| 7.01.168 | Cryoablation, Radiofrequency Ablation, and Laser Ablation for Treatment of Chronic Rhinitis | | |
|---|---|---|---|
| **Original Policy Date:** | November 1, 2021 | **Effective Date:** | May 1, 2024 |
| **Section:** | 7.0 Surgery | **Page:** | Page 1 of 25 |

## Policy Statement

I. Cryoablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.

II. Radiofrequency ablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.

III. Laser ablation for chronic rhinitis (allergic and nonallergic) is considered **investigational**.

**NOTE**: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

## Policy Guidelines

**Coding**
See the Codes table for details.

## Description

Chronic rhinitis is a common medical condition that encompasses allergic rhinitis, nonallergic rhinitis, and mixed rhinitis and can severely impact quality of life. The initial treatment for chronic rhinitis often involves medical management with pharmacotherapy that may include steroids, anticholinergics, nasal decongestants, and antihistamines. For individuals who do not attain improvement in chronic rhinitis symptoms after receiving adequate medical therapy (referred to as refractory chronic rhinitis), invasive surgical options to block posterior nasal nerve may be considered. Historically, vidian neurectomy which targets the vidian nerve was offered for refractory rhinitis. Although vidian neurectomy was shown to be effective in reducing symptoms like rhinorrhea, it is associated with side effects of cheek and palate numbness and dry eyes (in nearly 50% of cases, ranging between 35 to 72%). In an effort to improve on complications of vidian neurectomy such as xerophthalmia, interventions that specifically target the posterior nasal nerve branches of the vidian nerve have been developed. These interventions range from surgical ablation of the post-ganglionic posterior nasal nerve to minimally invasive options of cryotherapy, radiofrequency, or laser ablation of the nerve. These minimally invasive procedures can be performed under endoscopy. The efficacy of ablation of posterior nasal nerve is thought to result from the interruption of efferent parasympathetic stimulation of the nasal mucosa, which leads to reduction in submucosal gland secretions and blood flow.

## Related Policies

- Balloon Ostial Dilation for Treatment of Chronic and Recurrent Acute Rhinosinusitis
- Functional Endoscopic Sinus Surgery for Chronic Rhinosinusitis
- Steroid-Eluting Sinus Stents and Implants

## Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract

language will control. 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.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

## Regulatory Status

In February 2019, the ClariFix™ device (Stryker) was cleared for use in adults with chronic rhinitis by the FDA through the 510(k) process (K190356).[7,] Clearance was based on substantial equivalence to the predicate device, ClariFix (K162608). The only modification to the subject device was an update to the indications for use to include adults with chronic rhinitis. As per the FDA 510K summary, the ClariFix device is intended to be used as a cryosurgical tool for the destruction of unwanted tissue during surgical procedures, including in adults with chronic rhinitis.

In December 2019, the RhinAer™ stylus (Aerin Medical) was cleared by the FDA through the 510(k) process as a tool to treat chronic rhinitis (K192471).[8,] Clearance was based on equivalence in design and intended use of a predicate device, the InSeca ARC Stylus™ (K162810). The RhinAer stylus includes modification of the InSeca ARC stylus shaft components and flexibility. As per the FDA 510K summary, the RhinAer is indicated for use in otorhinolaryngology surgery for the destruction of soft tissue in the nasal airway, including in posterior nasal nerve regions in patients with chronic rhinitis.

There are currently no laser ablation devices with FDA clearance for treatment of chronic rhinitis.

## Rationale

### Background

Chronic rhinitis is a common medical condition that encompasses allergic rhinitis, nonallergic rhinitis, and mixed rhinitis and can severely impact quality of life.[1,]The initial treatment for chronic rhinitis often involves medical management with pharmacotherapy that may include steroids, anticholinergics, nasal decongestants, and antihistamines. Although medications are the mainstay treatment option, approximately 10% to 22% of the patients with chronic rhinitis still have persistent symptoms despite medical therapy and may require further interventions.[2,]For individuals who do not attain improvement in chronic rhinitis symptoms after receiving adequate medical therapy (referred to as refractory chronic rhinitis), invasive surgical options to block posterior nasal nerve may be considered. Historically, vidian neurectomy which targets the vidian nerve was offered for refractory rhinitis.[3,4,] Although vidian neurectomy was shown to be effective in reducing symptoms like rhinorrhea, it is associated with side effects of cheek and palate numbness and dry eyes (in nearly 50% of cases, ranging between 35% to 72%).[3,] In an effort to improve on complications of vidian neurectomy such as xerophthalmia, interventions that specifically target the posterior nasal nerve branches of the vidian nerve have been developed. It is thought that such interventions would help to reduce the morbidity associated with vidian neurectomy.[5,]These interventions range from surgical ablation of the post-ganglionic posterior nasal nerve to minimally invasive options of cryotherapy, radiofrequency, or laser ablation of the nerve. These minimally invasive procedures can be performed under endoscopy. The efficacy of ablation of posterior nasal nerve is thought to result from the interruption of efferent parasympathetic stimulation of the nasal mucosa, which leads to reduction in submucosal gland secretions and blood flow.[6,]

To quantify the severity of chronic rhinitis and to assess treatment response, various outcome measures can be used, including radiologic scores, endoscopic grading, and patient-reported quality of life measures. The primary outcome measures relevant for the treatment of chronic rhinitis are

patient-reported symptoms and quality of life. Examiner evaluation of the nasal and sinus appearance and polyp size may provide some information about treatment outcomes, but these evaluations are limited by the lack of universally accepted standards.

Frequently used outcome measures for treatments of chronic rhinitis in adults are shown in Table 1. A consensus on the minimally clinically important difference (MCID) for some of these outcomes has not been established. The U.S. Food and Drug Administration (FDA) guidance on drugs for rhinitis recommends patient-reported total nasal symptom scores as the primary measure of efficacy. The FDA guidance on drugs for rhinitis does not specify a MCID for patient-reported symptom measures, but notes that a MCID should be prespecified in studies and the rationale explained. Adverse events must be assessed immediately (perioperative complications and postoperative pain) and over the longer term.

