong headache services in Glasgow, Edinburgh and Aberdeen, with an excellent network of clinicians with interest in headache across Scotland.

### Patient population

NICE concluded that there was sufficient evidence of clinical benefit for people with chronic and episodic cluster headache to recommend adopting gammaCore if treatment is successful in the first 3 months.

Based on current evidence, NICE could not reliably make a therapeutic distinction between chronic and episodic headaches.

NICE noted that, due to the limitations of the evidence, it is not clear whether gammaCore offers a benefit for the treatment of refractory patients.

### Use of the technology in Scotland

gammaCore is currently available in two centres in Scotland (Aberdeen and Glasgow). In Aberdeen, it is used for prophylaxis and/or acute treatment as recommended by the Headache Team (Consultant Neurologist and General Practitioner with Specialist Interest in Headache (GPSIs)) where other standard treatments have failed. gammaCore has been used to treat chronic cluster headaches, and occasionally episodic cluster headaches (Dr Callum Duncan, Consultant Neurologist, Aberdeen Royal Infirmary, Personal communication, September 2020).

### Scottish Health Technology Council considerations

The draft SHTG Adaptation was considered by the Scottish Health Technology Council on 7 December 2020. A summary of the discussion is presented as follows:

- The Council acknowledged the severity of pain that is associated with cluster headaches and recognised the huge impact it can have on patients' lives.
- The Council noted the importance of reviewing the use of gammaCore after 3 months to ensure that the technology is targeted to people who have responded to the treatment.
- The Council recognised that the estimated cost saving derived from the NICE economic model is based on the assumption of an initial free 3-month trial use period, and that only people whose condition responds to treatment with gammaCore within that 3-month period continue to use it. Responders are assumed to require less sumatriptan medication.

## Reliability and transferability of the adapted HTA

The EUnetHTA HTA adaptation toolkit was used to assess the relevance, reliability and transferability of the NICE guidance. The toolkit focuses on five 'domains' (or sections of an HTA report):

- The use of the technology
- Safety
- Effectiveness
- Economic evaluation
- Organisational elements

One issue that this toolkit highlighted was a potential for bias in the included studies; the manufacturer was the sponsor in all but one of the studies. In addition, one of the authors in all but one of the studies was employed, or had received payments from the manufacturer.

No other issues relating to relevance, reliability and transferability of the NICE guidance were identified.

## What did the experts say?

Full details of the questions asked in each round, and the anonymised responses received, can be obtained from SHTG on request.

### First round of questioning

Nine experts responded to the first round of questioning. There was representation from neurologists, experts in headache disorders, anaesthesia and pain medicine and public health. The experts came from the following boards: NHS Greater Glasgow and Clyde, NHS Grampian, NHS Fife, NHS Lothian, NHS Highland. The key results from the first round of questioning are summarised as follows:

- All nine experts stated that they either agreed or strongly agreed with the recommendations within the guidance produced by NICE.
- All nine experts agreed or strongly agreed that the guidance produced by NICE was an accurate interpretation of the evidence base.

- All nine experts said that guidance for NHSScotland should support the case for the use of gammaCore in cluster headaches.
- Four experts said that the guidance for NICE should be adopted and implemented in its entirety, without any changes, in NHSScotland. Four experts felt that the guidance needed to be amended for the Scottish context. Two experts said that the use of gammaCore should be targeted for patients with chronic headaches, with one expert clarifying that gammaCore should follow three treatment failures and include three months of assessment.
- One expert highlighted that the cost-effectiveness results are for chronic cluster only and not for chronic cluster plus episodic combined.

