Title: Sphenopalatine Ganglion Block for Headache

**Medical Policy**

**Professional**

Original Effective Date: November 13, 2017  
Revision Date(s): November 13, 2017  
Current Effective Date: November 13, 2017

**Institutional**

Original Effective Date: November 13, 2017  
Revision Date(s): November 13, 2017  
Current Effective Date: November 13, 2017

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member’s benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Individuals:  
• With chronic migraine headache | Interventions of interest are:  
• Sphenopalatine ganglion block(s) | Comparators of interest are:  
• Medication  
• Self-management (eg, relaxation, exercise)  
• Botulinum toxin injection | Relevant outcomes include:  
• Symptoms  
• Functional outcomes  
• Quality of life  
• Treatment-related morbidity |
| Individuals:  
• With severe acute headache treated in the emergency setting | Interventions of interest are:  
• Sphenopalatine ganglion block(s) | Comparators of interest are:  
• Medication | Relevant outcomes include:  
• Symptoms  
• Functional outcomes  
• Quality of life  
• Treatment-related morbidity |
| Individuals:  
• With cluster headache | Interventions of interest are:  
• Sphenopalatine ganglion block(s) | Comparators of interest are:  
• Medication  
• Oxygen therapy | Relevant outcomes include:  
• Symptoms  
• Functional outcomes  
• Quality of life  
• Treatment-related morbidity |
DESCRIPTION
Chronic migraine and severe headaches are common conditions and the available treatments are not universally effective. A proposed treatment option is blocking the sphenopalatine ganglion (SPG) nerve by applying topical anesthetic intranasally. Several catheters approved by the Food and Drug Administration are available for the SPG blocking procedure.

OBJECTIVE
The objective of this policy is to evaluate whether sphenopalatine ganglion blocks improve health outcomes in patients with chronic or severe acute headaches, compared with other accepted headache treatments.

BACKGROUND
Headaches and Headache Treatments
Headaches are common neurologic disorders and are among the top reasons that patients seek medical care. Headaches affect approximately 50% of the general population in a given year and over 90% of people have a lifetime history of headache.¹ The 2 most common types of headache are tension-type headaches and migraines. Tension headaches have a prevalence of approximately 40%.² Diagnostic criteria include the presence of at least 2 of the following characteristics: bilateral headache location, nonpulsating pain, mild-to-moderate intensity, and headache not aggravated by physical activity.³ Migraines are the second-most common headache disorder, with a 1-year migraine prevalence of approximately 12% in the United States.² They are characterized by severe pain on 1 or both sides of the head, nausea, and, at times, disturbed vision. Migraines can be categorized by headache frequency, and by the presence or absence of aura. Chronic migraine is defined as attacks on at least 15 days per month for more than 3 months, with features of migraine on at least 8 days per month.³

Cluster headaches are less common than tension or migraine headaches, with an estimated prevalence of 0.1% of the population.² They are characterized by severe unilateral orbital, supraorbital, and/or temporal pain that also includes other symptoms in the eye and/or nose on the same side (eg, rhinorrhea, eyelid edema or drooping).

Treatment
A variety of medications are used to treat acute migraine episodes. They include medications taken at the onset of an attack to abort the attack (triptans, ergotamines) and medications to treat the pain and other symptoms of migraines once they are established (nonsteroidal anti-inflammatory drugs, antiemetics). Prophylactic medication therapy may be appropriate for people with migraines that occur more than 2 days per week. In addition to medication, behavioral treatments (eg, relaxation, cognitive therapy) are used to manage migraine headache. Botulinum toxin type A injections are a U.S. Food and Drug Administration–approved treatment for chronic migraine.
Severe acute cluster headaches may be treated with abortive therapy including breathing 100% oxygen, and triptan medications. Other medications used to treat cluster headaches include steroids, calcium channel blockers, and nerve pain medications. Due to the severity of pain associated with cluster headaches, patients may seek emergency treatment. Tension-type headaches are generally treated with over the counter pain medication.

**Sphenopalatine Ganglion Block**

Sphenopalatine ganglion (SPG) blocks are a proposed treatment option for chronic migraines and some severe non-migraine headaches. The SPG is a group of nerve cells located behind the bony structures of the nose. The nerve bundle is linked to the trigeminal nerve, the primary nerve involved in headache disorders. The SPG has both autonomic nerves, which in this case are associated with functions such as tearing and nasal congestion, and sensory nerves, associated with pain perception. SPG blocks involve topical application of local anesthetic to mucosa overlying the SPG. The rationale for using SPG blocks to treat headaches is that local anesthetics in low concentrations could block the sensory fibers and thereby reduce pain while maintaining autonomic function.