**Table 1. Outcome Measures for Chronic Rhinitis Interventions**

| Outcome | Measures | Description | Minimal Clinically Important Difference | Timing |
|---|---|---|---|---|
| **Symptoms** | reflective Total Nasal Symptom Score (rTNSS) | Sum of 4 individual subject-assessed symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing, each evaluated using a scale of 0 = none, 1 = mild, 2 = moderate, or 3 = severe. Maximum 12 points. | Not established; 30% change from baseline has been proposed | At least 6 months or longer |
| | The Chronic Sinusitis Survey (CSS) | Measure of symptoms and medication usage over an 8-week recall period. Includes 3 questions regarding symptoms and 3 regarding medication usage, yielding a total score, symptom subscore, and medication subscore. Ranges from 0 to 100 in which a low CSS score represents greater symptoms and/or medication usage. | Not established | At least 6 months or longer |
| | Visual Analog Scale (VAS) | Patient-reported. | Not established | At least 6 months or longer |
| **Disease-Specific Quality of Life** | Sino-Nasal Outcome Test-20 (SNOT-20) | Patients complete 20 symptom questions on a categorical scale (0 [no bother] to 5 [worst symptoms can be]). Average rankings can be reported over all 20 symptoms, as well as by 4 subclassified symptom domains. The possible range of SNOT-20 scores is 0 to 5, with a higher score indicating a greater rhinosinusitis-related health burden. SNOT-22, a variation of the SNOT-20, includes 2 additional questions (on "nasal obstruction" and "loss of smell and taste"). | SNOT-20: change in score of 0.8 or greater<br><br>SNOT-22: change in score of 8.9 points | At least 6 months or longer |
| | Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) | Measures the functional (physical, emotional, and social) problems associated with rhinitis. | Not established | At least 6 months or longer |
| | Visual analog scale (VAS) | Patient-reported. | Not established | At least 6 months or longer |
| **Adverse events** | Various; patient- and clinician reported | Potential procedure- and device-related adverse events include postoperative pain, epistaxis, and dry eyes. | Not applicable | Immediately post procedure to 6 months or longer |

## Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.
To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

## Ablative Procedures for Chronic Rhinitis

### Clinical Context and Therapy Purpose

The purpose of ablative procedures (cryoablation, radiofrequency ablation, and laser ablation) in individuals with chronic rhinitis who are refractory to medical management is to provide a treatment option that is an alternative to or an improvement on existing surgical invasive options. Chronic rhinitis is a common medical condition that can severely impact quality of life. While the initial medical treatment comprising of pharmacotherapy is adequate for majority of individuals, approximately 10% to 22% individuals may still have persistent symptoms despite medical therapy. Treatment options for individuals with chronic rhinitis that is refractory to medical management are limited and include vidian neurectomy and invasive surgical options to block posterior nasal nerve. However, these surgical interventions are associated with high frequency of post operative complications and requirement of general anesthesia. To overcome some of these limitations, minimally invasive ablative procedures using cryo, radiofrequency or laser based-interventions have been developed. These interventions do not require general anesthesia and can be performed using an endoscope. In order to evaluate if these minimally invasive ablative interventions improve the net health outcome, trials must enroll individuals with chronic rhinitis who are refractory to medical management and compare these ablative interventions with sham surgery or conventional surgical procedures to block posterior nasal nerve ideally in the setting of a RCT. Nonrandomized trials in similar populations can inform the durability of response after initial efficacy is demonstrated via RCTs.

The following PICO was used to select literature to inform this review.

#### *Population*

The relevant population of interest is adults age 18 years of age and older with chronic allergic or nonallergic rhinitis refractory to medical management.

Rhinitis is defined as symptomatic inflammation of the paranasal sinuses and nasal cavity. Chronic rhinitis is usually defined as rhinorrhea with or without nasal congestion symptoms despite medical therapy lasting longer than 3 months. Allergic rhinitis is defined as an immunoglobulin E (IgE)–mediated inflammatory response of the nasal mucous membranes after exposure to inhaled allergens. Symptoms include rhinorrhea (anterior or post nasal drip), nasal congestion, nasal itching, and sneezing. Allergic rhinitis can be seasonal or perennial, with symptoms being intermittent or persistent.

### *Interventions*

The therapies being considered are cryoablation, radiofrequency ablation and laser ablation. Procedure involves destruction of tissue in the posterior nasal nerve region and is thought to correct the imbalance of autonomic input to the nasal mucosa, reducing nasal antigen responses and vascular hyperreactivity.

- Cryoablation: The ClariFix system uses nitrous oxide to freeze nasal tissue, causing nerve damage. The procedure can be performed under local anesthesia.
- Radiofrequency ablation: The RhinAer Stylus is a handheld device designed for use under local anesthesia. The device delivers radiofrequency energy at a temperature of 60 degrees Celsius to the posterior nasal nerve region.
- Laser ablation: There are currently no laser ablation devices with FDA clearance for treatment of chronic rhinitis.

### *Comparators*

The comparator of interest is other surgical procedures.

### *Outcomes*

The general outcomes of interest are symptoms, change in disease status, quality of life, and treatment-related morbidity.

To quantify the severity of chronic rhinitis and to assess treatment response, various outcome measures can be used, including radiologic scores, endoscopic grading, and patient-reported quality of life measures. The primary outcome measures relevant for the treatment of chronic rhinitis are patient-reported symptoms and quality of life. Examiner evaluation of the nasal and sinus appearance and polyp size may provide some information about treatment outcomes, but these evaluations are limited by the lack of universally accepted standards.

