

# **Clinical Commissioning Policy Statement: Sphenopalatine Ganglion Stimulation for Refractory Chronic Cluster Headache (Adults)**

NHS England Reference: 170083P



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## 1. Plain Language Summary

Cluster headaches consist of attacks of severe one-sided pain that can last from a few minutes to several hours and can occur many times a day, over several days. Each attack develops suddenly, usually without warning. Typically, attacks occur in clusters over several weeks or months, after which the patient goes into remission. In a small number of cases, patients do not experience any remission and their cluster headaches are regarded as chronic.

It is believed that cluster headaches are associated with a bundle of nerves behind the nose called the sphenopalatine ganglion (SPG). Treatments that target these nerves have been shown to reduce the pain and frequency of cluster headaches. This usually involves a combination of breathing in pure oxygen through a face mask, or the use of medication such as nasal sprays and injections. Patients who do not respond to these medical treatments are said to be refractory and in these circumstances, surgical treatment can be considered.

## 2. Background

Cluster headaches are excruciating attacks of pain, often felt around the eye. Their exact cause is not clear. Cluster headaches begin quickly and without warning. The pain is severe and is often described as a sharp burning or piercing sensation on one side of the head. Symptoms include periorbital pain, a red and watering eye, and a blocked or runny nostril. Attacks usually last between fifteen minutes and three hours and typically occur between one and eight times a day. Attacks usually occur in clusters over several weeks or months, after which the patient goes into remission which can last months or years before the headaches start again.

Cluster headaches are deemed chronic if attacks occur for more than 1 year without remission, or with remission periods lasting less than 3 months (Headache Classification Subcommittee of the International Headache Society). Chronic Cluster Headache has a very low prevalence.

The usual treatments for acute cluster headache attacks are oxygen inhalation and/or with or without medications such as triptans. Medications such as corticosteroids, verapamil and occipital nerve blocks are used to prevent or reduce the number of attacks. Surgical treatments are reserved for patients with distressing symptoms that are refractory to medical treatments.

It is believed that cluster headaches are caused by a trigeminal-autonomic reflex mediated through the (SPG. SPG stimulation aims to relieve pain and reduce the frequency of cluster headache attacks. It involves the implantation of a neuro-stimulator device through a small incision in the gum, which stimulates the SPG with small electrical currents. When cluster headaches occur, the patient activates the neuro-stimulator (up to a pre-determined maximum dose) by placing a rechargeable handheld control unit on their cheek, over the area where the main body of the device is implanted.

### 3. Commissioning Position

NHS England has carefully reviewed the evidence to treat refractory chronic cluster headache with an implanted device for SPG stimulation. We have concluded that there is not enough evidence to consider making the treatment available at this time.

### 4. Effective From

This policy statement is effective from 5 October 2018.

### 5. Evidence Summary

#### 5.1. Overview of Clinical Evidence

One multicentre, randomised, sham-controlled clinical trial: Pathway CH-I (Schoenen et al 2013) has evaluated the use of SPG stimulation for the acute treatment of chronic cluster headache in patients whose condition was medically refractory. Two follow-up studies of patients in this trial have been reported (Jürgens et al 2017, Barloese et al 2016). A recent open-label study reported outcomes of this procedure (Barloese et al 2018).

The outcomes reported in the Pathway CH-I trial included pain relief, use of acute rescue medication, attack frequency and quality of life (Schoenen et al 2013).

Reported outcomes in the follow up studies were attack frequency, therapeutic response, preventative medication changes from baseline, headache disability improvements and patient satisfaction.

#### 5.2. Clinical Effectiveness

Twenty-eight of the 32 enrolled participants completed the randomised component of the Pathway CH-I trial. Participants were instructed to treat cluster attacks of moderate to severe intensity with 15 minutes of stimulation. Random insertion of placebo was used, meaning that when a participant initiated stimulation one of three possible stimulation doses was randomly applied in equal proportions for 15 minutes: full stimulation, sub-perception stimulation, or sham stimulation (Schoenen et al 2013).

A total of 566 cluster attacks were treated (190 full stimulation, 184 sub-perception stimulation and 192 sham stimulation). Two months post-insertion, SPG stimulation was found to be superior to sham stimulation for both pain relief at 15 minutes post-stimulation (67.1% vs. 7.4%,  $p < .0001$ ) and for pain freedom at 15 minutes post-stimulation (34.1% vs. 1.5%,  $p < .0001$ ) (Schoenen et al 2013). Mean cluster attack frequency dropped from 17.4 attacks per week at baseline to 12.5 attacks per week during the experimental period ( $p = 0.005$ ) (Schoenen et al 2013).