The proposed procedure for SPG blockade is to insert intranasally a catheter that is attached to a syringe carrying local anesthetic (eg, lidocaine, bupivacaine). Once the catheter is in place, the local anesthetic is applied to the posterior wall of the nasal cavity and reaches the SPG. Some form of SPG blocking procedure has been used for many years. Originally, SPG blocks were done by inserting a cotton-tipped applicator dabbed with local anesthetic into the nose; this technique may be less accurate and effective than the currently proposed procedure. Another variation is to insert a needle into the cheek and inject local anesthetic but this no longer appears to be used because it is more invasive and can be painful. Neurostimulation of the SPG and SPG blockade with radiofrequency lesioning have been used outside of the United States, but these treatments are not cleared or approved by FDA.

Three catheter devices are commercially available in the United States for performing SPG blocks. The catheters have somewhat different designs but all are attached to syringes that contain local anesthetic. The catheters are inserted intranasally and, once in place, the local anesthetic is applied through the catheter. With 2 of the 3 commercially available catheters (the SpenoCath®, Allevio™), patients are positioned on their back with their nose pointed vertically and their head turned to the side. With the Tx360® device, patients remain seated.

The company marketing the Tx360® device proposes its use in the context of the MiRx™ protocol. This 2-part protocol includes a medical component for immediate pain relief and a physical component to reduce headache recurrences. The medical component involves clinical evaluation and, if the patient is considered eligible, an SPG block
procedure. The physical component can include any of a number of approaches such as physical therapy, ergonomic modifications, massage, and dietary recommendations.

The optimal number and frequency of SPG treatments is unclear. Information from the American Migraine Foundation suggests that the procedure can be repeated as often as needed to control pain.5 A randomized controlled trial (RCT) has described a course of treatment for migraines consisting of SPG blocks twice a week for 6 weeks (total, 12 treatments).

SGB blocks are proposed for both short- and long-term treatment of headaches and migraines. When used in the emergency setting in patients with severe acute headaches, the goal of treatment is to abort the current headache while the patient is in the emergency department. In the RCT that provided a 6-week course of treatment with SPG blocks for chronic migraine (mentioned above), short-term outcomes were assessed up to 24 hours after each treatment, and the duration and frequency of chronic migraines were assessed at 1 and 6 months after the course of treatment.

**REGULATORY STATUS**
The Tx360® Nasal Applicator (Tian Medical), the Allevio™ SPG Nerve Block Catheter (JET Medical), and the SpenoCath® (Dolor Technologies) are considered class I devices by the U.S. Food and Drug Administration (FDA) and are exempt from 510(k) requirements. This classification does not require submission of clinical data regarding efficacy but only notification of FDA prior to marketing. These 3 devices are all used to apply numbing medication intranasally.

**POLICY**
Sphenopalatine ganglion blocks are considered experimental / investigational for all indications, including, but not limited to, the treatment of migraines and non-migraine headaches.

**RATIONALE**
This evidence review was originally created in May 2017 and based on a search of the MEDLINE database. The most recent literature search was conducted through March 23, 2017.

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.
Because the placebo response rate is typically high in patients with headache, assessment of the evidence for this review focuses on randomized, placebo-controlled trials.

**Chronic Migraine**

The published literature on sphenopalatine ganglion (SPG) blocks to treat chronic migraine consists of 1 double-blind, placebo-controlled randomized trial\(^7,8\) and a case report with 3 patients.\(^9\)

Findings from the RCT were published in two 2015 publications by Cady et al. The first publication\(^7\) reported on the primary outcome measure and key secondary outcomes, and the subsequent publication\(^8\) reported on supplemental secondary outcomes and longer term follow-up. The trial included patients who met International Classification of Headache Disorders-II diagnostic criteria for chronic migraine\(^10\) and had had chronic migraine for at least 3 months. Patients could use concomitant headache medication, but had to agree not to change medication use during the study period. Following an initial 28-day baseline period to confirm the diagnosis of chronic migraine, patients were randomized 2:1 to receive treatment with bupivacaine 0.5% or saline (placebo) applied using the Tx360 device. Patients received a series of 12 treatments—2 treatments a week for 6 weeks. The primary outcome was change in pain severity, measured using a 0-to-10 numeric rating scale (NRS). Pain severity was assessed 15 minutes, 30 minutes, and 24 hours after each treatment. Key secondary outcome measures were the Patient’s Global Impression of Change (PGIC), the Headache Impact Test (HIT-6) questionnaire, and patient satisfaction with treatment. In addition, patients kept headache diaries throughout the study.