Frequently-used outcome measures for treatments of chronic rhinitis in adults are shown above in Table 1 (see Background). Adverse events must be assessed immediately (perioperative complications and postoperative pain) and over the longer term.

### Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

## Cryoablation
## Review of Evidence

### Randomized Controlled Trials

One RCT conducted by Del Signore et al (2021)[9], compared cryoablation using the ClariFix device with a sham procedure in 133 adults (age ≥21 years) with chronic rhinitis (Tables 2 and 3 ). Duration of follow-up was 3 months. Although the trial results showed a statistical significant difference in response rate in favor of cryoablation group compared to the sham group, it is unclear if the trial enrolled individuals with chronic rhinitis who were refractory to medical management. This limitation precludes interpretation of results.

**Table 2. RCT of Cryoablation for Chronic Rhinitis - Characteristics**

| Study | Countries | Sites | Dates | Participants | Interventions | |
|---|---|---|---|---|---|---|
| | | | | | Active | Comparator |
| **DelSignore et al (2021)[9]** | U.S. | 12 sites | Not reported | N=133 adults with chronic rhinitis with moderate to severe symptoms (rTNSS rhinorrhea subscore ≥2, congestion subscore ≥2, and total score ≥4).<br><br>Baseline patient characteristics<br>• 66/133 had documented responses to a previous trial of ipratropium;<br>• Of these 66, 16.7% were classified as "nonresponders", 81.8% were classified as "responders", and 1.5% had an unknown response<br>• 47.1% of patients in the active group and 49.2% of patients in the sham group were using any allergy/rhinitis medication at baseline<br>• Documented trial and failure of medical management alone was not an inclusion criteria<br>• Mean age: 55 years<br>• 58% female<br>• 89% White, 6% Black, 3% Asian, <1% American Indian/ Alaska Native<br>Primary endpoint:<br>• Comparison between the treatment and sham arms for the percentage of responders at 90 days. Responders were defined as participants with a 30% or greater reduction in rTNSS relative to baseline. | Cryoablation with the ClariFix device; n=68 | Sham cryoablation; n=65 |

RCT: randomized controlled trial; rTNSS: reflective Total Nasal Symptom Score.

Table 3. RCT of Cryoablation for Chronic Rhinitis - Results

| Study | Symptoms (Proportion with ≥30% Improvement in rTNSS from Baseline) | Symptoms (rTNSS Mean Change from Baseline) | RQLQ Score (Mean Change from Baseline) | Concomitant Allergy/Rhinitis Medication Use (Proportion with Use at 3 Months) | Adverse Events |
|---|---|---|---|---|---|
| **DelSignore et al (2021)[9,]** | | | | | |
| **Cryoablation with ClariFix** | 73.4% (47/64) | -3.7 (95% CI, -4.3 to -3.1) | -1.5 (95% CI, -1.8 to -1.2) | 40.0% (26/65) | Post-procedural pain: 36.8% (25/68)<br>Headache: 5.9% (4/68) |
| **Sham cryoablation** | 36.5% (23/63) | -1.8 (95% CI, -2.5 to -1.1) | -0.8 (95% CI, -1.1 or -0.5) | 34.4% (22/64) | Post-procedural pain: 1.5% (1/65)<br>Headache: 0% (0/68) |
| **p-value** | <.001 | <.001 | <.001 | .51[a] | Post-procedural pain:.002[a]<br>Headache:.15[a] |

[a] p-value calculated by BCBSA staff.
CI: confidence interval; RCT: randomized controlled trial; RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire; rTNSS: reflective Total Nasal Symptom Score.

The purpose of the study limitations tables (see Tables 4 and 5 ) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement. The major limitation is the lack of clarity on whether the enrolled study participants were refractory to medical management or not. An adequately powered randomized sham-controlled trial that enrolls participants who are refractory to medical management is necessary to clearly ascertain effect of cryoablation on the net health outcome in patients with chronic rhinitis.

Table 4. Study Relevance Limitations

| Study | Population[a] | Intervention[b] | Comparator[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| **DelSignore et al (2021)[9,]** | 1. The intended use population is unclear (it is not clear if the trial enrolled participants who were refractory to medical management). 3. The studies were all comprised of racially homogenous participants with over 89% White and thus the conclusions may not be generalizable to the US population | | 2: Other (An alternative comparator could be other surgical interventions). | | 1, 2: Follow-up limited to 3 months |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 5. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **DelSignore et al (2021)[9],** | 3. Allocation concealment unclear; | 2, 4: Patients were blinded; blinding was not reported for study staff or outcome assessors. | | | | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

### Nonrandomized Studies

Three single-arm prospective studies including 149 patients evaluated efficacy and safety of cryoablation for patients with chronic rhinitis. Characteristics and results of these studies are shown in Tables 6 and 7. Out of the 3 studies, 2 studies enrolled individuals who were refractory to medical management. The definition of refractory varied from symptoms not adequately controlled with a minimum of 4 weeks of topical nasal steroid treatment or failure of medical therapy for a duration of at least 3 months. Key limitations of these studies are summarized in Tables 8 and 9. Although all 3 studies reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases. Additionally, loss to follow-up was high and minimally clinically important differences (MCID) were not prespecified for important outcome measures.

