# Occipital Nerve Injections and Ablation (Including Occipital Neuralgia and Headache) (for Kansas Only)

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➲ Instructions for Use

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**Related Policies**

- Ablative Treatment for Spinal Pain (for Kansas Only)
- Botulinum Toxins A and B
- Durable Medical Equipment, Orthotics, Medical Supplies, and Repairs/Replacements (for Kansas Only)
- Electrical Stimulation for the Treatment of Pain and Muscle Rehabilitation (for Kansas Only)
- Vagus and External Trigeminal Nerve Stimulation (for Kansas Only)

## Application

This Medical Policy only applies to the state of Kansas.

## Coverage Rationale

### Members 18 Years of Age and Older

For medical necessity clinical coverage criteria for occipital nerve ablation for severe cancer pain due to malignancy involving the head and neck, refer to the InterQual® CP: Procedures, Neuroablation, Percutaneous.

Click here to view the InterQual® criteria.

**Injection of local anesthetics and/or steroids used as greater occipital nerve blocks is proven and medically necessary for treating pain due to malignancy involving the head and neck.**

**The following are unproven and not medically necessary for diagnosing and/or treating occipital neuralgia or headaches, including migraine and Cervicogenic Headaches, due to insufficient evidence of efficacy:**

- Injection of local anesthetics and/or steroids, used as greater occipital nerve blocks
- Neurostimulation or electrical stimulation
- Occipital Neurectomy
- Partial posterior intradural C1-C3 Rhizotomy
- Radiofrequency ablation (thermal or pulsed) or denervation
- Rhizotomy of C1-C3 spinal dorsal roots
- Surgical decompression of second cervical nerve root and ganglion
- Surgical decompression of the greater occipital nerve

## Members Under 18 Years of Age

**The following are proven and medically necessary for treating pain due to malignancy involving the head and neck:**

- Injection of local anesthetics and/or steroids used as greater occipital nerve blocks (GONBs)
- Occipital nerve ablation (destruction by neurolytic agent)

**The following are unproven and not medically necessary for diagnosing and/or treating occipital neuralgia or headaches, including migraine and Cervicogenic Headaches, due to insufficient evidence of efficacy:**

- Injection of local anesthetics and/or steroids, used as greater occipital nerve blocks
- Neurostimulation or electrical stimulation
- Occipital Neurectomy
- Partial posterior intradural C1-C3 Rhizotomy
- Radiofrequency ablation (thermal or pulsed) or denervation
- Rhizotomy of C1-C3 spinal dorsal roots
- Surgical decompression of second cervical nerve root and ganglion
- Surgical decompression of the greater occipital nerve

# Definitions

**Cervicogenic Headache**: Referred pain perceived in the head from a source in the neck. In the case of Cervicogenic Headache, the cause is a disorder of the cervical spine and its component bony, disc, and/or soft tissue elements. (American Migraine Foundation, 2016)

**Migraine Disability Assessment Test (MIDAS)**: The MIDAS questionnaire is a tool utilized to measure the impact headaches have on your life. The information on the questionnaire is helpful for the primary care provider to determine the level of pain and disability caused by headaches and to find the best treatment. After the questionnaire is completed, the total number of days from questions 1-5 are added together.

| MIDAS Grade | Definition | MIDAS Score |
|---|---|---|
| I | Little or No Disability | 0-5 |
| II | Mild Disability | 6-10 |
| III | Moderate Disability | 11-20 |
| IV | Severe Disability | 21+ |

If the MIDAS score is 6 or more, discussion with a provider is necessary (National Headache Foundation, 2018).

**Migraine-Specific Quality of Life Questionnaire (MSQ)**: The MSQ is a self-report measure that assesses the impact of migraine on three domains of quality of life: role functioning, emotional functioning, and social functioning. The MSQ consists of 14 items that are rated on a 6-point Likert scale, ranging from 1 (very poor) to 6 (very good). The MSQ has been widely used and proven effective in various languages and population samples. (Giannouli et al. 2024)

**Neurectomy**: Partial or total excision or resection of a nerve. (Taber's Medical Dictionary)

**Rhizotomy**: Surgical section of a nerve root to relieve pain. (Taber's Medical Dictionary)

# Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

| CPT Code | Description |
|---|---|
| 63185 | Laminectomy with rhizotomy; 1 or 2 segments |
| 63190 | Laminectomy with rhizotomy; more than 2 segments |

| CPT Code | Description |
|---|---|
| 64405 | Injection(s), anesthetic agent(s) and/or steroid; greater occipital nerve |
| 64553 | Percutaneous implantation of neurostimulator electrode array; cranial nerve |
| 64555 | Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve) |
| 64568 | Open implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator |
| 64570 | Removal of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator |
| 64575 | Open implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve) |
| 64590 | Insertion or replacement of peripheral, sacral, or gastric neurostimulator pulse generator or receiver, requiring pocket creation and connection between electrode array and pulse generator or receiver |
| 64596 | Insertion or replacement of percutaneous electrode array, peripheral nerve, with integrated neurostimulator, including imaging guidance, when performed; initial electrode array |
| 64597 | Insertion or replacement of percutaneous electrode array, peripheral nerve, with integrated neurostimulator, including imaging guidance, when performed; each additional electrode array (List separately in addition to code for primary procedure) |
| 64598 | Revision or removal of neurostimulator electrode array, peripheral nerve, with integrated neurostimulator |
| 64633 | Destruction by neurolytic agent, paravertebral facet joint nerve(s), with imaging guidance (fluoroscopy or CT); cervical or thoracic, single facet joint |
| 64634 | Destruction by neurolytic agent, paravertebral facet joint nerve(s), with imaging guidance (fluoroscopy or CT); cervical or thoracic, each additional facet joint (List separately in addition to code for primary procedure) |
| 64722 | Decompression; unspecified nerve(s) (specify) |
| 64744 | Transection or avulsion of; greater occipital nerve |
| 64771 | Transection or avulsion of other cranial nerve, extradural |
| 64999 | Unlisted procedure, nervous system |



| HCPCS Code | Description |
|---|---|
| A4540 | Distal transcutaneous electrical nerve stimulator, stimulates peripheral nerves of the upper arm |
| L8679 | Implantable neurostimulator, pulse generator, any type |
| L8680 | Implantable neurostimulator electrode, each |
| L8685 | Implantable neurostimulator pulse generator, single array, rechargeable, includes extension |

| Diagnosis Code | Description |
|---|---|
| C76.0 | Malignant neoplasm of head, face and neck |
| G89.3 | Neoplasm related pain (acute) (chronic) |

# Description of Services

Cervicogenic Headache and occipital neuralgia are conditions whose diagnosis and treatment have been gradually refined over the last several years. This terminology refers to specific types of unilateral headache thought to arise from impingement or entrapment of the occipital nerves and/or the upper spinal vertebrae. Compression and injury of the occipital nerves within neck muscles and compression of the second and third cervical nerve roots are generally felt to be responsible for the symptoms, including unilateral and occasionally bilateral head, neck, and arm pain. The criteria for diagnosis of these entities currently include those of the International Headache Society (IHS) and the Cervicogenic Headache International Study Group.

Various treatments have been advocated for Cervicogenic Headache and occipital neuralgia. Oral analgesics and anti-inflammatory agents are effective for some individuals, but there is a population of individuals who do not experience pain relief with these medications. Local injections or nerve blocks, epidural steroid injections, radiofrequency ablation of the

planum nuchae, electrical stimulation, Rhizotomy, ganglionectomy, nerve root decompression, discectomy, and spinal fusion have all been investigated in the treatment of headache and occipital neuralgia.

Since medications provide only temporary relief and may cause side effects, surgical treatments, such as occipital Neurectomy and nerve decompression for migraine and other headaches, have been developed as a potential means to permanently prevent or to produce long-term remissions from headaches.

Radiofrequency ablation is performed percutaneously. During the procedure, an electrode that generates heat produced by radio waves is used to create a lesion in a sensory nerve to inhibit the transmission of pain signals from the sensory nerve to the brain.

Neurostimulation, or electrical stimulation is commonly used for control of chronic pain. Electrical stimulation can be delivered in three ways: transcutaneously, percutaneously, and using implantable devices. Peripherally implanted nerve stimulation entails the placement of electrodes on or near a selected peripheral nerve. Targets for stimulation include occipital nerves, auriculotemporal nerves, supraorbital nerves, and sphenopalatine ganglia.

# Clinical Evidence

## Greater Occipital Nerve Blocks (GONB), Diagnostic and Therapeutic

There is insufficient evidence that GONBs are effective as a specific diagnostic test for occipital neuralgia (ON) or headaches. The efficacy of local injection therapies for ON or cervicogenic headache and other headaches has not been established in well-designed clinical trials.

GONBs have been advocated as a diagnostic test for cervicogenic headache and ON. However, criteria and standards for diagnostic GONBs remain to be defined. No well-designed clinical trials clearly indicate that injection of the greater occipital nerve (GON) can be used as a specific diagnostic test for headaches and ON.

In a randomized, double-blind, placebo controlled parallel group trial (ANODYNE) of GONBs with methylprednisolone and lignocaine versus placebo, Chowdhury et al. (2024) assessed the efficacy and tolerability of GONB injections as a transitional preventative treatment for episodic cluster headaches (ECH). The trial included individuals with ECH and diagnosed by the international classification of headache disorders 3rd edition (ICHD-3) criteria from the ages of 18 to 65, with one or more attacks per 24 hours for seven days before randomizations (baseline) The individuals with ECH were either not on preventative medications or on stable doses for at least three months. The individuals with ECH were randomized to receive active GONB [2 mL methylprednisolone (80 mg) and 2 mL lignocaine (2%)] and placebo (4 mL saline injections). Prior to the administration of GONB, lignocaine jelly was applied to the skin to mask the effect of numbness following the GONB. The main endpoint evaluated was the average change in the frequency of weekly attacks from baseline to the fourth week. All individuals who received at least one injection of GONB and had a follow up for one week following the GONB were monitored for efficacy in a modified intention to treat population. The analysis of safety included treatment-emergent adverse effects (TEAE) for all individuals that received at least one dose of the investigational product. The change in weekly attack frequency from baseline to the fourth week was -11.1 for the active group versus -7.7 for the placebo group. The authors pointed out that TEAE in 18 (90%) of 20 participants who received the active drug and in 18 (90%) of 20 those who received a placebo. The common TEAE uncovered were local site bleeding and pain, which were mild and transient. No serious adverse events were reported. Although this trial has a robust study design using International Headache Society (IHS)-recommended outcome measures, local lignocaine jelly application before GONB for masking, and inclusion of CAS restlessness and various patient-reported outcome measures (PROMs) in the secondary outcomes, limitations did exist as well. The limitations of the trial included the use of verapamil as a preventative, relatively small sample size, and the trial being a single-center experience. However, the findings of the trial underscore the utility of GONB with methylprednisolone and lignocaine as a transitional preventative for individuals with ECH. The authors concluded that GONB with methylprednisolone and lignocaine reduced the weekly attack frequency from baseline to week one through week four for individuals with ECH compared to the placebo. Overall, GONB was well tolerated. To evaluate the efficacy for individuals with ECH further, a head-to-head study comparing GONB with oral prednisolone would be beneficial.

Through a systematic review and meta-analysis, Li & Tang 2024 assessed the efficacy of GONB to treat acute migraines. Out of four randomized controlled trials (RCTs), 224 participants were included in the meta-analysis that showed that when compared with control intervention in acute migraine, GONB intervention could significantly reduce pain scores at 45 to 60 minutes and pain scores at 30 minutes. The intervention demonstrated no impact on pain scores at 0 to 15 minutes, sustained headache relief or rescue medication. Limitations of the analysis were the small sample size, limited number of studies, short follow up time, and lastly the episodic migraine (EM) and persistent migraine were included in the

analysis which could have affected the efficacy assessment. The authors concluded that the intervention of GONB may be able to alleviate pain intensity for acute migraine with an average reduction of pain scores at 30 to 60 minutes by about two [Friedman et al. (2020) and Korucu et al. (2018) are included in this systematic review].

In 2024, Mustafa et al. conducted a systematic review and meta-analysis to assess the effectiveness of GONB in chronic migraine focusing on the impact of local anesthetics when compared to a placebo. Included in the review were case-controlled, cohort and RCTs for adults with chronic migraine (adhering to the ICHD-3). The outcomes primarily measured were the frequency, duration, and intensity of headache along with safety assessments. The results of the review demonstrated a remarkable reduction in intensity and frequency of headaches in the first and second months of treatment with GONB when utilizing anesthetics compared to placebo. Adverse events reported did not differ significantly between the intervention and placebo groups. The limitations of the review were the small sample size, absence of sufficient data from recent trials preventing consideration of baseline characteristics, hindering the ability to perform meta-regression, and not accounting for pretreatment medications the participants may have taken during the procedure. Furthermore, the analysis did not address comorbidities specifically which could potentially influence the safety of the procedure for those with various comorbidities. The authors concluded that the administration of GONB with local anesthetic leads to a notable reduction in the intensity and frequency of headaches when compared to placebo, while underscoring the effectiveness of GONB and affirms their satisfactory safety profile. The analysis emphasized the safety and efficacy of GONB, although with a cautious interpretation due to the limited number of studies and relatively small sample size. Further research and future studies could delve into different aspects to provide a more comprehensive assessment of the safety profile of the procedure in diverse populations while exploring various drugs, frequencies, and treatment plans to enhance the robustness and applicability of GONB for the management of chronic migraine [Cuadrado et al. (2017), Gul et al. (2017), Inan et al. (2015), Dilli et al. (2015), and Özer et al. (2019), are included in this review].

An Evidence Analysis Research Brief produced by Hayes in 2023a summarized the volume of publications to determine whether there is adequate published peer-reviewed literature to evaluate the evidence related to GONB for the treatment of ON. The evidence analysis suggested that there is currently not enough published peer-reviewed literature to evaluate the evidence related to GONB for treating ON in a full assessment.

In 2023b, Hayes produced an Evidence Analysis Research Brief on Local Injection Therapy for Cervicogenic Headache and ON. According to the brief, which summarized the most recent evidence, there are newly published studies on local injection therapy for cervicogenic headache and ON. The new evidence consisted of systematic reviews with and without meta-analysis. There were no RCTs, evaluating the therapy, or studies evaluating treatment guided by the therapy. The brief concluded that there were no position statements or guidelines for the treatment, showing that the lack of available guidance appears to confer with no or unclear support for local injection therapy.