### Second round of questioning

Seven experts responded to the second round of questioning. The key results from the second round of questioning are summarised as follows:

- All seven experts agreed or strongly agreed with the draft recommendation for NHSScotland.
- One expert suggested a Scottish audit of real world evidence and clinical experience in the first year of use.
- One expert highlighted the NICE cost-effective modelling, noting that the company provides the device for 3 months, only in the first year. NICE acknowledged that the model conclusions were sensitive to the first 3 months being free and that the cost-effectiveness without the free 3 months remains unclear.
- One expert stated that the evidence base was poor. NICE acknowledged the evidence base was small and stated the quality of the studies ranged from very low to moderate. NICE noted that the prevalence of cluster headaches in the UK is low and that a large, UK based, blinded randomised trial is unlikely to be possible. Their clinical experts estimated 25% to 50% of patients responded to gammaCore. The published evidence for the effectiveness of gammaCore was supported by a survey of 60 patients with cluster headaches.

## Acknowledgements

This adaptation is based on the following work:

National Institute for Health and Care Excellence. gammaCore for cluster headache 2019 [cited 10 Sep 2020]; Available from: <https://www.nice.org.uk/guidance/mtg46>

## Reviewers

SHTG Executive would like to thank the following individuals and experts who took part in a consultation exercise:

- Dr Ishaq Abu-Arafeh, Consultant Paediatrician, Paediatric Neurosciences, NHS Greater Glasgow & Clyde
- Dr Javier Carod-artal, Consultant Neurologist, NHS Highland
- Dr Callum Duncan, Consultant Neurologist, NHS Grampian
- Dr George Gorrie, Consultant Neurologist, NHS Greater Glasgow & Clyde
- Noelle O'Neill, Senior Public Health Scientist, NHS Highland
- Dr Kiran Sachance, Consultant in Pain Medicine Anaesthesia, NHS Lothian
- Dr Uwe Spelmeyer, Consultant Neurologist, NHS Fife
- Dr David Watson, General Practitioner, NHS Grampian

Declarations of interest were sought from all reviewers. Reviewers had no role in authorship or editorial control and the views expressed are those of HIS and the SHTG Council.

## SHTG Council

SHTG Executive would like to thank the following individuals and organisations on the SHTG Council for endorsing this recommendation:

- Mr Ed Clifton, SHTG Unit Head, Healthcare Improvement Scotland
- Mr Mark Cook, Director Government Affairs, Assn. of British Healthcare Industries
- Dr Karen Facey, Senior Research Fellow, Usher Institute, University of Edinburgh
- Ms Claire Fernie, Public Partner, Healthcare Improvement Scotland
- Dr Rodolfo Hernandez, Research Fellow, Health Economics Research Unit (HERU), University of Aberdeen
- Mr Colin Marsland, Director of Finance, NHS Shetland

- Ms Karen Macpherson, Lead Health Service Researcher, Healthcare Improvement Scotland
- Mr Ralph Roberts, Chief Executive, NHS Borders
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- Dr Iain Robertson, SHTG Council Chair, Consultant Interventional Radiologist, NHS Greater Glasgow and Clyde
- Dr Laura Ryan, Medical Director, NHS 24
- Dr Neil Smart, SHTG Council Vice-Chair, Consultant Anaesthetist, NHS Greater Glasgow and Clyde
- Mr Hugh Stewart, Public Partner, Healthcare Improvement Scotland
- Dr Safia Qureshi, Director of Evidence, Healthcare Improvement Scotland

## Healthcare Improvement Scotland development team

SHTG Executive would like to thank the following individuals for developing this health technology assessment:

- Julie Calvert, Lead Author/Health Services Researcher, Healthcare Improvement Scotland
- Tracey Mac Gann, Project Officer, Healthcare Improvement Scotland

## Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

## About SHTG Adaptation

SHTG Adaptations inform a decision at a particular point in time and are not routinely updated. The Adaptation will be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the recommendation for NHSScotland. For further information about the SHTG process see [this SHTG webpage](#).

To propose a topic for SHTG consideration, email [his.shtg@nhs.scot](mailto:his.shtg@nhs.scot)

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network [www.knowledge.scot.nhs.uk](http://www.knowledge.scot.nhs.uk), or by contacting your local library and information service.

A glossary of commonly used terms in Health Technology Assessment is available from [htaglossary.net](http://htaglossary.net).

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