Table 6. Nonrandomized Studies of Cryoablation for Chronic Rhinitis - Characteristics

| Study | Study Design | Location | Dates | Inclusion/Exclusion Criteria | Patient Characteristics | Treatment | Duration of Follow-up |
|---|---|---|---|---|---|---|---|
| **Hwang et al (2017)[10],** | Prospective, single-arm, open-label | 3 sites, US | Not reported | Inclusion:<br>• Adult patients with rhinorrhea with or without nasal congestion symptoms despite medical therapy longer than 3 months<br>• Minimum rhinorrhea and/or congestion subscores of 2 as part of the TNSS.<br><br>Exclusion:<br>• Patient-reported history of chronic rhinosinusitis<br>• Severe septal deviation precluding visualization of the middle meatus<br>• Endoscopic findings of polyps or purulence in the middle meatus, septal perforation, or prior sinus or nasal surgery that significantly altered the anatomy of the posterior nasal cavity. | N = 27<br>• Mean age, 53.3 (SD, 3.3) years<br>• 63% female<br>• race not reported<br>• 48% were atopic | Cryoablation performed in an office setting under local anesthesia | 1 year |
| **Chang et al (2020)[11], Ow et al (2021)[12]; NCT03181594** | Prospective, single-arm, open-label | 6 sites, US | 2017-2020 | Inclusion:<br><br>Age 21 years or older, with all of the following:<br>• Moderate-to-severe symptoms of rhinorrhea (defined as individual symptom rating of 2 or 3 on the rTNSS)<br>• Mild-to-severe symptoms of congestion (individual symptom rating of 1, 2, or 3 on the rTNSS) and minimum total score of 4 (out of 12) on the rTNSS at the time of the treatment visit | N = 98<br>• Mean age, 58.6 (SD, 16.2) years<br>• 64.3% female<br>• 91.8% identified as Caucasian<br>• 70 (71.4%) with nonallergic rhinitis and 28 (28.6%) with allergic rhinitis | Cryoablation performed in an office setting under local anesthesia | 2 years (n = 62) Primary data collection at 9 months |

| Study | Study Design | Location | Dates | Inclusion/Exclusion Criteria | Patient Characteristics | Treatment | Duration of Follow-up |
|---|---|---|---|---|---|---|---|
| | | | | • Chronic symptoms for 6 months or longer<br>• Inadequate symptom relief from at least 4 weeks of treatment with intranasal steroids<br>Exclusion:<br>• Clinically significant nasal or sinus anatomy that limits the ability to visualize/access the posterior nasal cavity or to accommodate the device<br>• Rhinitis medicamentosa, moderate-to-severe ocular symptoms, nasal or sinus infection, or recent history of epistaxis<br>• Coagulation disorder or anti-coagulant treatment<br>• Known sensitivity to the planned anesthetic agent(s)<br>• Cryoglobulinemia, paroxysmal cold hemoglobinuria, cold urticaria, or Raynaud's disease<br>• Pregnancy | | | |
| **Gerka Stuyt et al (2021)[13,]** | Prospective, single-arm, open-label | 7 sites, US | Not reported | Inclusion:<br>• Age over 18 years, diagnosis of chronic rhinitis, and failure of medical therapy for a duration of at least 3 months<br>Exclusion:<br>• Active or chronic nasal/sinus infections<br>• Structural abnormalities restricting device from accessing the | N = 24<br>• Mean age: 60.04 (SD, 16.7) years<br>• 50% female<br>• Race not reported<br>• 16 (67%) with non-allergic rhinitis; 3 (12.5%) with allergic; 5 (20.8%) with mixed | Cryoablation performed in an office setting under local anesthesia | 1 year |

| Study | Study Design | Location | Dates | Inclusion/Exclusion Criteria | Patient Characteristics | Treatment | Duration of Follow-up |
|---|---|---|---|---|---|---|---|
| | | | | posterior middle meatus<br>• Cerebrospinal fluid leaks<br>• Rhinitis medicamentosa<br>• Confounding systemic conditions (i.e. granulomatosis with polyangiitis, Sjogren's syndrome, cystic fibrosis, primary ciliary dyskinesia),<br>• Active intranasal recreational drug use<br>• Recurrent history of epistaxis, coagulopathy, pregnancy, or nasopharyngeal malignancy | | | |

rTNSS: reflective Total Nasal Symptom Score ; SD: standard deviation; TNSS: Total Nasal Symptom Score.

**Table 7. Nonrandomized Studies of Cryoablation for Chronic Rhinitis - Results**

| Study | Symptoms | Quality of Life | Concomitant Medication Use | Adverse Events | Periprocedural Pain |
|---|---|---|---|---|---|
| **Hwang et al (2017)[10],** | Mean reduction from baseline in rTNSS (SD):<br>• 30 days (n=27): 2.6 (0.3); p<.001<br>• 90 days (n=27): 2.7 (0.4); p<.001<br>• 180 days (n=21): 2.3 (0.5); p<.001<br>• 1 year (n=15):1.9 (0.3); p<.001 | Not assessed | Not assessed | Day 1 post procedure: 100% reported no or mild bleeding, 44% severe ear blockage, 4% severe nasal dryness; there was 1 moderate nosebleed 27 days post-procedure | 74% reported no or mild pain/discomfort |
| **Chang et al (2020)[11], (Outcomes through 9 months), Ow et al (2021)[12], (Outcomes from 12 through 24 months); NCT03181594** | Mean change from baseline in rTNSS score (SD):<br>• 30 days (n = 97): 2.9 (1.9); p<.001<br>• 90 days (n = 96): 3.0 (2.3); p<.001<br>• 180 days (n = 95): 3.0 (2.1); p<.001<br>• 270 days (n = 92): 3.0 (2.4); p<.001<br>Median change from baseline in rTNSS score (IQR):<br>• 12 months (n = 54): -3.0 (-4.0, -1.0); p<.001 | Mean change from baseline in RQLQ score (SD)<br>• 90 days (n = 96): 1.5 (1.2); p<.001<br>Median change from baseline in RQLQ score (IQR)<br>• 18 months (n = 54): - | 5 patients started using ipratropium bromide during the study period due to persistent rhinitis symptoms. Of 154 medications that 98 patients were using at baseline, 33 | 31 treatment-related adverse events (2 serious: nosebleed) | 16 of 72 (22.2%) patients assessed reported no pain or discomfort<br><br>17 reported severe headache, 5 severe nasal pain, 2 severe sinus pain |