In a 2023 randomized, double-blind, placebo-controlled study, Chowdhury and associates explored the use of GONB for preventing chronic migraine. The trial consisted of a baseline period of four weeks. Participants with chronic migraine were randomly assigned 1:1 to the placebo. The participants obtained four-weekly bilateral GONB with either 2 mL of 2% (40 mg) lidocaine (active group n = 22) or 2 ml of 0.9% saline (placebo n = 22) injections for 12 weeks. The primary endpoint was the change from baseline across weeks 9-12 in the average number of headaches and migraine days (MD). The key secondary endpoint was achieving a 50% reduction in headache days compared to baseline across weeks 9-12. Documenting and reporting serious adverse events were conducted to evaluate safety. The average headache and MD at baseline (±SD) were 23.4 ±4.4 and 15.6 ±5.7 days in the active group and 22.6 ±5.0 and 14.6 ±4.6 days in the placebo group, respectively. The active group had a considerable gain in least-squares mean reduction in the number of headaches and MD when compared to the placebo [-4.2 days (95% CI: -7.5 to -0.8; p = 0.018) and -4.7 days (95%CI: 7.7 to 1.7; p = 0.003), in that order]. In the active group, 40.9% of individuals reached a ≥ 50% reduction in headache days versus 9.1% of those receiving a placebo (p = 0.024). There were 64 mild and transient adverse events recorded from 16 individuals in the active group and 15 in the placebo group, and no death or serious adverse events were reported. Four-weekly GONB, with 2% lidocaine for 12 weeks, was superior to placebo in reducing the average number of headaches and MD for individuals with chronic migraine and a good tolerability profile. The study does not represent individuals with a chronic migraine history of 2-4 preventive treatment failures, which limits the generalizability of study results. More robust trials with longer follow up are necessary to decide whether to use GONB to prevent chronic migraines.

In 2023b, Evans and colleagues conducted a systematic review and meta-analysis to investigate the change in headache severity and frequency following a nerve block of the occipital trigger site. RCTs that use injection treatments for headaches with pain or tenderness in the occipital scalp were included in the review (12 RCTs treating 586 individuals). Evaluations included pain severity; a score was given from 0-10, and the headache frequency was reported as days per week. The results of the meta-analysis of pain severity, which compared nerve blocks to baseline, showed statistically significant reductions of 2.88 points at 5 to 20 min, 3.74 points at 1 to 6 weeks, and 1.07 points at 12 to 24 weeks. Meta-analyses of pain severity of nerve blocks compared with treatment groups of neurolysis, pulsed radiofrequency, and

botulinum toxin type A showed similar headache pain severity at 1 to 2 weeks and inferior improvements compared with the treatment groups after two weeks. Meta-analyses of headache frequency showed statistically significant reductions at 1- to 6-week follow-ups compared with baseline and at 1- 6 weeks with inactive control injections. The authors concluded that the severity and frequency of occipital headaches are reduced following occipital nerve blocks (ONB) and can be used to predict the success of migraine surgery. However, future research should investigate the long-term outcomes of the sub compartmental injection technique, particularly for changes in headache frequency.

Gordon and associates (2023) conducted a systematic review to evaluate the effectiveness and safety profile of GONB for individuals with cluster headaches. Participants included were those with a cluster headache diagnosis and received corticosteroid and local anesthetic suboccipital region injections. The outcomes measured were changes in the frequency/severity/duration of attacks, proportion of individuals responding to treatment, time to attack freedom from an attack, change in attack about length, and/or the presence of adverse effects of GON blockade. The review found that every effectiveness study found a significant response in one or more of the frequency/severity/duration of attacks or the proportion of individuals responding to the treatment (47.8%-100.0%). A higher injectate volume and use of concurrent prophylaxis may be associated with an increased likelihood of response. Methylprednisolone may have the best safety profile of available corticosteroids. The limitations of this study include the lack of exclusion criteria for study design, inability to undertake a quantitative data synthesis, and methodological and reporting inconsistency between studies. The authors concluded that GON blockade is safe and effective for CH prevention. Higher injectate volumes may improve the likelihood of response, and the possibility of serious adverse events may be reduced using methylprednisolone.

Elsayed et al. 2023, as part of a double-blinded RCT, aimed to compare the pain-relieving effect between distal and proximal ultrasound (US)-guided bilateral GONBs for post dural puncture headache (PDPH). This study included 50 PDPH participants and was randomized into two equal groups. Group D received a US-guided distal bilateral GONB (at the superior nuchal line level). Group p received a US-guided proximal bilateral GONB (at the second cervical vertebra level). Three milliliters of isobaric bupivacaine 0.5% and 4 mg dexamethasone were injected in both blocks. The study demonstrated a significant decrease in lying down and sitting Numeric Rating Scale (NRS)-11 at 10 minutes, 6, 12, 24, 36, and 48 hours after the intervention compared to before the intervention in both groups. Only sitting NRS-11 was significantly lower in group p than group D in all measurements after the intervention. The success rate (sitting NRS-11 < 4) at 24 hours was 60% in group D and 84% in group P, with an insignificant difference. The total 48-hour paracetamol and tramadol consumption were significantly lower in group p than in group D ($p = 0.038$ and 0.036, respectively). Transient cervicalgia occurred in 8% of each group. The limitations of the study included the small number of cases that proved the secondary outcomes, along with the absence of a control group. The authors concluded that US-guided proximal and distal GONBs were minimally invasive, simple, and effective ways to treat PDPH, with the superiority of proximal GONB in alleviating PDPH.

In a 2022 systematic review with meta-analysis, Velásquez-Rimachi and colleagues evaluated evidence and quality assessment of GONB local anesthetic combined or not with corticosteroids to prevent chronic migraine. The authors measured efficacy by assessing the change from baseline in the intensity and frequency of headaches in the intervention group compared to the placebo at a one-time point. The meta-analysis was performed with random effect models and evaluated random errors with the trial-sequential analysis (TSA), the risk of bias with the risk of bias tool, and the certainty of the evidence with Grading of Recommendations, Assessment, Development, and Evaluations (GRADE). The review uncovered 2864 studies that showed GONB reduced the intensity of headaches at the end of the first month (MD: -1.35, 95% CI: -2.12 to -0.59) and the second month (MD: -2.10, CI 95%: -2.94 to -1.26) as well as the frequency of headaches (first month: MD: -4.45 days, 95% CI: -6.56 to -2.34 days; second month: MD: -5.49, 95% CI -8.94 to -2.03 days). Corticosteroids did not show a significant decrease in the frequency of headaches during the first month of treatment (MD: -1.1 days, 95% CI: -4.1 to 1.8, $p = .45$). Adverse events between the groups were similar, and the exploratory TSA demonstrated inconclusive results. The authors concluded that the limited evidence shows that GONB with local anesthetics can reduce the frequency and intensity of headaches compared to a placebo and adding corticosteroids did not demonstrate any additional benefits. However, the quality of the evidence was deficient because of the substantial risk of bias and imprecision. Additionally, considering the TSA was inconclusive, more extensive, more specific trials are necessary.

Malekian et al. (2022) conducted a randomized, double-blind, placebo-controlled trial; individuals suffering from EMs without aura were randomized to triamcinolone or lidocaine, triamcinolone plus lidocaine, or saline groups. Individuals were evaluated at baseline, one week, two weeks, and four weeks after the injection. All 55 participants who completed the study were assessed for severity, duration of headaches, and side effects. In all four groups, the analysis of variance (ANOVA) measures revealed that the severity and duration reduced considerably after the greater occipital block ($p < 0.001$, $p = 0.001$, respectively). No difference was shown amongst groups at any point during the study ($p > 0.05$). A considerable decrease in frequency compared to baseline ($p = 0.002$, $p = 0.019$) was noted for groups two and three with lidocaine as part of the injection in paired sample T-test. Reported side effects with an association with triamcinolone were

seen in three participants. The authors concluded that GOB with a local anesthetic reduces the number of attacks in EM. No injection was better than the placebo regarding the duration and severity of the headaches. The trial uncovered that all four types of injections used effectively decreased the severity and the duration of headaches in EM, and no block solution was better than the 0.9% saline solution as a placebo at any of the time points. The trial uncovered a significant decrease in headaches for individuals receiving lidocaine alone or combined with triamcinolone compared to 0.9% saline injection or triamcinolone. Further studies exploring whether these results were caused by the compressive effect of injected solution, or the placebo effect are necessary.

Hasırcı Bayır et al. (2022) conducted a retrospective review of medical records to examine the efficacy of GONB for adults with primary headaches. The study included 53 participants from a single center outpatient clinic who presented with EM (n = 36), tension-type headache (n = 12), chronic migraine (n = 4), or cluster headache (n = 1) and who completed a three-month follow-up visit. The study population was predominately female (86.79%), with a median age of 43.06 years. The participants underwent evaluation before and after receiving a GONB for headache type, attack duration, attack frequency, the severity of pain, and analgesic intake. Their initial values were compared with the follow-up values at months one, three, and six. The participants underwent GONB once a week for three weeks then once a month if they reported a decrease in the duration, severity, or frequency of headache for a maximum of six months based on their clinical responses. The authors reported that the migraine group showed a statistically significant decrease in Visual Analog Scale (VAS) scores, attack duration, the mean value of monthly number of attacks and analgesics taken at months compared to their initial scores. Participants in the tension-type headache group showed a statistically significant decrease in their VAS scores, attack durations, mean value of the monthly number of attacks, and analgesics taken compared to their initial scores at the end of the three-month follow-up. The values for the tension-type headache group at six months were statistically not significant as only two of the 12 participants completed the six-month follow-up. Limitations of the study include the small sizes of each headache type, the preponderance of female participants, the use of various concomitant medications during the trial by some participants, and the study design. The authors concluded that repetitive GONB is an effective treatment method for migraine and tension-type headaches.

In a meta-analysis aimed at evaluating the therapeutic effectiveness of GONB against PDPH, Chang et al. (2021) reviewed seven studies (four RCTs and three non-RCTs) to determine the severity of pain at 24 hours post-procedure. The authors defined intervention failure as repeated GONBs, the use of analgesics, or the need for an epidural blood patch. Secondary outcomes analyzed in this study included the impact of GONB on pain relief at one hour and 12 hours post-procedure. Their meta-analysis included 275 adult individuals, and the sample sizes of the included studies ranged from 16 to 90 participants. The authors found a moderate risk of bias among the non-RCT studies overall. They reported that the pooled results showed a lower mean pain score at 24 hours and at one hour and 12 hours post-procedure. The analysis also showed that using GONB also decreased the risk of intervention failure. Limitations noted by the authors included high heterogeneity among the study populations, the difference in treatment provided to the control groups (placebo, bed rest, hydration, oral analgesics), the small number of RCTs available for analysis, and the short-term follow-up of 24 hours. The authors concluded that their meta-analysis showed that GONB has a therapeutic effect up to 24 hours post-procedure against PDPH with a low risk of intervention failure. They recommended further large-scale studies to evaluate the therapeutic benefit of GONB beyond the acute phase of PDPH.

Caponnetto et al. (2021) conducted a systematic review to summarize the effectiveness and safety of GONBs in treating cervicogenic headaches. The authors included seven studies; five observational studies, and two non- RCTs with a total of 140 participants. Follow-ups for outcomes evaluation varied among the studies, ranging from five minutes to nine months after the procedure. Pain intensity was evaluated through the VAS or the Numeric Pain Rating Scale (NPRS). The monthly mean frequency of pain was 27 days at baseline and changed to 3.2 after one week, 2.4 after two weeks, 3.6 after 1.5 months, and 2.3 after 3.5 months. In five studies, mean pain reduction ranged from 8.2 (at two weeks after the first block) to -0.1 (at one month after the third block). Three studies reported minor adverse events. The authors concluded that the limited available evidence suggested that GONBs effectively improve pain for individuals with cervicogenic headache, both as acute and as a preventative treatment. The available studies were either observational, non-controlled, or non-randomized trials with low-level evidence. Larger and randomized studies are needed to confirm the efficacy of the procedure. [Author Lauretti et al. (2014), previously cited in this policy, is included in this study].

Friedman et al. (2020) conducted an RCT to determine whether GONB was as effective as intravenous (IV) metoclopramide for migraine. A double-dummy, double-blind, parallel-arm, non-inferiority study was conducted in two emergency departments (EDs). Individuals with moderate or severe intensity migraines were randomized to receive bilateral GONB, with each side administered 3 mL of bupivacaine 0.5% or metoclopramide 10 mg IV. The primary outcome was improvement in pain on a 0-10 scale between time zero and one hour later. Secondary outcomes included sustained headache relief, defined as achieving and maintaining for 48 hours a headache level of mild or none without the use of additional analgesic medication and rescue medication in the ED. Over a 2.5-year study period, 99 participants were randomized, 51 to GONB and 48 to metoclopramide. Those who received the GONB reported a mean improvement

of 5.0, and those who received metoclopramide reported a mean improvement of 6.1. Sustained headache relief was reported by 11/51 (22%) GONB and 18/47 (38%) metoclopramide participants. Of the 51 individuals with GONB, 17 (33%) required rescue medication in the ED vs. 8/48 (17%) metoclopramide-participants. An adverse event was reported by 16/51 (31%) GONB participants and 18/48 (38%) metoclopramide-participants. The authors concluded that GONB with bupivacaine was less efficacious than IV metoclopramide for the first-line treatment of migraine in the ED. [Included in the (2024) systematic review by Li & Tang].

A 2019 Hayes Health Technology Assessment report focused on the efficacy and safety of GONB for the preventive treatment of chronic migraine headaches for individuals with an inadequate response to standard care. GONB with an injection of a local anesthetic is relatively safe and may improve most headache outcomes over the short term compared with placebo. Little to no evidence meeting inclusion criteria was found around benefit of chronic use of this therapy. There is a need for additional, larger, well-designed controlled trials with longer follow-up to adequately determine the optimal clinical role of GONB in the preventive treatment of chronic migraine. There was small or insufficient evidence for the use of GONB for the prevention of debilitating symptoms of EM or transformed migraine in adults who do not respond adequately to standard therapy. An updated literature search was performed by Hayes in October 2021 that found one newly published study that met the inclusion criteria; however, the data did not result in a change to their report recommendations. The overall quality of the body of evidence remained rated as low due to individual study limitations, some inconsistencies in outcomes, and imprecision in some comparisons or outcomes examined in only a few studies or a single study. In the 2022 annual review, an updated literature search was performed by Hayes, uncovering one newly published study meeting the inclusion criteria. Hayes did not change their rating, which is based on low-quality evidence that suggests GONB with an injection of a local anesthetic is relatively safe and could improve most headache outcomes over the short term when compared to placebo. The low rating reflects the heterogeneity in the patient populations and varying treatment protocols across studies. Additionally, there is little to no evidence that meets the inclusion criteria that found a benefit for chronic therapy use. The review again concluded that there is a need for added, well-designed controlled trials that have a longer follow-up to determine the optimal clinical role of GONB for preventing chronic migraines. Similarly, for the use of GONB in preventing debilitating symptoms of EM or transformed migraine in adults who do not respond to standard therapy, the review rating remained low based on the paucity of evidence on these types of migraines [Hayes, (2019), updated (2022)].