Thirty-three patients initially enrolled in the Pathway CH-I trial were followed for 24 months while receiving on-demand SPG stimulation. This number is inconsistent with the 32 subjects reported in the original trial. At 24 months, 45% (15/33) of patients experienced an acute response, 33% (11/33) experienced a frequency response and 6/33 patients experienced both types of response; a long-term overall responder rate of 61% was reported. A total of 64% (21/33) patients reduced or stopped at least one medication or remained free (9/33) of all preventive drugs (Jürgens et al 2017).

Eleven out of 33 patients (33%) followed up for 24 months reported having cluster attacks contralateral to the side of their inserted microstimulator. Five had contralateral attacks in the 6-month period before insertion of the device (Jürgens et al 2017).

Barloese et al (2018) is an open label study where 85 patients were followed up for 12 months. Patients had to have had cluster headaches for at least 16 weeks; most had tried several or all pharmaceutical options and were considered difficult to treat with a high headache burden. 68% of patients were responders, 55% of chronic patients were frequency responders (defined as at least a 50% reduction in frequency) and 32% of patients were acute responders (defined as being able to achieve effective therapy in at least 50% of attacks). 67% of patients reduced their medications.

The results of Barloese et al (2018) are comparable to those reported previously, as the authors themselves state: "Overall, the data presented here is very similar to previously published results of SPG stimulation with one exception: the proportion of acute uses of the stimulator achieving effective therapy was lower than previously reported (39% v 65%)".

Three of the publications in this review (Shoenen et al 2013, Jurgens et al 2017, and Barloese et al 2016) recruited the same patients and reported the results from one single study. The sample size was small – the authors analysed 28 out of the 32 patients initially enrolled although they reported adverse effects for all 32. The characteristics of the missing patients were not reported and it is therefore difficult to make any inferences from the results. The treatment duration in the experimental period was not clearly reported and it is not clear if it was the same for all 28 patients reported in the study.

The follow up for the initial randomised sham-controlled crossover trial was two months and the 24-month follow-up study was open label. The numbers of the patients enrolled were inconsistent – 32 (28 analysed) stated in the original trial and then 43 in the long term follow up trial (33 analysed) even though the authors stated in the inclusion criteria that only patients who had taken part in the original trial were included.

Participants in the long term follow up study were not randomised and there were no comparators so it is not possible to comment on how the results of effectiveness and safety compare with other acute medication or alternative surgeries. The results may be biased as both the participants and investigators were aware of the intervention being evaluated.

P-values were selectively reported. Where they were not reported, the statistical significance of the outcomes remains unknown. Statistically significant improvement was reported for the headache impact score and SF-36, although it is unclear how these outcomes translate to activities of daily living.

The evidence supporting implanted SPG stimulation device as a treatment option in refractory chronic cluster headaches is largely from one small study which is subject to significant bias and confounding of both study design, and the reporting of results. More reliable evidence is required to inform treatment policies.

### **5.3. Safety**

Serious adverse events were reported in five out of the 32 implantation procedures. This included the need for three stimulator lead revisions and two stimulator explants.

Sensory disturbance (26 of 32 patients) and pain (12 of 32 patients) were the most common adverse effects occurring immediately after implantation, mainly affecting maxillary nerve branches. After 3 months, only 16% of patients suffered from ongoing and mild sensory disturbance and 19% from local pain (Schoenen et al 2013).

Other adverse events included infection (one at the incision site, one in the maxillary sinus), mild paresis of muscles around the nasolabial fold (two participants), and operative maxillary sinus puncture (two participants) as well as common reports of pain, swelling, headache, hematoma, and dry eye (Schoenen et al 2013).

## **6. Equality Statement**

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

## **7. Responsible CRG**

Specialised Pain Services

## **8. Date Approved**

September 2018

## **9. Policy Review Date**

This document will be reviewed when information is received which indicates that the policy requires revision.

## **10. Links to Other Policies**

Not applicable.

## References

Barloese M, Jurgens T, May A, Lainez J, Schoenen J, Gaul C, Goodman A, Caparso A and Jensen R (2016). Cluster headache attack remission with sphenopalatine ganglion stimulation: experiences in chronic cluster headache patients through 24 months. *The Journal of Headache and Pain* 17(1): 67

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Schoenen J, Jensen R, Lanteri-Minet M, Lainez M, Gaul C, Goodman A, Caparso A and May A (2013). Stimulation of the sphenopalatine ganglion for cluster headache treatment. Pathway CH-1: a randomised sham-controlled trial. *Cephalalgia* 33 (10): 816-830

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