| Study | Symptoms | Quality of Life | Concomitant Medication Use | Adverse Events | Periprocedural Pain |
|---|---|---|---|---|---|
| | • 18 months (n = 54): -3.0 (-5.0, -2.0); p<.001<br>• 24 months (n = 57): -4.0 (-5.0, -2.0); p<.001 | 2.1 (-3.1, -1.1); p<.001<br>• 24 months (n = 57): -2.1 (-3.0, -0.8); p<.001 | (21.4%) medications were discontinued during the study period | | |
| **Gerka Stuyt et al 2021[13,]** | Mean 12-hour TNSS score (SD):<br>• Baseline: 6.92 (2.8); p<.001<br>• 30 days: 3.17 (2.4); p<.001<br>• 90 days: 2.92 (1.4); p<.001<br>• 1 year: 3.08 (2.6); p<.001<br>Mean 2-week TNSS score (SD):<br>• Baseline: 7.75 (3.1); p<.001<br>• 30 days: 3.79 (2.1); p<.001<br>• 90 days: 3.88 (1.8); p<.001<br>• 1 year: 3.76 (2.1); p<.001 | Not assessed | 12/18 patients assessed (66.7%) had eliminated or reduced the use of medication to manage their rhinitis when compared to their preoperative baseline | No patients developed epistaxis, palate numbness, or dry eye complications | Patients experienced only minimal discomfort during and post-procedure |

IQR: interquartile range; RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire; rTNSS: reflective Total Nasal Symptom Score ; SD: standard deviation; TNSS: Total Nasal Symptom Score.

## Table 8. Study Relevance Limitations

| Study | Population[a] | Intervention[b] | Comparator[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| **Hwang et al (2017)[10,]** | 1. The intended use population is unclear (it is not clear if the trial enrolled participants who were refractory to medical management) | | | | |
| **Chang et al (2020)[11,], Ow et al (2021)[12,]; NCT031815944** | | | | 5. Clinically significant difference for Total Nasal Symptom Score was not prespecified | |
| **Gerka Stuyt et al 2021[13,]** | | | | | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not

prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 9. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **Hwang et al (2017)[10],** | 1. Not randomized | 1. Open label | 1. Not registered | 1. 6/27 (22%) lost to follow-up at 180 days, 12 (44%) lost to follow-up at 1 year | 1. Power calculation not reported | |
| **Chang et al (2020)[11], Ow et al (2021)[12]; NCT03181594** | 1. Not randomized | 1. Open label | | 1. Through 9 months, 7/98 (7.1%) excluded from analysis: 4 lost to follow-up, 3 excluded due to resumption of ipratropium use during the study period 62 of 98 patients (63.2%) enrolled in the longer-term follow-up study 72/98 (73.5%) patients completed post-procedure pain questionnaire | 1. Power calculation not reported | |
| **Gerka Stuyt et al 2021[13],** | 1. Not randomized | 1. Open label | 1. Not registered | 1. 6 of 24 lost to follow-up at 1 year (25%) | 1. Power calculation not reported | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Section Summary: Cryoablation

Evidence for the use of cryoablation for the treatment individuals with chronic rhinitis who are refractory to medical management includes one RCT and several nonrandomized studies. One RCT that compared cryoablation using the ClariFix device with a sham procedure showed a statistical significant difference in response rate in favor of the cryoablation group compared to the sham group. However, it is unclear if the trial enrolled individuals with chronic rhinitis who were refractory to medical management. This limitation precludes meaningful interpretation of these results as the intended use of ClariFix device is for individuals with chronic rhinitis who are refractory to medical management. Three single-arm prospective studies evaluated efficacy and safety of cryoablation for patients with chronic rhinitis. Out of the 3, 2 studies enrolled individuals who were refractory to medical management. The definition of refractory varied from symptoms not adequately controlled with a minimum of 4 weeks of topical nasal steroid treatment to failure of medical therapy for a duration of at least 3 months. Although all 3 single arm studies reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases. Additionally, loss to follow-up was high.

## Radiofrequency Ablation

### Randomized Controlled Trials

Stolovitsky et al (2021) conducted an RCT comparing radiofrequency ablation using the RhinAer device with sham treatment.[14,] The trial enrolled 117 adults (age, 18 to 85 years; mean age, 57 years) with chronic rhinitis. Use of medication to treat chronic rhinitis throughout the trial was allowed in both groups (Table 10 ). Approximately 72.7% of patients in the active treatment group and 71.8% in the sham group were using antihistamines at baseline. Although the trial results showed a statistical significant difference in response rate in favor of radiofrequency ablation group compared to the sham group, it is unclear if the trial enrolled individuals with chronic rhinitis who were refractory to medical management. This limitation precludes interpretation of results. The study was unblinded at 3 months, and individuals in the control group were allowed to crossover to the active intervention group. Takashima et al (2022) reported 12-month follow-up for patients (n=77) initially randomized to the active intervention group.[15,] Study results for the active intervention group at 6- and 12-months are reported in Table 11. The study is ongoing, with planned 3-year follow-up.

**Table 10. RCT of Radiofrequency Ablation for Chronic Rhinitis - Characteristics**

| Study | Countries | Sites | Dates | Participants | Interventions | |
|---|---|---|---|---|---|---|
| | | | | | Active | Comparator |
| **Stolovitsky et al (2021)[14,]** | U.S. | 16 sites | July 2020 to December 2020 | N=117 adults with ≥6 months chronic rhinitis with moderate to severe symptoms (rTNSS rhinorrhea subscore 2 to 3, congestion subscore 1 to 3, and total score ≥6)<br>• Mean age: 57 years<br>• 65% female<br>• 90% White, 6% Black, 1% Asian, 3% mixed race or not reported | Radiofrequency ablation with the RhinAer device; n=77 | Sham radiofrequency ablation; n=39 |

RCT: randomized controlled trial; rTNSS: reflective Total Nasal Symptom Score.