A systematic review and meta-analysis were conducted by Shauly et al. (2019) to determine the efficacy of GONB in the treatment of chronic migraine headaches. Nine studies were analyzed that reported mean number of headache days per month in both intervention and control groups. The study included 440 participants (intervention, n = 224; control, n = 216). Six of the included RCTs reported intervention treatment as either bupivacaine or lidocaine versus saline injection. Three of the included RCTs reported intervention treatment as corticosteroid in addition to bupivacaine or lidocaine versus bupivacaine or lidocaine with saline as the control group. Eight of the studies that were analyzed reported the mean headache days per month in both intervention and control groups. A total of 417 individuals were studied, with a pooled mean difference of −3.6 headache days (95 percent CI, −1.39 to −5.81 headache days; $p < 0.00001$). Pooled mean difference in pain scores of -2.2 (95 percent CI, -1.56 to -2.84) also demonstrated a decrease in headache severity compared with controls ($p < 0.0121$). Seven of the studies assessed reported mean VAS pain scores. Pooled mean difference in pain scores of −2.2 (95 percent CI, −1.56 to −2.84; $p = 0.0121$). Two studies also reported those that experienced a greater than 50 percent reduction in headache frequency. Risk ratios were calculated in these two studies, and the average risk ratio was found to be 0.76 (95 percent CI, 0.97 to 0.55; $p < 0.00001$). The authors concluded that greater occipital nerve blocking should be recommended for use for individuals with migraines, particularly those that may require future surgical intervention. The block may act as steppingstone for those experiencing migraine headache because of its usefulness for potentially assessing surgical candidates for nerve decompression. The included studies had some limitations. For one, those in the control group in three of these studies were also given bupivacaine or lidocaine, whereas the intervention included corticosteroids. Variations between the control and intervention groups may skew the results of the meta-analysis. Another limitation of this study is the quality of included studies. Most of the included studies exhibited a relatively small sample population. Clinical trials with a much larger sample population and longer period of observation should be conducted.

Özer et al. (2019) performed a study aimed to evaluate the efficacy of GON and supraorbital nerve (SON) blockade with local anesthetics for the preventive treatment of migraine without aura (MWOA). Eighty-seven individuals diagnosed with MWOA were included in the study and randomly divided. One group was injected with 1% lidocaine; the other group was injected with 0.9% saline. GON and SON injections were done bilaterally. The injections were repeated weekly for three weeks. Participants were followed up for two months to assess clinical response. Seventy-one participants completed the study. After two months, the number of headache days decreased from 12.8 ±10.9 to 5.3 ±7.4, and VAS decreased from 8.3 ±1.0 to 5.5 ±1.9 in the blockade group. The number of headache days decreased from 12.4 ±10.3 to 7.5 ±7.2, and VAS decreased from 8.2 ±1.1 to 7.4 ±1.3 in the placebo group. Response was seen in 65.1% of the participants in the blockade group (65.4% for EM, 64.7% for chronic migraine) and 28.6% in the placebo group. The authors reported that

the results suggest that GON and SON blockade with lidocaine was more effective than the placebo in the prophylactic treatment of both episodic and chronic migraine [Included in the systematic review by Mustafa et al. (2024)].

A retrospective study was performed by Gönen et al. (2019), which included 51 individuals with episodic and chronic cluster headache that underwent GONB with a single dose of rapid and long-acting steroid injection without additional prophylactic treatment. Pain assessment was performed using the VAS. The participants were asked to keep a record of the frequency, severity, and duration of attacks after GONB. In 28 (54.9%) individuals, no attack occurred after GONB, and cluster bouts were halted. Mean duration of attacks was 86.67 ±37.45 min before the treatment. In the 23 individuals that had at least one attack after GONB, the mean duration of attacks was 31.73 ±36.10 min between post-treatment days 0-3, 29.35 ±40.49 min between post-treatment days 4-10, 28.48 ±42.17 min between post-treatment days 11-28, and 35.65 ±46.55 min after the post-treatment day 28 ($p < 0.001$). Between post-treatment days 0-3, the VAS score was 0 in 70.6% (n = 36), between 1 and 5 in 13.7% (n = 7), and between 6 and 10 in 15.7% (n = 8) of the participants. Between post-treatment days 4-10, the VAS score was 0 in 76.5% (n = 39), between 1 and 5 in 7.8% (n = 4), and between 6 and 10 in 15.7% (n = 8) of the participants. Between post-treatment days 11-28, the VAS score was 0 in 80.4% (n = 41), between 1 and 5 in 3.9% (n = 2), and between 6 and 10 in 15.7% (n = 8) of the individuals. After the post-treatment day 28, the VAS score was 0 in 86.3% (n = 44) and between 6 and 10 in 13.7% (n = 7) of the participants. The authors concluded that GONB is a practical, reliable, and cost-effective treatment option for individuals with episodic and chronic cluster headache. The study is limited by its retrospective observations and small sample size [Included in the Gordon et al. (2023) systematic review].

A systematic review and meta-analysis were conducted by Zhang et al. (2018) to investigate the impact of GONB on pain management of migraine. Seven RCTs (n = 323) assessing the efficacy of GONB versus placebo for migraine were included. The primary outcome was pain intensity. The authors concluded that GONB intervention can significantly reduce pain intensity and analgesic medication consumption but has no remarkable impact on headache duration and adverse events compared with control intervention for individuals with a migraine. The analysis was based on only seven RCTs, with relatively small sample size (n < 100) and short follow-up time.

A prospective-randomized controlled study was conducted by Korucu et al. (2018) to evaluate the effectiveness of a GONB against a placebo and classical treatments (non-steroidal anti-inflammatory drugs and metoclopramide) among those who were admitted to the ED with acute migraine headaches. Sixty participants were randomly assigned to three treatment groups: the GONB group (nerve blockade with bupivacaine), the placebo group (injection of normal saline into the GON area), and the IV treatment group (IV dexketoprofen and metoclopramide). The pain severity was assessed at 5, 15, 30, and 45-minutes with a 10-point pain scale score (PSS). The mean decreases in the 5-, 15-, 30-, and 45-minutes PSS scores were more significant in the GONB group than in the dexketoprofen and placebo groups. The authors concluded that a GONB was as effective as an IV dexketoprofen + metoclopramide treatment and superior to a placebo for individuals with acute migraine headaches. No follow-up was noted [Included in the (2024) systematic review by Li & Tang].

Tang et al. (2017) conducted a systematic review and meta-analysis to explore the efficacy of GONB for individuals with migraines. Six RCTs assessing the efficacy of GONB versus placebo for individuals with migraine were included. Compared with control intervention for individuals with migraines, GONB intervention was found to significantly reduce pain score, number of headache days, and medication consumption but demonstrated no influence on duration of headache per four weeks. The authors concluded that GON block intervention can significantly alleviate pain, reduce the number of headache days and medication consumption, but have no significant influence on the duration of headache per four weeks for individuals with migraine. The short-term follow-up did not allow for assessment of intermediate and long-term outcomes.

Gul et al. (2017) evaluated the efficacy of GONB for individuals with chronic migraine in randomized control study. The study included 44 individuals with chronic migraine who were randomly divided onto two groups: group A (bupivacaine) and group B (placebo). GONB was administered four times (once per week) with bupivacaine or saline. After four weeks of treatment, participants were followed up for three months, and findings were recorded once every month for comparing each month's values with the pretreatment values. The primary endpoint was the difference in the frequency of headache (headache days/month). The VAS pain scores were also recorded. No severe adverse effects were reported. Group A showed a significant decrease in the frequency of headache and VAS scores at the first, second, and third months of follow-up. Group B showed a significant decrease in the frequency of headache and VAS scores at the first month of follow-up, but second and third months of follow-up showed no significant difference. The authors concluded that their results suggest that GONB with bupivacaine was superior to placebo, has long-lasting effect than placebo, and was found to be effective for the treatment of chronic migraine. More studies are needed to better define the safety and cost-effectiveness of GONB in chronic migraine [Included in the systematic review by Mustafa et al. (2024)].

Cuadrado et al. (2017) assessed the short-term clinical efficacy of GON anesthetic blocks in chronic migraine in a double-blind, randomized, placebo-controlled clinical trial. Thirty-six women with chronic migraine were treated either with bilateral GON block with bupivacaine 0.5% (n = 18) or a sham procedure with normal saline (n = 18). Headache frequency was recorded a week after and before the procedure. Pressure pain thresholds (PPTs) were measured in cephalic points (supraorbital, infraorbital, and mental nerves) and extracephalic points (hand, leg) just before the injection (T0), one hour later (T1) and one week later (T2). Anesthetic block was superior to placebo in reducing the number of days per week with moderate-or-severe headache, or any headache. Overall, PPTs increased after anesthetic block and decreased after placebo; after the intervention, PPT differences between baseline and T1/T2 among groups were statistically significant for the supraorbital and infraorbital sites. The authors concluded that GON anesthetic blocks appear to be effective in the short term in chronic migraine, as measured by a reduction in the number of days with moderate-to-severe headache or any headache during the week following injection. This study was limited by its heterogeneous population and small sample size [Included in the systematic review by Mustafa et al. (2024)].

## Surgical Treatment of Occipital Neuralgia (ON) or Cervicogenic Headache

A number of different surgical procedures such as dorsal nerve root section, occipital neurectomy, partial posterior rhizotomy, cervical spine disc excision with fusion, and surgical nerve release, have been studied for the treatment of ON and cervicogenic headache.

The available evidence is insufficient to conclude that surgery is an effective treatment for ON or cervicogenic headaches. The long-term efficacy of surgical procedures for ON or cervicogenic headaches has not been established in well-designed clinical trials.

In a 2024a Hayes Evidence Analysis Research Brief, neuroplasty for the treatment of ON was reviewed. The aim of the review was to summarize the volume of publications related to neuroplasty for treating ON, and to determine if there is adequate published peer-reviewed literature to conduct a full assessment of the evidence. Adequate published peer-reviewed literature to evaluate the evidence was uncovered although conclusions about the safety and effectiveness cannot be made within the report due to the lack of full text being reviewed. If this technology is found to be emerging, evolving, controversial or disruptive and the degree to which it is a priority to consumers then a full appraisal will be conducted. There were no RCTs or clinical studies evaluating neuroplasty. There were six studies uncovered that evaluate the treatment guide by neuroplasty and one systematic review without a meta-analysis. There were no position statements or guidelines identified which suggests there is no or unclear support for using neuroplasty for individuals with ON [Pietramaggiori & Scherer (2023) is included in this review; Li et al. (2012) and Choi et al. (2015) which was previously cited in this policy is also included in this review].

In 2023a, Evans and associates conducted a systematic review and meta-analysis to summarize the effect of migraine surgery on headaches, severity, frequency, and migraine headache index (MHI) scores derived by multiplying migraine severity, frequency, and duration. Included in the review were clinical trials treating headaches with surgery, and the meta-analyses were performed on outcomes using a random effects model and determined the pooled average change from baseline, when possible, to compare treatment to control. Included in the review were 18 studies with six RCTs, one clinical trial, 11 controlled clinical trials treating 1143 individuals with pathologies including migraine, occipital migraine, frontal migraine, occipital nerve triggered headache, frontal headache, occipital neuralgia, and cervicogenic headache. It was found that migraine surgery reduced the headache frequency at one year postoperative by 13 days per month when compared to baseline (I2 = 0%), reduced headache severity at eight weeks to 5 years postoperative by 4.16 points on a 0-10 scare when compared to baseline (I2 = 53%), and reduced MHI at one to five years postoperative by 83.1 points when compared to baseline (I2 = 2%). The limitations of the meta-analyses are the small number of studies that could be analyzed, including studies with a high risk of bias. The authors concluded that the migraine surgery supplied a clinically statistically significant reduction in headache frequency, severity, and MHI scores. Additional studies, including RCTs with a low risk of bias, should be performed to improve the precision of the outcome.

Goyal et al. (2022) performed a systematic review to evaluate various interventional treatment for cervicogenic headache and compare their relative efficacies. The final analysis consisted of 23 articles published between January 2001 and March 2021. Eleven studies evaluated the effect of radiofrequency ablation (RFA); five evaluated ONB, two for facet joint injections, two for cervical epidural injection, and two for cryoneurolysis. The ONB [GON, lesser occipital nerve (LON)] showed only limited evidence, as most of the studies were non-controlled and yielded only transient benefits. Radiofrequency lesioning may be preferable over other interventions because of its long duration of effect, better efficacy, and fewer side effects. Conventional RFA is neuro-destructive and is associated with high complication rates such as neuritis or deafferentation pain. The authors noted several limitations in their review including the lack of available RCTs, the structure, the heterogeneity of the inclusion/exclusion criteria and outcomes assessed among the studies, the small sample sizes and short follow-up periods in the studies and the flaws and inconsistencies in some of the study designs. Based on available literature, the authors concluded that ONB may be a reasonable option for cervicogenic headache

treatment. Radiofrequency lesioning was found to be better with long-term positive outcomes, and pulsed therapy had better safety. However, the review revealed only limited evidence, and additional large, prospective, well-designed RCTs are needed to provide more concrete evidence and to establish relative efficacy of the various available interventions discussed for the management of cervicogenic headache [Included in the (2023a) Hayes Evidence Analysis Research Brief].

A systematic review and meta-analysis to evaluate the proportion of individuals with migraine reporting elimination of migraine headache (MH) after migraine trigger site surgery and whether surgery compared to sham or no surgery is more effective in the elimination of MH was conducted by Vincent et al. (2019). A total number of 627 participants with a diagnosis of migraine in compliance with the classification of the International Headache Society (IHS) were included. The treatment consisted of one or more surgical procedures involving the extracranial nerves and/or arteries with outcome data available at minimum six months. A proportion of 0.38 of participants [random effects model, 95% CI (0.30–0.46)] experienced elimination of migraine headaches at 6-12 months follow-up. Using data from three RCTs, the calculated odds ratio for 90-100% elimination of migraine headaches is 21.46 [random effects model, 95% CI (5.64–81.58)] for individuals receiving migraine surgery compared to sham or no surgery. The authors reported that migraine surgery leads to elimination of migraine headaches in 38% of individuals with migraines. However, more elaborate randomized trials are needed with transparent reporting of patient selection, medication use, and surgical procedures and implementing detailed and longer follow-up times.