Forty-one patients met eligibility criteria and had chronic migraine diagnoses confirmed during the baseline period. These patients were randomized to bupivacaine (n=27) or to placebo (n=13). Mean baseline scores on the NRS were 4.8 in the bupivacaine group and 4.5 in the placebo group. When findings for all treatments were pooled, patients in the bupivacaine group reported a significantly greater reduction in NRS scores than the placebo group at 15 minutes, 30 minutes, and 24 hours after treatment. Bupivacaine-treated patients also had significantly lower PGIC scores than saline-treated patients at 30 minutes and 24 hours posttreatment. No statistically significant between-group differences were found in HIT-6 scores or in average acute mediation use. Only 1 serious adverse event was reported and it was not treatment-related.

The second publication by Cady et al reported on 1- and 6-month follow-up results and on supplemental secondary end points.\(^8\) To control for multiple comparisons, the cutoff for statistical significance for the supplemental secondary end points was \(p < 0.01\). There were no statistically significant differences between groups in the reported supplementary secondary outcomes. These outcomes included the number of headache days per month, the mean pain score, and quality of life measures. A post hoc power analysis revealed that the trial was underpowered to detect significant differences in secondary outcomes. Some results were suggestive of a long-term effect. For example, the bupivacaine group had a lower, albeit nonsignificant number of headache days in the month posttreatment (17 days) than the placebo group (23 days). However, a trial with a larger sample size would be needed to confirm whether 1- or 6-month results are significantly better after bupivacaine than after placebo treatment.

**Section Summary: Chronic Migraine**

One double-blind, placebo-controlled, randomized trial has evaluated transnasal SPG blocks for chronic migraine. The trial found a significantly greater short-term (up to 24 hours) reduction in
pain severity after active treatment versus placebo. However, there were no significant longer
term effects on other outcomes (ie, 1 and 6 months after 12 treatments over 6 weeks). The trial
was underpowered to detect outcomes at 1 and 6 months. It had some risks of bias due to a
high rate of dropouts. Additional adequately powered trials are needed to determine the impact
of SPG blocks on health outcomes.

Severe Acute Headache Treated in the Emergency Setting
The published literature on SPG blocks to treat severe acute headache consists of 1 double-blind,
placebo-controlled, randomized trial (2015). The trial included patients between the ages of 18
and 65 who presented to the emergency department with a frontal-based crescendo-onset
headache and a negative neurologic examination. The trial focused on frontal-based headaches
because they are considered most likely to respond to SPG blocks. Headaches were not classified
into specific types but patients with sudden-onset headache were excluded. Ninety-three patients
met eligibility criteria and were randomized 1:1 to treatment with bupivacaine 0.5% (n=45) or to
a saline placebo (n=48) applied using the Tx360 device. The intervention consisted of 1
treatment session. The primary outcome was a 50% absolute pain reduction on a 100-mm visual
analog scale (VAS) 15 minutes posttreatment. Four patients, 2 in each group, withdrew before
receiving the intervention and 2 were deemed ineligible after randomization. Thus, 41 patients in
the bupivacaine group and 46 in the placebo group were included in the primary analysis.

For the primary outcome, 20 (49%) patients in the bupivacaine group and 19 (41%) patients in
the placebo group had at least a 50% reduction in the mean VAS score. The difference between
groups (7.5%) did not differ statistically (95% confidence interval, -13% to 27%). Secondary
outcomes, including at least a 19-mm reduction in VAS score, percentage of patients who were
headache-free 15 minutes postintervention, and percentage of patients who were nausea-free 15
minutes postintervention, also did not differ significantly between groups. Seventy-six (88%)
patients were available for follow-up after 24 hours. The percentage of patients headache-free at
24 hours was significantly higher in the bupivacaine group (n=26 [72%]) than in the placebo
group (n=19 [48%]; difference, 25%; 95% CI, 2.6% to 44%). No serious adverse events were
reported in either group. The trialists stated that, in retrospect, outcome assessment at 1 hour
after treatment would have been useful because headache relief at 1 hour, but not at 24 hours,
is clinically relevant for emergency department headache patients.

Section Summary: Severe Acute Headache Treated in the Emergency Setting
One double-blind, placebo-controlled, randomized trial has evaluated a single transnasal SPG
block for treating patients with acute headache presenting to an emergency department. The
authors did not find a statistically significant benefit for active treatment compared with placebo
15 minutes postintervention. Significantly more patients were headache-free at 24 hours in the
active treatment than in the placebo group, but, in the absence of short-term pain relief, SPG
blocks would not be a clinically useful treatment in the emergency setting. Future studies
conducted in the emergency setting should assess outcomes for an intermediate time period (eg,
1 or 2 hours posttreatment).