**Table 11. RCT of Radiofrequency Ablation for Chronic Rhinitis - Results**

| Study | Symptoms (Proportion with ≥30% Improvement in rTNSS from Baseline) | Symptoms (rTNSS Mean Change from Baseline) | Concomitant Medication Use (Proportion with Increased Use) | Periprocedural Pain (VAS 0-10) | Adverse Events |
|---|---|---|---|---|---|
| **Stolovitsky et al (2021)[14,] and Takashima et al (2022)[15,]** | | | | | |
| **Radiofrequency ablation with RhinAer** | • 3 months: 67.5% (95% CI, 55.9 to 77.8)<br>• 6 months: 75.0% (95% CI, 63.4 to 84.5)<br>• 12 months: 80.6% (95% CI, 69.1 to 89.2) | • 3 months: -3.6 (95% CI, -4.2 to -3.0)<br>• 6 months: -4.4 (95% CI, -5.0 to -3.8)<br>• 12 months: -4.8 (95% CI, -5.5 to -4.1) | • 3 months: 9.1% (7/77)<br>• 6 months: 16.8% (13/77)<br>• 12 months: 20.8% (16/77) | Immediately post-procedure: 2.1 (95% CI, 1.6 to 2.6) | Any treatment-related adverse event<br>12 months: 10.4% (8/77) |

| Study | Symptoms (Proportion with ≥30% Improvement in rTNSS from Baseline) | Symptoms (rTNSS Mean Change from Baseline) | Concomitant Medication Use (Proportion with Increased Use) | Periprocedural Pain (VAS 0-10) | Adverse Events |
|---|---|---|---|---|---|
| **Sham radiofrequency ablation** | 3 months: 41.0% | 3 months: -2.2 (95% CI, -3.2 to -1.3) | 12.8% (5/39) | Immediately post-procedure: 1.4 (95% CI, 0.7 to 2.0) | Not reported |
| **p-value** | 3 months:.009 | 3 months:.013 | 3 months:.53[a] | Immediately post-procedure:.078 | Not calculable |

[a] p-value calculated by BCBSA staff.
CI: confidence interval; RCT: randomized controlled trial; rTNSS: reflective Total Nasal Symptom Score; VAS: visual analog scale.

The purpose of the study limitations tables (see Tables 12 and 13) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement. The major limitation is the lack of clarity on whether the enrolled study participants were refractory to medical management or not. An adequately powered randomized sham-controlled trial that enrolls participants who are refractory to medical management is necessary to clearly ascertain effect of radiofrequency ablation on the net health outcome in patients with chronic rhinitis.

**Table 12. Study Relevance Limitations**

| Study | Population[a] | Intervention[b] | Comparator[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| **Stolovitsky et al (2021)[14,]** | 1. The intended use population is unclear (it is not clear if the trial enrolled participants who were refractory to medical management). | | 2: Other (An alternative comparator could be other surgical interventions) | 3: Only adverse events deemed related to treatment were reported for the active intervention group; there was no adverse event reporting for the control group. | 1, 2: Follow-up of randomized active treatment and control groups limited to 3 months; 12-month follow-up reported in Takashima et al (2022) provided for active treatment group only. |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 13. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **Stolovitsky et al (2021)[14,]** | 3: Allocation concealment unclear | 2, 4: Patients were blinded; blinding was not reported for study staff or outcome assessors; it is unclear if the treating physician was the outcome assessor; patients were unblinded at 3 months. | | | | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

### Nonrandomized Studies

Two single-arm prospective studies including 179 patients evaluated efficacy and safety of radiofrequency ablation for patients with chronic rhinitis.[16,17,] Characteristics and results of these studies are shown in Tables 14 and 15. Out of the 2 studies, 1 study enrolled individuals who were refractory to medical management.[17,] Refractory was defined as an inadequate response after at least 4 weeks usage of intranasal steroids and rTNSS score ≥6. Results of long term follow-up for 2-years were reported in an extension study of 34 patients. Ehmer D, McDuffie CM, McIntyre JB, et al. Long-ter.... 526575221096045. PMID 35663498] Key limitations of these studies are summarized in Tables 16 and 17. Although both studies reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases. Additionally, loss to follow-up was high and minimally clinically important differences (MCID) were not prespecified for important outcome measures.

**Table 14. Nonrandomized Studies of Radiofrequency Ablation for Chronic Rhinitis - Characteristics**

| Study | Study Design | Location | Dates | Inclusion/Exclusion Criteria | Patient Characteristics | Treatment | Duration of Follow-up |
|---|---|---|---|---|---|---|---|
| **Lee et al (2022)[16,]** | Prospective, single-arm, open label | 16 sites, U.S. and Germany | 2020-2021 | Adults with chronic rhinitis ≥6 months duration and total rTNSS ≥6, | N=129<br><br>Mean age 57.9 years (SD, 13.4); 54% female; | Radiofrequency ablation with the RhinAer device heated | 6 months |

| Study | Study Design | Location | Dates | Inclusion/Exclusion Criteria | Patient Characteristics | Treatment | Duration of Follow-up |
|---|---|---|---|---|---|---|---|
| | | | | rTNSS rhinorrhea subscore 2 to 3, and rTNSS congestion subscore 1 to 3<br>• Documented trial and failure of medical management was not an inclusion criterion | 91% white, 4% Black, 3% Asian, 2% other race/ethnicity; 72% nonallergic rhinitis, 8% allergic rhinitis, <1% mixed allergic and nonallergic rhinitis, 20% unknown etiology<br>• 50% of patients at baseline were on antihistamines<br>• 64.1% of patients at baseline were on intranasal steroids<br>• 25.8% of patients at baseline were on intranasal anticholinergic sprays | to 60° C performed in an office setting | |
| **Ehmer et al (2021[17],and 2022[18],)** | Prospective, single-arm, open label | 5 sites, U.S. | 2018-2021 | Chronic rhinitis of at least 6 months duration refractory to medical management (defined as an inadequate response after at least 4 weeks usage of intranasal steroids) and rTNSS score ≥6 | N=50<br>• Mean age 57.9 years (SD, 11.9);<br>• 42% female;<br>• 94% white, 4% Asian, 2% American Indian/Alaska Native;<br>• 42% allergic rhinitis, 34% non-allergic rhinitis, 24% unknown etiology | Radiofrequency ablation with the RhinAer device heated to 60° C performed in an office setting | 2 years |

rTNSS: reflective Total Nasal Symptom Score; SD: standard deviation.