## Nerve Decompression and Occipital Neurectomy for Headaches

The available evidence is insufficient to conclude that occipital neurectomy or nerve decompression, including decompression of the supraorbital, supratrochlear, zygomaticotemporal, or GONs, is an effective treatment for headaches. The long-term efficacy of these procedures for headaches has not been established in well-designed clinical trials.

In a systematic review and meta-analysis, Alrahbeni et al. (2024) aimed to analyze surgical approaches for refractory or intractable migraines. The literature collected focused on studies related to migraines and surgical outcomes, clinical trials or observational studies that included any surgical intervention for refractory or intractable migraines emphasizing key outcomes as such reductions in the intensity of the migraine, MIDAS, and 50% MHI reduction rates. A total of 11 studies were included in the systematic review while a meta-analysis of four studies involving overall 95 individuals showing a reduction in the average intensity of the migraine using ONS. An average MIDAS score reduction of -52.3 was seen through three studies involving 85 individuals, although this was not statistically significant. A substantial decreased in the average migraine intensity was seen with nerve decompression surgery (from 8.31 down to 4.06). The median MIDAS score dropped from 57 to 20, while two studies indicated a success rate of 40 to 82%, respectively for achieving a 50% reduction in the migraine MHI through nerve decompression. Two of the study's findings suggested that septorhinoplasty and sinus surgery effectively decreased the migraine intensity scores. The limitations of the study were the restriction of inclusion criteria to articles published solely in English, outcomes such as migraine intensity, MHI, and MIDAS were based on patient-reported outcomes, study design, the absence of direct statistical comparison between intervention and control groups which limits the strength of the conclusions, and the limited number of trials included in the analysis. The authors concluded that the evidence puts an emphasis on the potential advantages of surgical interventions as a promising approach to managing intractable or refractory migraines, however more robust, comprehensive research is necessary to refine and solidify the efficacy of the methods that aim for widespread benefits, while considering cot-effectiveness [Rodrigo et al. (2017) which was previously cited in this policy is included in this review].

Through a 2024b Hayes, Evidence Analysis Research Brief, the volume of publications related to auriculotemporal nerve decompression (ATN) for treating migraine was evaluated. Through a review of abstracts, it was determined that there is not enough published peer-reviewed literature to evaluate the evidence in a full assessment. There were no RCTs identified. There was one study found that evaluated ATN decompression that compared ATN sparing vs. ATN and superficial temporal artery sparing resection. One study that evaluated treatment guided by nerve decompression was identified along with a systematic review without a meta-analysis. There were no position statements or guidelines identified suggesting no or unclear support for the use of ATN decompression for treating migraine headache [Pietramaggiori & Scherer (2023), and Baldelli et al. (2020) are included in this analysis].

In 2024c, Hayes conducted an Evidence Analysis Research Brief to summarize the volume of publications related to supratrochlear or SON decompression for treating migraine headache to determine if there is adequate published peer-reviewed literature to evaluate the evidence in a full assessment. Through a review of abstracts, it was determined that there is adequate published peer-reviewed literature although conclusions about safety and effectiveness cannot be made within the report due to the lack of a full-text review. If supratrochlear or SON decompression becomes emerging, evolving, controversial or disruptive a full assessment will likely be completed. There were no randomized control trials identified. There were two studies found that evaluated supratrochlear or SON decompression comparing glabellar

myectomy alone vs. combined with supraorbital foraminotomy, or front, occipital, or temporal trigger site decompression identified. Also uncovered were three studies that evaluated the treatment guided by supratrochlear or SON decompression, although no position statements or guidelines were identified suggesting no or unclear support for the treatment. The evidence that was uncovered consisted of two comparative studies, three single-arm studies, and one systematic review with a meta-analysis [Jose et al. (2018)] which was previously cited in this policy is included in this review).

In the 2023 literature analysis by Pietramaggioria and Scherer, the authors describe a minimally invasive nerve and muscle-sparing technique to decompress the occipital nerves. The outcomes measured were the MDs per month, use of medications, pain evaluation, and decrease in MHI analyzed by a retrospective chart review which included 87 individuals who underwent nerve and muscle-sparing surgical decompression of the greater and lesser monoliteral or bilateral occipital nerves while being followed up for 12 months. The review showed that Surgical decompression significantly reduced ON burden (at least 50% improvement) in 91% of individuals, with 45% reporting a complete remission of occipital pain. Days with pain per month decreased by 80%, chronic background pain intensity decreased by 81%, and pain intensity during crisis decreased by 76%. Accordingly, drug use dropped by approximately 70%. The authors concluded that a surgical technique could contribute to and support surgical decompression as the first option among the invasive approaches to treat occipital neuralgia. The results of the analysis corroborate \ previous findings [included in the (2024a) Hayes Evidence Analysis Brief on neuroplasty treatment for ON, and the (2024b) Hayes Evidence Analysis Brief on Auriculotemporal Nerve Decompression for Treatment of Migraine Headache].

McNutt et al. (2020) conducted a systematic review of 12 articles [Including Pisapia (2012), Ducic et al. (2009), Choi (2015), Jose et al. (2018), and Li et al. (2012) below] that directly addressed the question of neurolysis (NL) versus neurectomy (NR) for the treatment of ON after failure of conservative therapy to provide clarity regarding differences between the two approaches and a recommendation on the superiority of one treatment over the other. The articles included seven observational studies and five single case reports. No RCTs were identified in their literature search, and all were found to be level IV, low-quality evidence so they were unable to complete a meta-analysis. There was a total of 473 participants in the analysis with follow-up between two months and 5.6 years. Their analysis showed that individuals had a positive outcome when they had a positive response to GONB or Botox, tenderness over the GON and were under the care of a neurology specialist or pain specialist; however, the longer duration of the headache (greater than 13 years) and retro-orbital/frontal radiation were associated with treatment failure. The authors noted that the included studies utilized various inclusion and exclusion criteria as well as outcome measures. Other limitations they noted included the number of case reports, lack of comparison group in many studies, high dropout rates, small sample sizes, lack of blinding and a lack of correlating outcomes to a particular surgical treatment. After reviewing the data, the authors found there was conflicting results for NL and no consistent outcome identified for NR. They found that many participants had concomitant headache diagnoses and additional confabulators, and they were not screened for other causes of occipital headache. The authors determined there was insufficient evidence to recommend one treatment method over the other. The authors stated that higher-quality studies including RCTs are needed to evaluate these surgical options.

A systematic review and meta-analysis were conducted by Baldelli et al. (2020). The nine selected studies included seven retrospective studies (4 case-control; 3 case series), one blinded randomized controlled clinical trial, and one a prospective cohort study. A total of 1135 individuals were included in studies on occipital nerve decompression with different surgical techniques. The sample size of each study ranged from 11 to 476. Surgical outcome was measured with the migraine headache questionnaire, the percentage of postoperatively pain relief, and the MHI. Follow-up was at least six months in each study. General positive response after surgery (> 50% reduction in occipital migraine headaches) ranged from 80.0% to 94.9%. The authors concluded that success in occipital decompression surgery is high, surpassing 90% in several studies but other RCTs are necessary to definitively confirm the findings. A main limitation is the retrospective nature of most of the studies. [Authors Ducic et al. (2009) and Guyuron et al. (2009), which were previously cited in this policy, are included in this study] [Included in the (2024) Hayes Evidence Analysis Research Brief on Auriculotemporal nerve decompression].

## Radiofrequency Ablation (RFA)

The available evidence from published studies is not sufficient to conclude that RFA or denervation is an effective treatment for ON or headaches. Well-designed studies are needed to evaluate the potential advantages of RFA for these conditions and to identify which individuals would benefit from this procedure.

Ertilav et al. (2024) conducted an RCT to compare the efficacy of repeated GONB and pulsed radiofrequency therapy for individuals with chronic migraine. To carry out the trial, the authors included 70 individuals who were admitted to the Neurology and Algology outpatient clinic between September 2023 and December 2023 who were diagnosed with chronic migraine according to the ICHD-3 criteria. The individuals were randomized into two groups to receive US-guided repeated GONB and pulsed radiofrequency (PRF). The outcomes measured were recorded before the procedure, and at

the first and sixth months after the procedure. In both groups (35 with GONB and 32 with GONB PRF), the pain scores at the first- and sixth-months post procedure were significantly lower compared to before the procedure. The VAS scores were significantly lower in the PRF group more than in the GONB group at the sixth month. In both groups, the post procedural MIDAS scores at the first and sixth months were significantly lower when compared to before the procedure. In the GONB PRF group, MIDAS scores at the sixth month were significantly lower than MIDAS scores at first month. The MIDAS scores were significantly lower in the PRF group compared to the GONB group at six months. The limitations of the study were the small sample size and the absence of blinding for individuals which may reduce the reliability of the results due to the placebo effect. The authors concluded that the interventional procedures such as GONB and PRF are safe and effective methods for chronic migraines when many medical treatments are unresponsive. When applied with the right techniques the authors found that PRF and GONB for treating migraines is pleasing in appropriate individuals. It was also determined that PRF is an effective and safe option for long term pain relief in chronic migraines and is a better alternative to GONB, whose effectiveness is known.

Through an updated systematic review by Jain et al. 2024, the authors aimed to investigate the primary and secondary outcomes of RFA for chronic headache pain. The review resulted in a total of 580 articles found, and 32 utilized and included in the review. The studies primarily focused on pain scores, duration of relief, function, and patient satisfaction. RFA was utilized to target various nerves as the pain generator and compared with other modalities such as local anesthetic or corticosteroid in several studies. The limitations of the review include the retrospective nature of the studies and the lack of consistency of approach and targeted nerves. The authors concluded that in all, RFA showed favorable outcomes in managing chronic headache pain. It was determined that RFA can serve as an alternative treatment option for individuals who fail other conservative treatment regimens. All the included studies showed positive outcomes towards RFA for managing headache. To provide individuals and clinicians with evidence for the most appropriate treatment strategies, understanding the outcomes of RFA for headache pain is necessary. Further studies are necessary to establish a RFA treatment protocol for headache and provide clinicians with stronger strategies for treatment. Additionally, larger RCT studies are necessary to analyze the efficacy and safety of RFA for individuals with chronic headaches [Fang et al (2016), Guo et al. (2021), and Lee et al. (2020) are included in this review].

Tanyel et al. (2024) conducted a double blind, RCT aimed at evaluating the effects of combining PRF therapy with GONB therapy for individuals with chronic migraine. The participants were divided into two groups: the GONB and the GONB and PRF group. Each group consisted of 16 individuals with chronic migraine. Using 0.5-Hz sensorial stimulation, a 5-cm-long radiofrequency needle was inserted under US-guidance in both groups. Subsequently, all participants received GONB by administering 2 mL of 0.25% bupivacaine. In the GONB and PRF group, participants underwent 4 min of PRF at 42℃, whereas the GONB group did not receive any PRF treatment. Follow-up examinations were performed at one, two, three and six months after the procedure to evaluate the frequency and severity of migraine attacks, number of headache days, and analgesic consumption. The trial results showed that In the GONB and PRF group, VAS score, number of migraine attacks, number of headache days, and analgesic consumption were significantly lower compared to the GONB group. Significant decreases (60%) in mean VAS scores, number of migraine attacks, number of headache days, and consumption of analgesic medications were observed in the GONB and PRF group at the 1, 2, 3, and 6-month follow-ups compared with the pre-treatment period. The limitations of the study included the lack of assessment of quality of life, disability, and headache impact, and the sole focus on clinical effects of combining GONB for PRF for those individuals with chronic migraine. The authors concluded that the combination of GONB with PRF presents as a promising new treatment option for individuals with chronic migraine. The approach has demonstrated efficiency in minimizing analgesic use, decreasing the frequency of migraine attacks, reducing the number of headache days, and decreasing the severity of migraine attacks.

Abd-Elsayed et al. (2024) retrospectively assessed the efficacy of RFA therapy for treating ON and headaches at health clinics throughout the United States. They hypothesized that RFA is a minimally invasive treatment supplying significant pain relief long term for ON and associated headaches. The retrospective analysis studies data collected from 277 individuals who underwent occipital nerve RFA with adequate pre-procedure and post-procedure follow-up for data analysis. The data collected included the individual's age, sex, BMI, headache diagnosis, pre- and post-procedure pain score using the VAS, improvement in symptoms through subjective percentage, and duration of symptom relief. The results of the assessment showed that the mean pre-procedure pain score before RFA therapy for those who completed at least six months of follow-up was 5.57 (SD = 1.87), and the mean post-procedure pain score after RFA therapy was 2.39 (SD = 2.42). The improvement in pain scores between pre-procedure and post-procedure was statistically significant, with a p-value < 0.001. The mean patient-reported percent improvement in pain following RFA therapy was 63.53% (SD = 36.37). The mean duration of pain improvement was 253.9 days after the initiation of treatment (SD = 300.5). When excluding participants who did not have any relief following their RFA procedure, the average pre-procedure pain score was 5.54 (SD = 1.81), and the post-procedure pain score was 1.71 (SD = 1.81) with a p-value < 0.001.The limitations of the study include the retrospective nature of the study, and limited data for collection. The authors concluded through the study that the minimally invasive, safe, and effective treatment of RFA is for individuals with refractory occipital neuralgias

and headaches. More studies are needed to illuminate the ideal individual characteristics for RFA treatment and the potential for procedural complications and long-term side effects associated with occipital nerve RFA therapy.

In a 2023c Hayes Evidence Analysis Research Brief nonpulsed (Thermal) percutaneous RFA for treating ON the volume of publications were summarized to determine whether there is adequate published peer-reviewed literature to evaluate the evidence. The review of abstracts suggested that there currently is not enough published peer reviewed literature to evaluate the evidence in a full assessment. There were no RCTs or systematic reviews, no studies evaluating nonpulsed (thermal) RFA identified, and one study evaluating the treatment guided by nonpulsed (thermal) RFA.