Cluster Headache
No RCTs or nonrandomized controlled studies were identified that evaluated intranasal SPG
blocks for treating cluster headache. Two case series in patients with chronic drug-resistant
cluster headache were published by a research group in Italy. Both studies used a needle
(20-gauge in 1 study, 18-gauge in the other) under endoscopic control to inject a mixture of local

Contains Public Information
anesthetics and steroid as close as possible to the SPG. The mixture consisted of triamcinolone acetonide (40 mg), 1% bupivacaine (4 mL), and 2% mepivacaine with 1/100,000 adrenaline (2 mL). The earlier study, published in 2006 by Felisati et al, included 21 patients who received between 2 and 4 total treatment sessions, provided 1 week apart. Including 1 patient in whom the treatment could not be applied, 9 (45%) experienced no efficacy, 3 (15%) experienced a partial benefit, and 8 (40%) experienced a complete temporary benefit. In the 8 patients who had complete disappearance of attacks, the benefit lasted 2 to 4 weeks in 3 patients, 3 to 6 months in 3 patients, and 12 to 24 months in 2 patients. Four (19%) patients experienced treatment-related complications, which consisted of 1 case of marked nasal epistaxis 3 days after the procedure and 3 cases of temporary diplopia.

In 2010, Pipolo reported on 15 patients who received 3 SPG block treatments a mean of 3 days apart. Eight (53%) of the 15 patients experienced complete remission of cluster headache symptoms. Three (20%) of these continued to be in remission at last follow-up (mean, 18 months). One (7%) patient experienced partial benefit and 6 (40%) reported either no benefit or a benefit for less than 2 weeks. Three (20%) patients experienced complications, including 2 cases of severe epistaxis and 1 of reduced buccal opening that resolved after 5 months.

Section Summary: Cluster Headache
The literature includes 2 case series, both of which were published by the same research group in Italy. The approach to treatment was similar in the 2 studies but differed in terms of medication and application technique currently used in the United States. It is unclear how the safety or efficacy of the procedure used in the case series differs from an intranasal SPG block applying local anesthetics and using an FDA cleared device. In these series, 40% to 50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. These studies had small sample sizes and lacked a sham treatment or alternative therapy for treating cluster headache.

SUMMARY OF EVIDENCE
For individuals who have chronic migraine who receive sphenopalatine ganglion (SPG) block(s), the evidence includes a randomized controlled trial (RCT) and a case report. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The randomized trial evaluated a regimen of 12 SPG blocks over 6 weeks and was double-blind and placebo-controlled. The trial found significantly greater short-term (up to 24 hours) benefits from active treatment than from placebo. There were no significant longer term effects (ie, 1 and 6 months after 12 treatments), although the trial was underpowered to detect longer term efficacy. Given that SPG blocks are being proposed as a preventive therapy for chronic migraines, evidence demonstrating reduced migraine frequency, severity, or other objective outcomes from robust trials is still needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe acute headache treated in the emergency setting who receive SPG block(s), the evidence includes 1 RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The randomized, double-blind, placebo-controlled trial was evaluated a single SPG block for severe acute headache of mixed etiologies. There was no statistically significant difference between active treatment and placebo for the primary outcome (pain reduction 15 minutes postintervention). The trialists did not collect pain again data until 24 hours posttreatment, at which time significantly more patients were
headache-free in the active treatment arm than in the placebo arm. Additional studies, preferably RCTs, are needed to determine whether SPG blocks are an effective treatment in the emergency setting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cluster headache who receive SPG block(s), the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Two small case series, both of which evaluate an approach for intranasal SPG blocks that differs from the intervention currently available in the United States, were identified. In these series, 40% to 50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. However, it is not clear from these series the degree to which the procedures evaluated differ in safety and efficacy from an intranasal SPG block using a device cleared by the Food and Drug Administration. Additional studies, preferably RCTs, are needed to evaluate SPG blocks for treating cluster headaches. The evidence is insufficient to determine the effects of the technology on health outcomes.

**PRACTICE GUIDELINES AND POSITION STATEMENTS**

No guidelines or statements were identified.

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**

Not applicable.

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**

Some currently unpublished trials that might influence this review are listed in Table 1.

### Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02365909</td>
<td>Study Evaluating Sphenopalatine Ganglion Block (SPGB) for Treatment of Postdural Puncture Headache (PDPH)</td>
<td>30</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02090998</td>
<td>Sphenopalatine Ganglion Nerve Block vs. Elavil for Treatment of Transformed Migraines</td>
<td>200</td>
<td>May 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

**CODING**

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

### CPT/HCPCS

- 64400 Injection, anesthetic agent; trigeminal nerve, any division or branch
- 64505 Injection, anesthetic agent; sphenopalatine ganglion
- 64999 Unlisted procedure, nervous system

- This service is reported by some providers with CPT code 64505 along with the CPT code for trigeminal block: 64400.
ICD-10 Diagnoses
Experimental / Investigational for all diagnoses related to this medical policy.

REVIEWS

REFERENCES