**Table 15. Nonrandomized Studies of Radiofrequency Ablation for Chronic Rhinitis - Results**

| Study | Symptoms | Concomitant Medication Use | Quality of Life | Adverse Events | Periprocedural Pain |
|---|---|---|---|---|---|
| **Lee et al (2022)[16],** | Mean rTNSS score:<br>• Baseline: 7.8<br>• 3 months: 3.6; mean change from baseline -4.2 (95% CI, -4.6 to -3.7)<br>• 6 months: 2.9; mean change from baseline -4.9 (95% CI, -5.5 to -4.3)<br>Proportion of responders based on ≥30% improvement | | MiniRQLQ score, adjusted mean change from baseline:<br>• 3 months: -1.6 (95% CI, -1.8 to -1.4)<br>• 6 months: -1.8 (95% CI, -2.1 to -1.5)<br>MiniRQLQ, proportion of patients with ≥0.4 point | Any treatment-related adverse event: 6.2% (8/129) | Mean pain score (VAS 0 to 100): 19.0 (95% CI, 14.7 to 23.3) |

| Study | Symptoms | Concomitant Medication Use | Quality of Life | Adverse Events | Periprocedural Pain |
|---|---|---|---|---|---|
| | from baseline in rTNSS score:<br>• 3 months: 76.2% (95% CI, 68.1 to 82.8)<br>• 6 months: 83.5% (95% CI, 75.8 to 89.0) | | improvement from baseline:<br>• 3 months: 80.3% (95% CI, 72.6 to 86.3)<br>• 6 months: 87.7% (95% CI, 80.7 to 92.4) | | |
| **Ehmer et al (2021[17] and 2022[18])** | Mean rTNSS score:<br>• Baseline: 8.5 (95% CI, 8.0 to 9.0)<br>• 12 weeks: 3.4 (95% CI, 2.8 to 4.1)<br>• 1 year : 3.6 (95% CI, 3.0 to 4.3)<br>• 2 years: 2.9 (95% CI, NR); mean change from baseline -5.5 (95% CI, -6.4 to -4.6)<br>Proportion of responders based on ≥30% improvement from baseline in rTNSS score:<br>• 12 weeks: 87.8% (95% CI, 75.8 to 94.3 )<br>• 26 weeks: 91.7% (95% CI, 80.4 to 96.7 )<br>• 1 year: 80.9% (95% CI, 67.5 to 89.6 )<br>• 2 years: 88.2% (95% CI, 73.4 to 95.3) | Proportion with increased concomitant medication use at 1 year :<br>• Antihistamines/ decongestants: 12.8%<br>• Decongestant nasal spray: 4.3%<br>• Steroid nasal spray: 6.4% | | 1 year: Serious adverse events: 2 (N=NR) ; any adverse event: 16 (N=8)<br><br>2 years: NR; narrative report of no treatment -related adverse events from year 1 to year 2 | Mean post-treatment pain score (VAS 0 to 100): 18.1 |

CI: confidence interval; miniRQLQ: mini Rhinoconjunctivitis Quality of Life Questionnaire; NR: not reported; rTNSS: reflective Total Nasal Symptom Score ; VAS: visual analog score.

**Table 16. Study Relevance Limitations**

| Study | Population[a] | Intervention[b] | Comparator[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| **Lee et al (2022)[16]** | 1. The intended use population is unclear (it is not clear if the trial enrolled participants who were refractory to medical management) | | | | |

| |
|---|
| **Ehmer et al (2021[17],and 2022[18],)** |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 17. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **Lee et al (2022)[16],** | 1. Not randomized | 1. Open label | | | 1. Power calculations not reported | |
| **Ehmer et al (2021)[17],and 2022[18],)** | 1. Not randomized | 1. Open label | | 1. High loss to follow-up or missing data (of the 50 participants in the original study, 34 reconsented for the extension study and completed the 24-month follow-up visit) | 1. Power calculations not reported | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Section Summary: Radiofrequency Ablation

Evidence for the use of radiofrequency ablation for the treatment individuals with chronic rhinitis who are refractory to medical management includes one RCT and several nonrandomized studies. One RCT that compared radiofrequency using the RhinAer device with a sham procedure showed a statistical significant difference in response rate in favor of radiofrequency ablation group compared to the sham group. However, it is unclear if the trial enrolled individuals with chronic rhinitis who were refractory to medical management. This limitation precludes meaningful interpretation of these results as the intended use of RhinAer device is for individuals with chronic rhinitis who are refractory

to medical management. Two single-arm prospective studies evaluated efficacy and safety of radiofrequency ablation for patients with chronic rhinitis. Out of the 2, 1 study enrolled individuals who were refractory to medical management. Although both single arm studies reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases.

### Laser Ablation

#### Nonrandomized studies

Krespi et al (2020) reported the results of a nonrandomized study evaluating laser ablation for treatment of chronic rhinitis.[19,] The study enrolled 32 adults who were treated with an endoscopic diode laser in an outpatient setting. While the study stated that study participants were resistant to medical management, the authors did not define treatment resistance. Duration of follow-up was 3 months. Mean rTNSS was reduced from 6.0 (standard deviation [SD], 0.7) at baseline to 2.3 (SD, 0.4) at 3-month follow-up. Adverse events were not reported. Although the study reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases.