In 2022, Suer and colleagues conducted a systematic review evaluating RCTs of cervical facet joint pain and cervicogenic headaches to establish the current level of evidence for treating the etiologies of pain with RFA. The primary outcome measured was pain relief and duration of pain relief, with the secondary outcomes measured being function, sleep, mood, return to work, additional treatments, and complications. The exploration uncovered four RCTs with a low ROB. The primary outcome measure of pain relief and duration of relief demonstrating a successful relief ranging from 30% to 50%. Secondary outcomes such as function and psychological distress were variable for treatment relief, and no significant difference was noted between groups in two of the studies included. The authors concluded the efficacy of cervical facet RFA for treating chronic neck pain. The evaluation is limited due to variability in the population and heterogeneous treatment outcomes with follow-up intervals that do not allow for meta-analyses. Questions remain, and further research is warranted on this treatment.

A systematic review by Orhurhu et al. (2021) was performed to summarize available evidence behind RFA for headaches, including pain outcome measures, secondary outcomes, and complications. A total of 18 studies composed of six RCTs, six prospective studies, and six retrospective studies were included in the review. All the studies assessed pain improvement with RFA for individuals with headaches. Most studies targeted the occipital nerve for treatment. Complications were mostly mild and self-limiting, including eyelid swelling, rash, superficial infection of the procedural site, and worsening of headache. The review discussed multiple studies that suggest the efficacy of RFA in the treatment of headaches. Outcomes varied based on the difference in approaches regarding continuous radiofrequency versus pulsed radiofrequency, temperature, and duration of administration. Most studies discussed in the review indicate a therapeutic benefit of RFA for headaches over a short-term period. The authors concluded that pain outcomes beyond one year are under-studied and further studies are needed to determine the long-term effects of RFA for headaches. Limitations included a large variability in definitions of trigeminal neuralgia, radiofrequency technique, and selection bias. There is a paucity of strong longitudinal RCTs and prospective studies.

A retrospective review by Guo et al. (2021) was performed to evaluate the effect of low-temperature plasma radiofrequency ablation (LTPRA) of the sphenopalatine ganglion (SPG) in treating chronic and episodic cluster headache. A total of 76 participants treated using LTPRA between January 2015 and October 2017 were reviewed. Fifty individuals suffered from episodic CH and the remaining 26 from chronic cluster headache. The primary outcomes were clinical improvement rate, defined as the percentage of partial and complete pain relief results at one day, 12 months, and 24 months of follow-up after the operation. Clinical improvement rates were 92.3%, 92.3%, and 73.1% in chronic cluster headache and 73.1%, 84% and 68% in episodic CH at each follow-up time point, respectively. Three individuals with chronic cluster headache and seven individuals with episodic CH showed no pain relief after the operation. Drooping eyelids were found in two cases, one recovered at the three-month follow-up, but another one did not in the 24-month follow-up. No serious complications occurred intraoperatively or postoperatively. The authors concluded that LTPRA can be considered an effective and alternative surgical modality for treating individuals with chronic and episodic CH based on SPG block. Further research with RCTs is needed to validate these findings [Included in the (2024) systematic review by Jain et al.].

Robinson et al. (2021) conducted a systematic review to summarize the current state of surgical ON management. Twenty-two studies met the inclusion criteria with a total of 766 individuals. Fifteen studies evaluated interventions on the GON and/or LON and seven studies evaluated interventions on the C2 nerve root. Interventions included decompression, ablation (radiofrequency and cryoablation), and stimulation. The studies used patient-reported pain scores as an outcome metric. Other outcome metrics included complication rates, patient satisfaction, quality of life, and analgesic usage. The average duration of follow-up ranged from 3 to 67 months. The authors found that GON decompression decreased mean ON pain intensity from 7.18 ±1.33 to 1.73 ±1.95. Studies that addressed ablation, including RFA and cryoablation found an overall success rate of 85%, with an average VAS score decreased from 7.4 ±1.7 to 2.9 ±1.7. The authors found that C2 ganglion decompression led to therapeutic success, as defined by > 50% reduction in patient-reported preoperative pain without analgesia use in 70% of individuals at 2.5-year follow-up. Cervical dorsal rhizotomy provided full pain relief in 64% of individuals, partial relief in 20%, and no relief in 16% at the five-year follow-up. The authors concluded that ON treatment identified peripheral nerve decompression, ablation, and stimulation as useful therapeutic options for medically refractory occipital pain. This study is limited by the low level of evidence and significant risk of bias of most of the articles.

[Authors Acar et al. (2008), Blake et al. (2019), Choi et al. (2015), Gande et al. (2016), Jose et al. (2018). Keifer et al. (2017), Li et al. (2012), and Pisapia et al. (2012), which were previously cited in this policy, are included in this study].

Lee et al. (2020) performed a retrospective chart review to evaluate the efficacy and complications of C2 dorsal root ganglion (DRG) pulsed RFA for cervicogenic headache and to identify factors related to the outcome of the procedure. Electronic medical records of consecutive participants who underwent C2 DRG block for cervicogenic headache from January 2012 to May 2018 at a pain center were reviewed. Consequent C2 DRG pulsed RFA was performed for individuals whose headache recurred after an initial period of relief 24 hours after the C2 DRG block. A *successful outcome* was defined as at least 50% pain relief at six months after C2 DRG pulsed RFA. Fluoroscopy-guided C2 DRG block was performed in 114 participants. Forty-five participants received C2 DRG pulsed RFA and 40.0% among them (18/45, success group) had ≥ 50% pain relief after six months. There were no post-procedure complications throughout the study period. More people in the success group than in the failure group had a definite positive response (≥ 50% pain relief) to a previous C2 DRG block ($p < .001$). The authors concluded that C2 DRG pulsed RFA may be an effective treatment for individuals with cervicogenic headache, particularly for those who have previously experienced definite pain reduction after C2 DRG block. The limitations of the study design and small number of individuals preclude firm conclusions [Included in the (2024) systematic reviews by Jain et al. and Oliveira et al.].

Grandhi et al. (2018) performed a systematic review to examine the use of RFA and pulse radiofrequency for the management of cervicogenic headache. A review of the literature was conducted, and 10 studies met inclusion for review. The authors concluded that RFA and pulse RFA provided very limited benefit in the management of cervicogenic headache and there needs to be high-quality RCTs and/or strong non-RCTs to support the use of these techniques, despite numerous case reports demonstrating benefit.

Luo et al. (2018) prospectively investigated the long-term effects of US-guided percutaneous pulsed radiofrequency for treating 22 individuals with refractory idiopathic supraorbital neuralgia. A reduction in the verbal pain NRS score of more than 50% was used as the standard of effectiveness. The effectiveness rates at different time points within two years were calculated. After a single pulsed radiofrequency treatment (PRFT), the effectiveness rate at one and three months was 77%, and the rates at six months, one year, and two years were 73%, 6%, and 50%, respectively. Twenty-three percent of individuals experienced mild upper eyelid ecchymosis that gradually disappeared after approximately two weeks. The authors concluded that the study demonstrated percutaneous pulsed radiofrequency may be a safe and effective treatment choice for individuals with refractory idiopathic supraorbital neuralgia. The findings of this study need to be validated by well-designed studies.

Fang et al. (2016) conducted a study to evaluate the efficacy and safety of a non-ablative computerized tomography guided PRFT of SPG for individuals with refractory cluster headaches. Sixteen consecutive individuals with cluster headache who failed to respond to conservative therapy treated with PRFT of SPG were analyzed. Eleven of 13 individuals with ECH (85%) and one of three individuals with chronic cluster headaches (33%) were completely relieved of the headache. Two individuals with ECH and two individuals with chronic cluster headache showed no pain relief following the treatment. The mean time following PRFT for partial pain relief was 1.3 days (ranging from 1 to 3 days) and the mean time following PRFT for complete pain relief was 6.3 days (ranging from 1 to 20 days). All participants enrolled in this study showed no treatment-related side effects or complications. The authors concluded that those with refractory ECH were quickly, effectively, and safely relieved from the cluster period after computerized tomography guided PRFT of SPG, suggesting that it may be a therapeutic option if conservative treatments fail. Large sample sizes and long-term follow-up research will be useful to evaluate the efficacy of PRFT for individuals with chronic cluster headache [Included in the (2024) systematic review by Jain et al.].

## Neurostimulation or Electrical Stimulation for Headaches/Occipital Neuralgia

The available studies were limited and had significant methodological flaws, making it difficult to draw conclusions regarding the efficacy of electrical stimulation for the treatment of headaches or ON. No well-designed RCTs in the medical literature compare neurostimulation to established treatment options or a sham procedure. Studies on larger populations with longer follow-up are needed to establish the benefits of neurostimulation and electrical stimulation for treating these conditions.

Kollenburg et al. (2024) conducted a systematic review to provide a comprehensive overview of the effectiveness, safety, mechanisms, and practical application of ONS for treating headache disorders. The findings were an overall response rate of ONS is 35.7-100%, 17-100%, and 63-100% for individuals with cluster headache, chronic migraine, and ON respectively. Regarding the long-term effectiveness in all groups, 41.6-88.0% of participants remain responders after ≥ 18.3 months. The most frequently reported adverse events include lead migration/fracture (13%) and local pain (7.3%). Based on the author's results, they concluded that ONS can be considered a safe and effective treatment for chronic intractable headache disorders. To support more widespread application of ONS, additional research with larger sample

sizes should be conducted [Dodick et al. (2015), and Rodrigo et al. (2017) which were previously cited in this policy are included in this systematic review].

In 2024, Perdecioğlu et al. conducted a single-blinded, RCT to show the changes in pain severity and frequency per month in chronic migraine with NipRF treatment. The participants were those diagnosed with chronic migraine according to the ICHD-3 beta diagnostic criteria. For 50% of the participants, a pulsed radiofrequency (pRF) was applied for treatment with transcutaneous electrodes to the GON trace. For the other 50% a GONB was placed under US -guidance. The MIDAS was administered to the participants, and those with scores > 2 was included in the study. The pain intensity and frequency were evaluated using the VAS and headache diary completed before and four weeks post treatment. The results of the trial showed that when both groups were compared, the pre and post treatment VAS scores and headache frequencies were similar. VAS scores and headache frequency decreased significantly after treatment in both groups when comparing the pre and post treatment values within the groups. The limitations of the study are that the mean values for determining the study population did not include headache specific people. Also, the control group was not designed with sham electrodes, therefore the placebo effect could not be excluded. The authors concluded that NipRF treatment is safe and effective for treating chronic migraine. The participants pain and frequency decreased with NipRF treatment, like that in the GONB group. Further studies are needed to establish clear protocols for this easy-to-administer, comfortable, and safe treatment.

Oliveira et al. (2024) created a narrative systematic review to explore the effectiveness and safety of GON Pulsed radiofrequency neuromodulation PRFN for headaches. The primary endpoint measured was the change in headache intensity. The secondary outcomes measured were the effect on monthly headache frequency (MHF), mental and physical health, mood, sleep, analgesic consumption, and side effects. The results of the review demonstrated PRFN to provide significant analgesia and reduction of MHF in chronic migraine from three to six months; and significant pain relief for ON from six to ten months. Mild adverse effects were reported in 3.1% of cohort. A minority of studies reported on secondary outcomes. The limitations of this study include the small amount of high quality prospective RCTs that have evaluated this topic. Much of the included data for the review came from observational studies, with inherent ROB. Most of the studies did not include a control group. There is a significant heterogeneity across studies, with large differences in terms of headache indication, intervention parameters, image guidance technique, and comparators that made interstudy comparison challenging. The authors concluded that there is a low-quality body of evidence that indicates an analgesic benefit from PRFN of GON for ON and chronic migraine, but it's role for other headache types needed more investigation. The optimal PRFN target and settings remain unclear. High-quality RCTs are necessary to further explore the role of this intervention [Lee et al. (2020) is included in this review].

Through a systematic review, Finnern et al. (2023) sought to appraise the literature for the efficacy of cervical spinal cord stimulation (cSCS) for treating any intractable chronic headache, including migraine headaches (with or without aura), cluster headache, tension headache, and other types of headaches. The primary outcomes measured were headache intensity and frequency and adverse effects. A total of 16 studies with 107 individuals were included with the findings of type of headache, cluster headache, trigeminal neuropathy, occipital neuralgia, posttraumatic headache, cervicogenic headache, short-lasting unilateral neuralgiform headache with automatic symptoms, and poststroke facial pain. The results showed that there was very low-quality evidence that cSCS is associated with a decrease in migraine headache frequency, migraine headache intensity, and trigeminal neuropathy intensity. The placement for cSCS leads ranged from C1 to C4. The authors concluded that promising data from observational studies showed that cSCS may help decrease the frequency and intensity of chronic intractable headaches; however, future well-powered RCTs are needed.

Veilleux et al. (2023) performed a systematic review of the efficacy of ONS for treating trigeminal autonomic cephalalgias (TACs). The primary outcomes measured are a reduction in headache intensity, duration, and frequency, adverse event rate, and reduction in medication use. The data for those suffering from short-lasting, unilateral, and neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and cranial autonomic symptoms (SUNA) were reported separately, and the ROB was assessed using the NIH Quality Assessment Tools. Out of 417 individuals, 14 published papers were included in the analysis, with an average reduction in headache intensity and duration of 26.2% and 31.4% in that order. The average reduction in headache frequency was 50%, a 61.2% reduction in the use of abortive medications, and a 31.1% reduction in the utilization of prophylactic medicines. The mean decrease in headache intensity and duration in the SUNCT/SUNA cohort was 56.8% and 42.8%. The overall responder rate, defined as a > 50% reduction in attack frequency, was 60.8% for the non-SUNCT/non-SUNA cohort and 66.7% for the SUNCT/SUNA cohort. Adverse events requiring repeat surgery were reported in 33% of cases. ROB assessment suggests that articles included in this review had reasonable internal validity. The limitations of the study include the heterogeneous nature of the study, and the need for uniform diagnosis criteria of medically refractory TACs due to the definition varied across available literature. The authors concluded that ONS may be an effective surgical treatment for approximately two-thirds of individuals with medically refractory TACs.

In a 2023 prospective, double-blind, randomized, placebo-controlled, multicenter clinical trial, Tepper and colleagues enrolled 248 participants to assess the clinical efficacy of remote electrical neuromodulation (REN) for preventing migraine. Participants were randomized to a 1:1 ratio and observed for four weeks with an eight-week double-blind intervention in which participants utilized either REN or placebo stimulation (128 actives, 120 placebos). To assess results, participants recorded their symptoms daily through an electronic diary. The modified intention-to-treat analysis consisted of 95 active and 84 placebo participants who qualified. The primary endpoint was measured from the mean number of MD per month from baseline, and the results showed a mean reduction of 4.0 ±SD of 4.0 days [1.3 ±4.0 in placebo, therapeutic gain = 2.7 (CI−3.9 to −1.5), p < 0.001]. The significance was maintained when analyzing the episodic (−3.2 ±3.4 vs. −1.0 ±3.6, p = 0.003) and chronic (−4.7 ±4.4 vs. −1.6 ±4.4, p = 0.001) migraine subgroups separately. REN was also superior to placebo in reduction of moderate/severe headache days (3.8 ±3.9 vs. 2.2 ±3.6, p = 0.005), reduction of headache days of all severities (4.5 ±4.1 vs. 1.8 ±4.6, p > < 0.001), percentage of those achieving 50% reduction in moderate/severe headache days [51.6% (49/95) vs. 35.7% (30/84), p = 0.033], and reduction in days of acute medication intake (3.5 ±4.1 vs.1.4 ±4.3, p = 0.001). Comparable results were obtained in the intention to treat (ITT) analysis. No serious device-related adverse events were reported in any group. The authors concluded that these results show that REN is a safe and effective preventive treatment for migraine, offering a much-needed non-pharmacological alternative as a stand-alone preventive therapy or combined with pharmacological therapies to enhance preventive impact further. The trial's limitations consist of a small sample size of participants who took additional preventative medications and those who did not; also, the definition of a migraine day included a possible combination of headache and aura, which does not comply with the IHS guidelines. Lastly, the inclusion criteria allowed for a single preventative agent, which limits the generalizability of the results in participants taking two or more preventatives [Included in the (2024) Hayes evolving evidence review].

In a 2022 randomized, sham-controlled, double-blind, multicenter trial, Tepper and colleagues evaluated the efficacy and safety of concurrent non-invasive stimulation of occipital and trigeminal nerves for the acute treatment of migraine with or without aura. The intention-to-treat group consisted of 131 participants, with 67 in the active group and 64 in the sham. One hundred nine participants were treated for at least one migraine episode, with 50 in the active group and 59 in the sham. The primary endpoint measured was the decrease of pain two hours subsequent treatment initiation. The secondary endpoints were pain relief at one hour and freedom from the most bothersome symptom at 2 hours post-treatment initiation. Exploratory endpoints consisted of freedom from the most painful symptom at two hours and sustained pain freedom 24 hours following treatment. Sixty percent of contributors (30/50) in the active arm described pain relief at two hours after the start of the first eligible treatment (primary outcome) versus 37% (22/59) in the control arm (difference, 23%; 95% CI, 2%-41%; p = 0.018). Pain freedom at two hours without rescue medicine was described by 46% (23/50) of contributors in the active arm and by 12% (7/59) of individuals in the sham arm (p < 0.001). Pain freedom two hours after the treatment and after 24 hours was described by 4.25 times more participants in the active arm (36%; 18/50) compared to the sham arm (8%; 5/59). The 28% difference was statistically significant (95% CI, 1%-43%; p < 0.001). A 4.25-fold difference was also seen associating the proportion of individuals free from pain and most bothersome symptom two h after the stimulation [47% (17/36) and 11% (5/45) in the active and sham arms, correspondingly; 95% CI, 14%-54%; p < 0.001].

A single-center, prospective, long-term open-label study was performed by Al-Kaisy et al. (2022) to evaluate the efficacy and safety of paresthesia-free high cervical 10 kHz spinal cord stimulation (SCS) in the treatment of refractory chronic migraine (rCM). Twenty adults with rCM (mean numbers of preventive treatments failed: 12.2 ±3.1) were enrolled and implanted with a 10 kHz SCS system (Senza™ system, Nevro Corp), with the distal tip of the lead(s) positioned epidurally at the C2 vertebral level. Safety and effectiveness outcomes including adverse events, headache and migraine reductions, responder rates (RR), MIDAS, Headache Impact Test-6 (HIT-6), and Migraine-Specific Quality-of-Life (MSQ), were captured up to 52 weeks after implantation. Compared to baseline, at 52 weeks post-implantation, there was a reduction of mean monthly migraine days (MMD) by 9.3 days (p < 0.001). Sixty percent and 50% of individuals obtained respectively at least 30% and at least 50% reduction in mean MMD. By week 52, 50% of patients' chronic pattern converted to an episodic pattern. The proportion of subjects classified with severe headache-related disability on the HIT-6, decreased from 100% to 60% at week 52. Meaningful improvements of headache-related quality of life measured by the MSQ scale were observed with mean gain of 24.9 ±23.1 (p < 0.001) points at 52 weeks. No unanticipated adverse device effects occurred. No participants required any additional device surgical revision. The authors concluded that 10 kHz SCS may a be safe and effective neurostimulation option for individuals with rCM stating that the paresthesia-free waveform constitutes an advantage for future methodologically sound sham-controlled studies in headache neuromodulation. A small sample size makes it difficult to decide whether these conclusions can be generalized to a larger population. Further research with RCTs is needed to validate these findings [Included in the Finnern et al., (2023) systematic review].

In 2021, Hayes conducted an Evolving Evidence Review on the Nerivio device (Theranica Bio-Electronics Ltd.) for the Treatment of Acute Migraine Episodes. At that time, the exploration of clinical studies and systematic reviews uncovered

minimal support for using Nerivio for managing acute migraine episodes. After reviewing clinical practice guidelines and position statements, the review concluded there needed to be more guidance for using Nerivio to manage acute migraine episodes. The review suggests evidence comparing Nerivio with standard migraine care is needed to inform its real-world value as a treatment possibility. The review was updated in 2023, with the same conclusions for systematic reviews (minimal support) and weak support from clinical practice guidelines and position statements. Evaluation of the literature indicated that new evidence for the safety and efficacy has become available since the 2021 publication, which offers a possible upgrade in the current level of support from clinical studies to 'minimal support.' Overall, there was no new evidence with longer-term follow-up, or evidence comparing Nerivio with standard migraine care since the 2021 publication, leaving the conclusion of continued minimal support for the technology. In the 2024 update, there were eight newly published clinical studies, one systematic review with meta-analysis, and one new guideline that may meet the inclusion criteria set out in the report, which was published in 2021 and does not change the current level of support.

Joswig et al. (2021) performed a retrospective review of 96 individuals with migraine, cervicogenic headache, cluster headache, neuropathic pain of the scalp, tension-type headache, and new daily persistent headache who had undergone ONS (61.5%), supraorbital nerve stimulation (SONS) (11.5%), or combined ONS plus SONS (27.1%) trial implantation and definitive implantation from 2007 to 2017. Changes in pain perception over time were monitored using the VAS for pain. The cohort consisted of 60.4% women and 39.6% men, with a mean age of 46.9 ±11.5 years and pain duration of 14 ±14.1 years. Of the 96 participants, 65 (67.7%) were treatment responders to a trial (≥ 30% amelioration in the average or maximum VAS score for pain and/or number of headache days) that had lasted 22.5 ±8.8 days. The reduction in their average VAS score for pain was to 37% ±24.4% of baseline compared with 99.1% ±24.1% of baseline for those without a response ($p < 0.01$). Of the 56 people who had undergone implantation and had long-term follow-up data available for ≤ 10 years, 32 (57.1%) reported a ≥ 50% reduction in their average VAS score for pain. Four individuals (6.5%) had requested hardware explanation. Stage II complications included one infection (1.6%) and six electrode dislocations (9.7%). The authors concluded that following careful patient selection, according to a positive response to a trial of ONS and/or SONS, clinically meaningful long-term benefit was achieved in 57.1% of those with various chronic headache conditions. Study limitations included the retrospective nature, lack of controls receiving placebo intervention, and randomization.

Pohl et al. (2021) completed a RCT to test the hypothesis that self-administered anodal transcranial direct current stimulation (tDCS) over the visual cortex significantly decreases the number of MMD in EM. The study was single-blind, randomized, and sham-controlled. Inclusion criteria were individuals aged 18-80 years and diagnosis of EM. Exclusion criteria were pregnancy, a neurodegenerative disorder, a contraindication against MRI examinations, and less than two MD during the 28-day baseline period. Individuals whose baseline period suggested chronic migraine were excluded. After baseline, participants applied daily either verum (anodal-1 mA to 20 min) or sham tDCS (anodal-1 mA to 30 sec) at Oz (reference Cz electrode) for 28 days. Headache diaries were used to record the number of MD at baseline, during the stimulation period, and during four subsequent 28-day periods. Twenty-eight participants were included; two were excluded after the baseline period because less than two MD occurred; three were excluded because their headache diaries suggested the diagnosis of chronic migraine. Twenty-three datasets were taken for further analysis. Compared to sham tDCS (n = 12), verum tDCS (n = 11) resulted in a lower number of MD ($p = 0.010$) across all follow-up periods. There was no change in total headache days ($p = 0.165$), anxiety ($p = 0.884$), or depression scores ($p = 0.535$). No serious adverse events occurred; minor side effects were similar in both groups. The authors concluded that this study provides Class II evidence that self-administered anodal tDCS over the visual cortex in EM is safe, and results in a lower number of MMD. However, it has neither an immediate nor a long-term effect. Data suggest that tDCS has no effect on headaches other than migraine or on comorbid anxiety or depressive symptoms. Study limitations included the retrospective nature, lack of controls receiving placebo intervention, and the classification of individual attacks was based on the headache diary; non-migraine days were not classified. The findings of this study need to be validated by well-designed studies.

A systematic review of the efficacy and safety of peripheral nerve stimulation (PNS) in managing acute or chronic pain was conducted by Xu et al. (2021). The review included RCTs and observational studies (n = 5) with Level I and II evidence of PNS in chronic migraine headache and Level II evidence in cluster headaches. The authors concluded that PNS of the occipital nerves reduced pain and disability and should be considered as an option for migraine and cluster headache when other noninvasive measures fail. There was a lack of high-quality RCTs. Meta-analysis was not possible due to wide variations in experimental design and heterogeneity of the study population.

Göbel et al. (2021) completed a prospective, randomized, interventional study to evaluate the effect of ONS on pain-modulatory mechanisms in the trigeminocervical area for individuals with chronic migraine. In a balanced-repeated-measurements design in eight individuals with chronic migraine with and without active ONS, the authors analyzed which effects ONS had on the orbicularis oculi reflex dynamically elicited by corneal air flow. To stimulate the reflex response, instead of an artificial electrical stimulus, a standardized airflow is directed onto the cornea of the eye. The reflex response

is recorded using a video camera detecting eyelid closure frequency (documented as eyelid closures per minute). This method aims to measure the anti-nociceptive protective mechanism of the orbicularis oculi reflex in a way as physiological as possible. At the same time, it allows recording the reflex response dynamically averaged over a longer period. The study was divided into two parts, the ON phase with active ONS, and the OFF phase with inactive ONS. In the former, the orbicularis oculi reflex was recorded quantitatively with active ONS. The OFF phase included the measurement of the orbicularis oculi reflex with ONS deactivated. There was a one-h break between the two test runs. To rule out a sequence effect, the individuals were randomized into two groups: One group (A) first went through the ON-phase measurement and, after an hour's break, the OFF-phase measurement. In the second group (B), the OFF-phase measurement was started, and the ON-phase measurement was carried out 1 h later. Results showed the orbicularis oculi reflex in active ONS (7.38 ±20.14 eyelid closures/minute) compared to inactive ONS (18.73 ±14.30 eyelid closures/minute) to be reduced ($p = 0.021$). The authors concluded that this suggests ONS can directly counteract the trigeminally mediated central sensitization in chronic migraine and protectively reduce the effects of aversive peripheral stimulation. A small sample size makes it difficult to decide whether these conclusions can be generalized to a larger population. Further research with RCTs is needed to validate these findings.

A 2020 ECRI Clinical Evidence Assessment on Nerivio Migra reviewed clinical evidence from two sham controlled RCT, two nonrandomized comparison studies, and one large multicenter case series that addressed migraine pain, symptom relief, and adverse events. There was a total of 1,722 participants. Two RCTs reported more individuals experienced pain relief with Nerivio (64% and 66.7%, respectively) than a sham treatment (26% and 38.8%). One study reported that 89.7% of participants avoided medication during attacks. The authors concluded that more RCTs are needed to characterize Nerivio's effectiveness as an alternative or adjunct to conventional treatments. Limitations included ROB from small sample size and lack of a control group. The updated 2022 ECRI Clinical Evidence Assessment states that consistent evidence shows Nerivio can decrease acute pain and medication use at 2 to 24-hour follow-up in 50% of individuals experiencing episodic, chronic, and/or menstrual migraine. The assessment notes that the technology is safe, with few mild adverse events reported. However, the studies reviewed are small, and confirmatory RCTs with long-term follow-up are necessary to determine safety and efficacy in the long term.

A Hayes Health Technology Assessment report on ONS for chronic migraine headache identified eight studies which included, four RCTs, of which two were crossover design; one was an uncontrolled, open-label extension study of an RCT; and four were prospective, uncontrolled studies. Sample size ranged from eight to 157 individuals and follow-up ranged from three months to nine years. In all but one study, individuals were selected for permanent ONS implantation based on a positive response to a temporary trial of ONS, typically, a ≥ 50% reduction in pain that lasted for a few weeks. The most reported outcome measures were the reduction in headache frequency and headache pain intensity. Other commonly reported outcome measures were response rate (most often defined as ≥ 50% reduction in headache frequency and/or intensity) and/or a ≥ 30% reduction, headache-related disability, and quality of life. The report concluded that based on the available evidence, ONS appeared to have a positive but variable treatment effect on headache outcomes in selected individuals, particularly in reductions of frequency and intensity. There was a risk of complications that may require additional surgery. This conclusion was based on an overall low-quality body of evidence, inconsistent study designs and lack of a defined population. One newly published study was uncovered in the 2022 Health Technology annual review. Hayes did not change their current rating, which reflects low-quality evidence of a potential benefit of ONS for improving headache outcomes in some individuals with chronic migraine. The update outlines how ONS is usually well tolerated; it may result in complications requiring additional surgeries (Hayes, 2020a; updated 2022). [Authors Dodick et al. (2015) and Rodrigo et al. (2017) which were previously cited in this policy, are included in this study].