### Section Summary: Laser Ablation

Evidence for the use of laser ablation for the treatment individuals with chronic rhinitis who are refractory to medical management includes one nonrandomized study. Although the single-arm prospective study reported improvement in symptom control, the major limitation is lack of a comparator group and open-label nature of the study design, which likely introduces biases. In addition, the authors did not define how study participants were classified as refractory to medical management.

## Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### American Academy of Allergy, Asthma, and Immunology

The 2023 International Consensus Statement on Allergy and Rhinology stated the following for cryotherapy/radiofrequency ablation of posterior nasal nerve. [20,]

- Aggregate grade of evidence: C (Level 3: 2 studies, level 4: 4 studies, level 5: 5 studies)
- Benefit: Improvement in rhinorrhea.
- Harm: Risk of complications (e.g., epistaxis, temporary facial pain and swelling, headaches), limited long-term results.
- Cost: Surgical/procedural costs, cost of device, potential time off from work.
- Benefits-harm assessment: Potential benefit must be balanced with low risk of harm, especially considering limited long-term results.
- Value judgments: Patients may experience an improvement in symptoms.
- Policy level: Option.
- Intervention: Cryoablation and radiofrequency ablation of the posterior nasal nerve may be considered in allergic rhinitis patients that have failed medical management, particularly for rhinorrhea.

Grade of evidence "C" implies that body of evidence consisted of observational studies (case control and cohort design). Policy level "Option" implies "either that the evidence quality that exists is suspect or that well-designed, well conducted studies have demonstrated little clear advantage to one approach versus another. Options offer clinicians flexibility in their decision-making regarding appropriate practice, although they may set boundaries on alternatives. Patient preference should have a substantial role in influencing clinical decision-making, particularly when policies are expressed as options." As per the consensus statement, "because the current evidence is primarily based on industry-sponsored studies with limited long-term data, these office-based interventions remain an option for properly selected patients".

### American Academy of Otolaryngology

In January 2023, the American Academy of Otolaryngology issued a position statement on peripheral nerve ablation for the treatment of chronic rhinitis.[21,] The position statement was not based on a systematic review or strength of evidence rating. According to the position statement, " Based on these safety and efficacy data, the American Academy of Otolaryngology endorses the use of posterior nasal nerve ablation for the treatment of medically-refractory chronic rhinitis. We do not consider these treatments to be experimental."

### American Rhinologic Society

In January 2022, the American Rhinologic Society issued a position paper on posterior nasal nerve ablation.[22,] The position statement was not based on a systematic review or strength of evidence rating. According to the position statement, "The American Rhinologic Society supports the use of posterior nasal nerve ablation for the treatment of chronic rhinitis, including both allergic and non-allergic subtypes. This procedure should not be considered experimental, but should be considered as an effective option in treating chronic rhinitis and improving patient quality of life in those suffering from rhinorrhea and nasal congestion based on the following data."

### U.S. Preventive Services Task Force Recommendations

Not applicable.

### Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

### Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 18.

**Table 18. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| *Ongoing* | | | |
| **NCT04154605**[a] | ClariFix Rhinitis Randomized Controlled Trial | 133 | Jul 2022 |
| **NCT04533438**[a] | The RhinAer Procedure for Treatment of CHronic RhInitis - A Prospective, MulticeNter Randomized ConTrolled TRial Comparing RhinAer to Sham Control (RHINTRAC) | 116 | Apr 2024 |
| **NCT05648565** | Effects of Radiofrequency Ablation of Posterior Nasal Nerves on Inflammatory Cytokines, Peak Nasal Inspiratory Flow, and Nasal Blood Flow in Patients with Chronic Rhinitis | 36 | Dec 2023 |

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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## Documentation for Clinical Review

- No records required

## Coding

*This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.*

*The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.*

| Type | Code | Description |
|---|---|---|
| CPT® | 30117 | Excision or destruction (e.g., laser), intranasal lesion; internal approach |
| | 30999 | Unlisted procedure, nose |
| | 31242 | Nasal/sinus endoscopy, surgical; with destruction by radiofrequency ablation, posterior nasal nerve ***(Code effective 1/1/2024)*** |
| | 31243 | Nasal/sinus endoscopy, surgical; with destruction by cryoablation, posterior nasal nerve ***(Code effective 1/1/2024)*** |
| | 31299 | Unlisted procedure, accessory sinuses |
| HCPCS | C9771 | Nasal/sinus endoscopy, cryoablation nasal tissue(s) and/or nerve(s), unilateral or bilateral |

## Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

| Effective Date | Action |
|---|---|
| 11/01/2021 | New policy. |
| 05/01/2022 | Annual review. Policy statement and literature updated. Policy title changed from Cryoablation for Chronic Rhinitis to current one. |
| 04/01/2023 | Annual review. No change to policy statement. Literature review updated. |
| 03/01/2024 | Coding update |
| 05/01/2024 | Annual review. No change to policy statement. Policy guidelines and literature review updated. |

## Definitions of Decision Determinations

**Medically Necessary:** Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

## Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

*Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.*

## Appendix A

| POLICY STATEMENT (No changes) | |
|---|---|
| **BEFORE** | **AFTER** |
| **Cryoablation, Radiofrequency Ablation, and Laser Ablation for Treatment of Chronic Rhinitis 7.01.168**<br><br>**Policy Statement:**<br>I. Cryoablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.<br><br>II. Radiofrequency ablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.<br><br>III. Laser ablation for chronic rhinitis (allergic and nonallergic) is considered **investigational**. | **Cryoablation, Radiofrequency Ablation, and Laser Ablation for Treatment of Chronic Rhinitis 7.01.168**<br><br>**Policy Statement:**<br>I. Cryoablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.<br><br>II. Radiofrequency ablation for chronic rhinitis (allergic or nonallergic) is considered **investigational**.<br><br>III. Laser ablation for chronic rhinitis (allergic and nonallergic) is considered **investigational**. |