A Hayes Health Technology Assessment report focused on ONS for the treatment of chronic cluster headache that had failed to respond to available drug treatments. The evidence bases for this report included one retrospective comparative cohort study, four prospective or retrospective pretest/posttest studies, and two prospective case series that evaluated ONS for treatment of individuals with chronic cluster headache (n = 15-67 individuals followed for three months to 6.1 years). The reviewed studies did not provide sufficient evidence to evaluate the effectiveness of ONS for chronic cluster headache. Across the studies that evaluated ONS for treatment of chronic cluster headache, individuals achieved a clinically meaningful ≥ 50% decrease in cluster headache attacks from baseline in 41% to 90% of those treated. Reduction in intensity of pain during a cluster headache attack from baseline varied widely (range, 11%-96%) across studies, although one study found a 2.3% increase in pain intensity that was not statistically significant. The study found that deep brain stimulation (DBS) was more effective than ONS with a greater number of individuals achieving a ≥ 50% decrease in cluster headache attacks from baseline in the DBS group than in the ONS group (100% versus 41%). Reduction in pain intensity scores was greater for the those receiving DBS than individuals receiving ONS (50% versus 11% reduction). Complications of ONS included uncomfortable or intolerable paresthesia (13%-35%), infection (2%-27%), pain or discomfort at wound or implant site (3%-24%), hardware or stimulation dysfunction (19%), wire or electrode breakage or migration (2%-17%), neck stiffness (16%), battery replacement needed < 1 year after implantation (12%), wire externalization or pressure ulcer due to wire or electrode (4%-9%), allergy to surgical material (4%), and wound

issues (2%-4%). For infections and certain other complications, up to 27% of stimulators needed to be surgically removed or replaced. The body of evidence concerning ONS for chronic cluster headache was small in size and very low in quality. One of the reviewed studies was a comparative cohort study that was rated as poor quality. The other six studies were case series that were rated as poor or very poor. Larger, well-designed studies are needed to determine whether ONS is an effective treatment for refractory, chronic cluster headache. In the updated 2022 Health Technology annual review, new evidence was uncovered; however, there was no new evidence with longer-term follow-up and no new technology applications. Hayes maintained their rating, which reflects very low-quality evidence that ONS provides some benefits for individuals with refractory symptoms due to chronic cluster headaches. Substantial uncertainty remains, with no concrete conclusions drawn due to the lack of controlled studies of ONS for cluster headaches and the small size of the controlled studies. The review shows that while ONS is generally safe, there is a risk of complications or need to remove the device over time. In the 2023 update, there were three newly published studies, however there was no change in the current rating of D2 for ONS for treatment of debilitating, medically refractory CH for adult individuals. [Hayes, (2020b); updated (2023)]. [Authors Magis et al. (2011) and Miller et al. (2017) which were previously cited in this policy, are included in this study].

Moisset et al. (2020) performed a systematic review and meta-analysis of RCTs focusing on migraine treatment using neurostimulation methods. Outcomes for the quantitative synthesis were two-hour pain-free for acute treatment and headache days per month for preventive treatment. Thirty-eight studies were included in the analysis (seven acute, 31 preventive). The authors concluded that REN seemed effective for acute treatment. Invasive ONS was effective for chronic migraine prevention. Supra-orbital transcutaneous electrical nerve stimulation (TENS), percutaneous electrical nerve stimulation (PENS), and high-frequency repetitive transcranial magnetic stimulation (rTMS) over the motor cortex (M1) were effective for migraine prevention. The quality of the evidence was very poor. Future large and well-conducted studies are needed to confirm efficacy.

Aibar-Durán et al. (2020) describe two prospective cohorts of individuals with refractory cluster headache treated with ONS and DBS and compare preoperative to postoperative status at six and 12 months after the surgery and at final follow-up. Efficacy analysis using objective and subjective variables is reported, as well as medication reduction and complications. The ONS group consisted of 13 men and four women. The median number of attacks per week (Naw) before surgery was 28, and the median follow-up duration was 48 months. The DBS group comprised five men and two women. The median Naw before surgery was 56, and the median follow-up was 36 months. The Naw and VAS scores were significantly reduced for the ONS and DBS groups after surgery. However, while all the individuals from the DBS group were considered responders at final follow-up, with more than 85% being satisfied with the treatment, approximately 29% of initial responders to ONS became resistant by the final follow-up ($p = 0.0253$). The authors concluded that ONS is initially effective as a treatment for refractory cluster headache, although a trend toward loss of efficacy was observed. No clear predictors of good clinical response were found in the present study. Conversely, DBS appears effective and provides a more stable clinical response over time with an acceptable rate of surgical complications [Included in the Kollenburg et al. (2024) systematic review].

Halker et al. (2020) performed a systematic review to evaluate the effectiveness and comparative effectiveness of pharmacologic and nonpharmacologic therapies for the acute treatment of EM in adults. Seventeen RCTs and one comparative observational study with 1,758 participants were included for nonpharmacologic therapies. The authors concluded that compared with placebo, several nonpharmacologic treatments may improve various measures of pain, including REN [moderate strength of evidence (SOE)], magnetic stimulation (low SOE), acupuncture (low SOE), chamomile oil (low SOE), external trigeminal nerve stimulation (low SOE), and eye movement desensitization re-processing (low SOE). These interventions, including the noninvasive neuromodulation devices, have been evaluated only by single or very few trials.

A randomized, sham-controlled, parallel-group, double-blind safety and efficacy study at 21 headache centers in the USA was conducted by Goadsby et al. (2019). Eligible participants were 22 years or older and had chronic cluster headaches (at least four attacks per week) that were either previously or currently inadequately controlled with available therapies. Participants were randomly assigned (1:1) to receive either SPG stimulation (n = 45) or sham stimulation (n = 48). Thirty-six individuals in the SPG stimulation group and 40 in the control group had at least one attack during the experimental phase and were included in efficacy analyses. The proportion of attacks for which pain relief was experienced at 15 minutes was 62·46% (95% CI 49·15-74·12) in the SPG stimulation group versus 38·87% (28·60-50·25) in the control group [odds ratio 2·62 (95% CI 1·28-5·34); p = 0·008]. Nine serious adverse events were reported. Three of these serious adverse events were related to the implantation procedure (aspiration during intubation, nausea and vomiting, and venous injury or compromise). A fourth serious adverse event was an infection that was attributed to both the stimulation device and the implantation procedure. The other five serious adverse events were unrelated. The authors concluded that SPG stimulation seems efficacious and is well tolerated and potentially offers an alternative approach to the treatment of chronic cluster headache. Further research is needed to clarify its place in clinical practice.

A monocenter, prospective, open-label, pilot trial (Birlea et al., 2019) explored the therapeutic utility and safety of external trigeminal neurostimulation (eTNS) as a preventive treatment for individuals suffering from chronic migraine. Participants were adults with a history of chronic migraine meeting International Classification of Headache Disorder-3 beta (2013) diagnostic criteria with or without medication overuse. After a one-month baseline period, 58 participants applied at least one daily 20-min session of eTNS for three months. Primary outcomes were monthly changes in frequency of headache days and in overall acute headache medication intake. Compared to baseline, frequency of headache days decreased by 3.12 days (16.21%, $p < 0.001$) and acute medication intake decreased from 26.33 to 18.22 (30.81%, $p < 0.001$) during the third month of treatment. Twenty-six people reported 47 minor adverse events, of which only two were related to the use of the device (skin irritation under the electrode and headache worsening with vertigo). The authors concluded that this open-label pilot trial suggests that eTNS with the Cefaly® device is safe and effective as prophylactic treatment for chronic migraine in adults. The treatment effect is greatest for individuals with noncontinuous headache; it is hardly significant in those with continuous headache. The study's open-label design and the lack of placebo arm are a limitation. The fact that the number of daily eTNS sessions was not the same for all individuals could be considered another weakness of the trial protocol, producing unnecessary variability.

A 2019 ECRI Health Technology Assessment on ONS for treating medically refractory chronic cluster headache found that evidence from six small case series at high ROB is insufficient to determine how well ONS works or how it compares with other electrical stimulation options for individuals with chronic cluster headache that has not responded well to medical therapy. Side effects from ONS are common and include lead migration and local inflammation. Although studies reported reductions in headache frequency in more than half of participants, results need validation from RCTs.

Tao et al. (2018) conducted a meta-analysis to analyze TENS effectiveness and safety for individuals with migraines. The study included four RCTs, which compared the effect of TENS (n = 161) with sham TENS (n = 115). Change in the number of monthly headache days (MHD), RR, painkiller intake, adverse events and satisfaction were extracted as outcome. The authors concluded that there is low-quality evidence suggesting that TENS may be effective in increasing RR, reducing headache days and painkiller intake, serving as a well-tolerated alternative for migraineurs. Future well-designed RCTs with extensive follow-up are needed.

A randomized blind control study aimed to assess the effectiveness and safety of PENS in migraine treatment was conducted by Li and Xu (2017). Sixty-two individuals with at least two migration attacks each month were recruited and randomly divided into a PENS group and a sham PENS group in a ratio of 1:1. All participants received PENS or sham PENS 30 minutes daily, five times weekly for 12 weeks. All outcome measurements were performed at treatment initiation to establish a baseline and after 12 weeks of treatment. The authors report that at the end of the 12 weeks, the group receiving PENS exhibited statistically significant decrease in the mean in MMD compared with the group receiving sham PENS intervention. The 50% RR was significantly higher in the PENS group than that in the sham PENS group. The monthly migraine attacks (MMA), MHD, and monthly acute antimigraine drug intake (MAADI) were also significantly lower in the PENS group that those in the sham PENS group. The authors concluded that the results of the study demonstrated that PENS is more effective and safer than Sham PENS for the treatment of migraine. Follow-up regarding both short and long-term effectiveness of PENS for treatment of migraine still needs to be assessed.

Liu et al. (2017) performed a randomized, controlled trial of transcutaneous occipital nerve stimulation (tONS) for prevention of migraine to evaluate the efficacy and tolerability of tONS for individuals with migraine. Participants(n = 110) were randomized to one of five therapeutic groups before treatment for one month. Groups A through C received tONS at different frequencies, group D underwent sham tONS intervention, and group E received topiramate orally. The authors report that the 50% RR was significantly greater in the groups undergoing active tONS and topiramate, compared with sham-treated group. A significant reduction in headache intensity was noted in each test group compared with the sham group. They concluded that tONS therapy is a new promising approach for migraine prevention. It has infrequent and mild adverse events and may be effective among those who prefer nonpharmacological treatment. The findings of this study need to be validated by well-designed studies with long-term follow-up.

## Clinical Practice Guidelines

### *American Academy of Pain Medicine (AAPM) Foundation*

The AAPM developed a multidisciplinary panel of eight physicians, two psychologists, and one person representative to review the multidisciplinary preventative options for migraine management in three categories: medications, behavioral, and interventional strategies. The panel concluded there is low certainty of evidence that GONBs with local anesthetic are more effective than saline injections in reducing headache days or acute medication use per month. There is insufficient evidence that GONBs with local anesthetic are more effective than saline in reducing impairment, as defined by PROs. The adverse event profile is minimal. Overall, the committee gave GONBs a weak recommendation for the prevention of

chronic migraine and found insufficient evidence of efficacy for EM. This treatment may be more effective for acute or short-term preventive therapy, and further research should be directed to those areas (Barad et al., 2022).

### *American Interventional Headache Society (AIHS)/American Society of Regional Anesthesia and Pain Medicine (ASRA)/American Society of Spine Radiology (ASSR)/European Society of Regional Anaesthesia and Pain Therapy (ESRA)/ Obstetric Anaesthetists' Association (OAA)/Society for Obstetric Anesthesia and Perinatology (SOAP)*

In 2023, a multidisciplinary panel of 21 collaborators outlined recommendations for the prevention, identification, and management of PDPH, including the strength and certainty of evidence of various patient, procedural, diagnostic, and management aspects of PDPH.

- The efficacy of GONB for PDPH after dural puncture with wider-gauge needles was unclear (level of certainty: low).
- GONBs may be offered to those with PDPH after spinal anesthesia with a narrower-gauge (≤ 22 needle, although headache may recur in a substantial proportion of individuals, with more severe headache requiring an EBP (evidence grade: C; level of certainty: moderate).

Several interventional techniques, such as GONB or SPG blocks, are novel therapies that need more robust evidence (Uppal et al., 2023).

### *American Society of Anesthesiologists (ASA)*

In their practice statement on PDPH, the ASA stated that there is insufficient evidence to recommend the use of GONBs or SPG blocks in the treatment of obstetric PDPH (ASA, 2021).

### *American Society of Anesthesiologists (ASA)/American Society of Regional Anesthesia and Pain Medicine (ASRA)*

In practice guidelines created jointly in 2010, the ASA and ASRA state the following: "Subcutaneous PNS may be used in the multimodal treatment of individuals with painful peripheral nerve injuries who have not responded to other therapies" (ASA/ASRA, 2010).

### *American Headache Society (AHS)*

In 2021, the AHS incorporated recent research findings, expert consensus, and patient perspectives into updated guidance on the utilization of new acute and preventive treatments for migraines in adults. The AHS indicates that all patients with a confirmed diagnosis of migraine may be offered treatment with a neuromodulatory device, which modulates pain mechanisms involved in headache by stimulating the nervous system centrally or peripherally with an electric current or a magnetic field. Although the efficacy and safety of neuromodulation is supported by positive results from multiple clinical trials, the use of neuromodulatory devices in clinical practice has been limited. Patients with an inadequate response to a migraine-specific medication, as well as those with frequent attacks who may be at risk of developing medication-overuse headache and/or chronic migraine due to overuse of acute medication, should be considered for a trial of a neuromodulatory device as an adjunct to the existing treatment plan (Ailani et al., 2021).

A 2019 AHS position statement on integrating new migraine treatments into clinical practice states that neuromodulation and biobehavioral therapy may be appropriate for preventive and acute treatment, depending on the needs of individuals. Neuromodulation may be helpful for individuals who prefer nondrug therapies, respond poorly, cannot tolerate, or have contraindications to pharmacotherapy (AHS, 2019).

A 2016 AHS guideline for treating cluster headaches recommends (Level A) sumatriptan subcutaneously, zolmitriptan nasal spray, and high-flow oxygen for acute treatment. SPG stimulation has been administered as a Level B recommendation for acute treatment. Suboccipital steroid injections have emerged as the only treatment to receive a Level A recommendation. Other newly evaluated treatments have been given a Level B recommendation (negative study: DBS), a Level C recommendation (positive study: warfarin; negative studies: cimetidine/chlorpheniramine, candesartan), or a Level U (data inadequate or conflicting) recommendation (frovatriptan). Further studies are warranted to demonstrate the safety and efficacy of established and emerging therapies (Robbins et al., 2016).

To draw attention to tests and procedures associated with low-value care in headache medicine, the AHS joined the Choosing Wisely initiative of the American Board of Internal Medicine Foundation. One of the recommendations approved by the Choosing Wisely task force of the AHS was not to recommend surgical deactivation of migraine trigger points outside of a clinical trial (Loder et al., 2013).

AHS has issued a position statement about the surgical intervention in migraine treatment that indicates that surgery for migraine is a last-resort option and is probably not appropriate for most sufferers. According to the AHS, there are no convincing or definitive data, to date, which show its long-term value. Besides replacing the use of more appropriate treatments, surgical intervention also may produce side effects that are not reversible and carry the risks associated with any surgery (AHS 2012).

## *American Society of Interventional Pain Physicians (ASIPP)*

A 2013 ASIPP guideline recommends that "therapeutic neurotomy may be provided based on the response from controlled diagnostic blocks."

## *American Society of Pain and Neuroscience (ASPN)*

According to the latest evidence-based application for radiofrequency neurotomy (LEARN) best practice guidelines from the ASPN consensus statement: occipital neurotomy may be selectively offered for the treatment of ON pain when greater or lesser nerves have been identified as the etiology of pain via diagnostic blocks. GRADE II-2 C.
Best Practices Summary

- Use of occipital nerve RFN is primarily for symptoms of ON causing posterior head pain and has also been described for use in migraine syndromes with occipital tenderness.
- Implementation of the International Headache Society diagnostic criteria for ON is standard practice.
- Diagnostic blockade of the occipital nerves should precede the use of RFN.
- Before RFN of the occipital nerves, other possible etiologies should be ruled out through either magnetic resonance imaging (MRI) and/or computerized tomography (CT) imaging. Imaging is not itself a diagnostic for ON.
- Evidence best supports the use of PRFN over other RFN options. Time settings for lesion creation range from a single lesion at 90 seconds to up to three lesions for 120 seconds. Further studies are necessary to compare procedural techniques.
- Several studies have documented six months of pain relief. Longer follow-up periods are needed to recommend repeat sessions of RFN in successfully treated people (Lee et al., 2021).

## *Congress of Neurological Surgeons*

In 2023, the Congress of Neurological Surgeons Guidelines Task Force systematically reviewed the relevant literature on ONS for ON to update the original 2015 guidelines, ensuring timeliness and accuracy for clinical practice. This minor update includes the following recommendation: Clinicians may use ONS as a treatment option for those with medically refractory ON (Level III) (Staudt et al., 2023).

The Congress of Neurological Surgeons published an evidence-based guideline in 2015 supporting the use of ONS as a treatment option for individuals with medical refractory ON. The population in the nine studies reviewed was small and there was a short duration of follow-up (Sweet, 2015). Class III evidence: Level III recommendation (Evidence from case series, comparative studies with historical controls, case reports, and expert opinion, as well as significantly flawed randomized, controlled trials).

## *Department of Veterans Affairs and the Department of Defense (VA/DoD)*

In the 2023 VA/DoD Clinical Practice Guideline for Management of Headache the following recommendations for headache and/or migraine were made:

- There is insufficient evidence to recommend for or against any form of neuromodulation for the treatment and/or prevention of migraine:
  - Non-invasive vagus nerve stimulation
  - Supraorbital, or external trigeminal, nerve stimulation
  - Remote electrical neurostimulation
  - External combined occipital and trigeminal
  - Neurostimulation system
  - Repetitive transcranial magnetic stimulation
  - Transcranial direct current stimulation
- There is insufficient evidence to recommend for or against GONB for preventing chronic migraine (Neither for nor against | Reviewed, New-added)
- We suggest against AbobotulinumtoxinA or OnabotulinumtoxinA injection to prevent EM
- We suggest OnabotulinumtoxinA injection for the prevention of chronic migraine
- There is insufficient evidence to recommend for or against the following for headache:
  - Transcranial magnetic stimulation
  - Transcranial direct current stimulation

    - External trigeminal nerve stimulation
    - Supraorbital electrical stimulation
- We suggest OnabotulinumtoxinA injection for the prevention of chronic migraine (Weak for | Reviewed, Not changed) A 2020 VA/DoD Clinical Practice Guideline for the primary care management of headache found there is insufficient evidence to recommend for or against the following for headache:
- Transcranial magnetic stimulation
- Transcranial direct current stimulation
- Pulsed radiofrequency or SPG block
- External trigeminal nerve stimulation
- Supraorbital electrical stimulation
- Neuromodulation

## *European Headache Federation*

In a set of recommendations regarding neuromodulation for chronic headaches, the European Headache Federation states that despite a growing field of stimulation devices in headaches treatment, further controlled studies are warranted to validate, strengthen, and disseminate the use of neurostimulation. The European Headache Federation states that until these data are available, any neurostimulation device should only be used for individuals with medically intractable syndromes from tertiary headache centers either as part of a valid study or have shown to be effective in such controlled studies with an acceptable side effect profile (Martelletti et al., 2013).

## *International Neuromodulation Society (INS)*

The INS board of directors chose an expert panel, the Neuromodulation Appropriateness Consensus Committee (NACC), to evaluate the peer-reviewed literature, current research, and clinical experience and to give guidance for the appropriate use of these methods. The NACC found that evidence supports extracranial stimulation for facial pain, migraine, and scalp pain but is limited for intracranial neuromodulation (Deer et al. 2014).

## *National Institute for Health and Care Excellence (NICE)*

The 2022 NICE guidelines on transcutaneous electrical stimulation of the SON for treating and preventing migraine offered the following recommendations:

- Evidence on the safety of transcutaneous electrical stimulation of the SON for treating and preventing migraine is adequate and raises no major safety concerns. For efficacy:
    - The evidence for treating an acute migraine attack is adequate but, for treating subsequent attacks, is limited in quality and quantity. So, for treating acute migraine, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.
    - Find out what special arrangements mean on the NICE interventional procedure's guidance page.
    - The evidence for preventing migraine is inadequate in quality. So, for preventing migraine, this procedure should only be used in the context of research.
- Clinicians wanting to do transcutaneous electrical stimulation of the SON for acute treatment of migraine should:
    - Inform the clinical governance leads in their healthcare organization.
    - Give people and their families and carers clear written information to support shared decision making, including NICE's information for the public.
    - Ensure that people and their families and carers understand the procedure's safety and efficacy, and any uncertainties about these.
    - Audit and review clinical outcomes of everyone having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedures outcomes audit tool (for use at local discretion).
    - Discuss the outcomes of the procedure during their annual appraisal to reflect, learn, and improve.
- Healthcare organizations should:
    - Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
    - Regularly review data on outcomes and safety for this procedure.
- Patient selection should usually be done by clinicians (including clinical nurse specialists) with expertise in managing migraine.
- NICE encourages further research on transcutaneous electrical stimulation of the SON for treating and preventing migraine. Studies should describe clearly whether the procedure is used for treatment or prevention. They should include details of patient selection, and the intensity, duration, and frequency of use. Outcome measures should include the number and severity of migraine episodes, quality of life in the short and long term, any changes in

medication and management of subsequent attacks. The development of any complications after starting treatment should be documented.

- The usual treatment options for migraines are medical therapies, to either stop or prevent attacks (refer to NICE's guideline on headaches in over 12s). For acute migraine attacks, these include analgesics, triptans and antiemetics. Treatments to stop or reduce the frequency of migraine attacks include beta blockers, calcium-channel blockers, tricyclic antidepressants, antiepileptics and calcitonin gene-related peptide inhibitors.
- Invasive treatments are reserved for people with distressing symptoms that are refractory to medical therapy. These include nerve blocks, botulinum toxin (see NICE's technology appraisal guidance on botulinum toxin type A for the prevention of headaches in adults with chronic migraine), acupuncture, and interventional procedures (see NICE's interventional procedures guidance on ONS, transcutaneous stimulation of the cervical branch of the vagus nerve and transcranial magnetic stimulation).
- Transcutaneous electrical stimulation of the SON uses small electrical currents to stimulate the SONs (branches of the ophthalmic nerve, the first division of the trigeminal nerve) through the skin overlying the nerves. It is also called external trigeminal nerve stimulation or eTNS. The aim is to relieve headache and, when used regularly, to reduce the severity and the frequency of migraine attacks. 2.5 People with migraine administer the therapy themselves using a small battery-operated device. For example, one device consists of a headband with a central button connected to a self-adhesive electrode patch. This is applied to the forehead above the eyebrows. When the device is activated, small electrical impulses stimulate the SONs (branches of the ophthalmic nerve, the first division of the trigeminal nerve). The intensity of the electrical pulses increases periodically and can be self-adjusted. Stimulation is applied daily for about 1 to 2 hours during an acute migraine attack, and for 20 minutes for prevention between attacks.
- NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 14 sources, which was discussed by the committee. The evidence included two RCTs, three case series and one observational survey for acute treatment of migraine. It included four RCTs, two case series, one observational survey and one Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience database adverse event report for prevention. It is presented in the summary of key evidence section in the interventional procedures overview. Other relevant literature is in the appendix of the overview.
- The professional experts and the committee considered the key efficacy outcomes to be: reduced frequency, duration and severity of migraine episodes, reduced medication use and improved quality of life.
- The professional experts and the committee considered the key safety outcomes to be: pain, weakness, poststimulation headaches and worsening of migraine.
- Twelve commentaries from people who have had this procedure and a submission from a patient organization were discussed by the committee.
- The committee noted that migraine is often a chronic condition with a detrimental effect on quality of life. It recognized that, for some people, there is a lack of effective prevention and treatment options.
- The committee noted that many people having this procedure continued to take medications to treat or prevent migraine.
- The committee was pleased to receive individual’s commentary and a submission from a patient organization for this procedure. It noted that several people reported a negative experience of the procedure, including unpleasant side effects.

In the updated 2021 NICE clinical guideline for Headaches in over 12s diagnosis and management cluster headache and treatment were addressed. The recommendations include:

- Discuss the need for neuroimaging for people with a first bout of cluster headache with a GP with a special interest in headache or a neurologist (2012).
- Offer oxygen and/or a subcutaneous or nasal triptan for the acute treatment of cluster headache. (2012) In November 2015, this was an off-label use of subcutaneous triptans in under 18s. Nasal triptans did not have a UK marketing authorization for this indication.
- When using oxygen for the acute treatment of cluster headache:
  - Use 100% oxygen at a flow rate of at least 12 liters per minute with a non-rebreathing mask and a reservoir bag; and
  - Arrange provision of home and ambulatory oxygen (2012).
- When using a subcutaneous or nasal triptan, ensure the person is offered an adequate supply of triptans calculated according to their history of cluster bouts, based on the manufacturer's maximum daily dose. (2012) In November 2015, this was an off-label use of subcutaneous triptans in under 18s. Nasal triptans did not have a UK marketing authorization for this indication. See NICE's information on prescribing medicines.
- Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache (2012).

A 2015 NICE guideline for the implantation of a SPG stimulation device for chronic cluster headache has the following states that current evidence on the efficacy of implantation of a SPG stimulation device for chronic cluster headache, in the short term (up to 2 months), is adequate. A variety of complications have been documented, most of which occur early and resolve; surgical revision of the implanted system is sometimes needed. The procedure should only be used with special arrangements for clinical governance, consent and audit or research. NICE encourages further research on SPG stimulation for chronic cluster headache.

NICE stated that the evidence on ONS for intractable chronic migraine shows some efficacy in the short term but there is very little evidence about long-term outcomes. Regarding safety, there is a risk of complications, needing further surgery. Therefore, NICE recommends that this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. NICE encourages publication of further information from comparative studies and from collaborative data collection to guide future use of this procedure and to provide individuals with the best possible advice (NICE 2013).

# U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

## Local Injection Therapy

Various local anesthetics are approved by the FDA for use in diagnostic and therapeutic nerve blockade. Botulinum toxin-A (BTX-A or BOTOX) is a neurolytic agent that has also been approved by the FDA for treatment of some conditions. However, BTX-A is not specifically approved for treatment of cervicogenic headache or occipital neuralgia; the use of BTX-A for these diagnoses is off-label use.

## Radiofrequency Ablation (RFA)

RFA is a procedure and, therefore, is not subject to regulation by the FDA. However, the devices used to perform RFA are regulated by the FDA premarket approval process. There are numerous devices listed in the FDA 510(k) database approved for use in performing RFA. Two product codes are dedicated to these devices, one for radiofrequency lesion generators (GXD) and one for radiofrequency lesion probes (GXI). Additional information is available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed March 17, 2025)

## Electrical Stimulation

Electrical stimulation of the occipital/cranial nerves for the treatment of occipital neuralgia, cervicogenic headache and migraines is a procedure and, therefore, not subject to regulation by the FDA; however, the devices used to perform electrical stimulation are regulated via the FDA 510(k) premarket approval process. There are numerous devices listed in the FDA 510(k) database with product codes GZF, GZB and PCC. Additional information is available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed March 17, 2025)

Nerivio Migra was granted a class II designation through the De Novo review process as a trunk and limb electrical stimulator. While originally authorized for use in adults with acute migraine (≤ 12 headache days per month) who do not have chronic migraine, Nerivio was subsequently cleared for adults with chronic migraine in 2020 and expanded for use in adolescents with ≥ 2 migraines per month in 2021. Additional information is available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K203181. (Accessed March 17, 2025)

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# Policy History/Revision Information

| Date | Summary of Changes |
|---|---|
| 10/01/2025 | **Coverage Rationale**<br>***Members Under 18 Years of Age***<br>• Added language to indicate occipital nerve ablation (destruction by neurolytic agent) is proven and medically necessary for treating pain due to malignancy involving the head and neck<br>• Removed instruction to refer to the InterQual® CP: Procedures, Neuroablation, Percutaneous for medical necessity clinical coverage criteria for occipital nerve ablation for severe cancer pain due to malignancy involving the head and neck<br>**Definitions**<br>• Added definition of:<br>  ○ Migraine Disability Assessment Test (MIDAS)<br>  ○ Migraine-Specific Quality of Life Questionnaire (MSQ)<br>**Supporting Information**<br>• Updated *Clinical Evidence* and *References* sections to reflect the most current information |

| Date | Summary of Changes |
|---|---|
| | • Archived previous policy version CS086KS.01 |

# Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare uses InterQual® for the primary medical/surgical criteria, and the American Society of Addiction Medicine (ASAM) criteria for substance use disorder (SUD) services, in administering health benefits. If InterQual® does not have applicable criteria, UnitedHealthcare may also use UnitedHealthcare Medical Policies that have been approved by the Kansas Department of Health and Environment. The UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.