
Medicare Advantage Medical Policy



***Current Policy Effective Date: 11/1/22**
(See policy history boxes for previous effective dates)

Title: Steroid-Eluting Sinus Implants

Description/Background

Steroid-eluting sinus stents are devices used postoperatively following endoscopic sinus surgery (ESS) or for treatment of recurrent sinonasal polypsis following ESS. These devices maintain patency of the sinus openings in the postoperative period, and/or to serve as a local drug delivery vehicle. Reducing postoperative inflammation and maintaining patency of the sinuses may be important in achieving optimal sinus drainage and may impact recovery from surgery and/or reduce the need for additional surgery.

Background

CHRONIC RHINOSINUSITIS

Chronic rhinosinusitis is an inflammatory sinus condition that has a prevalence between 1% and 5% in the U.S. population.(1)

Treatment

Endoscopic sinus surgery (ESS) is typically performed on patients with chronic rhinosinusitis unresponsive to conservative treatment. The surgery is associated with high rates of improvement in up to 90% of more appropriately selected patients. However, there are no high-quality RCTs comparing functional ESS to continued medical management or alternative treatment approaches. Because of the high success rates and minimally invasive approach, these procedures have rapidly increased in frequency, with an estimated 250,000 procedures performed annually in the United States.(2) They can be done either in the physician's office under local anesthesia or in the hospital setting under general anesthesia.

ESS involves the removal of small pieces of bone, polyps, and debridement of tissue within the sinus cavities. There are a number of variations on the specific approach, depending on the disorders being treated and the preferences of the treating surgeon. For all procedures, there is

a substantial postoperative inflammation and swelling, and postoperative care is therefore a crucial component of ESS.

There are a number of postoperative treatment regimens, and the optimal regimen uncertain. Options include saline irrigation, nasal packs, topical steroids, systemic steroids, topical decongestants, oral antibiotics, and/or sinus cavity debridement. Several randomized controlled trials (RCTs) have evaluated treatment options, but not all strategies have been rigorously evaluated.(3-6) A 2011 systematic review has evaluated the evidence for these therapies.(2) Reviewers concluded that the evidence was not strong for any of these treatments but that some clinical trial evidence supported improvements in outcomes. The strongest evidence supported use of nasal saline irrigation, topical nasal steroid spray, and sinus cavity debridement.

Some form of sinus packing is generally performed postoperatively. Simple dressings moistened with saline can be inserted manually following surgery. Foam dressings are polysaccharide substances that form a gel when hydrated and can be used as nasal packs for a variety of indications.(7) Middle meatal spacers are splint-like devices that prop open the sinus cavities post-ESS but are not designed for drug delivery. There is some RCT evidence that middle meatal spacers may reduce the formation of synechiae following ESS, although the available studies have significant heterogeneity in this outcome.(8)

Sinus Stents and Implants

Implantable drug-eluting sinus stents are another option for postoperative management following ESS. These implants are intended to stabilize the sinus openings and the turbinates, reduce edema, and/or prevent obstruction by adhesions. They can also be infused with medication delivered topically over an extended period of time, and this local delivery of medications may be superior to topical application in the postoperative setting.

Regulatory Status

In 2011, the PROPEL® system (Intersect ENT, Menlo Park, CA) was approved by the U.S. FDA through the premarketing approval process (P100044). This device is a self-expanding, bioabsorbable, steroid-eluting stent that is intended for use in the ethmoid sinus. It is placed via endoscopic guidance using a plunger included with the device. Steroids (mometasone furoate) are embedded in a polyethylene glycol polymer, which allows sustained release of the drug over an approximate duration of 30 days. The device dissolves over several weeks and therefore does not require removal. In 2012, a smaller version of the PROPEL® device, the PROPEL® Mini Sinus Implant, was approved for use in patients older than age 18 years following ethmoid sinus surgery to maintain patency. In 2017, the PROPEL Contour was approved through a PMA supplement. The PROPEL® Contour Sinus Implant is an adaptable implant that is designed to maximize drug delivery to the frontal and maxillary sinus.

SINUVA™ Sinus Implant (Intersect ENT, Inc., Menlo Park, CA) was initially approved in 1987. In 2017, the SINUVA™ Sinus Implant was approved with a new dose (1350 µg mometasone furoate) under a New Drug Application (NDA 209310). The corticosteroid is released over 90 days and the bioabsorbable polymers soften over this time. The implant is removed at Day 90 or earlier using standard surgical instruments. The SINUVA™ Sinus Implant is indicated for the treatment of nasal polyps in adult patients who have had ethmoid sinus surgery.

Medical Policy Statement

The use of steroid-eluting sinus implants for postoperative treatment following endoscopic sinus surgery and for treatment of recurrent sinonasal polyposis is considered experimental/investigational.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

J3490	J7402	S1091	31237	31299
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Rationale

Randomized controlled trials (RCTs) are important in the evaluation of sinus implants as an adjunct to endoscopic sinus surgery (ESS) to adequately compare implantable stents with alternative treatment regimens and to minimize the effects of confounders on outcomes. Case series and trials without control groups offer little in the way of relevant evidence, because improvements in symptoms is expected after ESS and because there are multiple clinical and treatment variables which may confound outcomes.

Steroid-Eluting Implant as an Adjunct to Endoscopic Sinus Surgery

Clinical Context and Therapy Purpose

The purpose of a steroid-eluting sinus stent in patients who have chronic rhinosinusitis (CRS) who have (ESS) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the adjunctive use of a steroid-eluting sinus stent improve the net health outcome in patients who have endoscopic sinus surgery?

The following PICOs were used to select literature to inform this review.

Populations

The relevant population(s) of interest are patients who have endoscopic sinus surgery for chronic rhinosinusitis.

Interventions

The therapy being considered is a bioabsorbable steroid-eluting sinus stent (eg, PROPEL Sinus Stent, PROPEL mini Sinus Stent, PROPEL Countour Sinus Stent) for post-operative care following ESS.

Comparators

The most relevant comparison for sinus stents is unclear because there is no standardized optimal postoperative treatment regimen. Ideally, the “standard care” comparison group should include some form of packing, intranasal steroids, and irrigation. An important consideration in evaluating controlled trials is that the control arm may not be treated with optimal intensity, thereby leading to a bias in favor of the device. For example, a study design that compares a steroid-eluting stent with a non-steroid-eluting stent will primarily evaluate the efficacy of steroids when delivered by the device but will not evaluate the efficacy of a stent itself. If the control group does not receive topical or oral steroids postoperatively, then this might constitute under treatment in the control group and result in a bias favoring the treatment group. Another concern is comparison of the efficacy of a drug with the efficacy of a drug delivery system. For example, if a steroid-eluting spacer is compared with a control of saline irrigation alone, it will be difficult to separate the efficacy of the drug itself (steroids) from the drug delivery system (stent).

Outcomes

The Perioperative Sinus Endoscopy score sums the combined scores determined from middle turbinate position, middle meatal status, ethmoid cavity appearance, as well as secondary sinus blockage (frontal and sphenoid). Each category is scored from 0-2, with 0 being not present, 1 as partially present, and 2 being fully present. The highest total score is 16, with scores ranging from 18-20 when the frontal and sphenoid sinuses are also included. The higher the score, the worse the status of the nasal cavity.

Post-ESS synechiae formation, the Sino-Nasal Outcome Test (SNOT-22) Questionnaire and the Rhinosinusitis Disability Index may also be used to evaluate perioperative outcomes.

A beneficial outcome would be an improvement in symptoms.

A harmful outcome would be adverse events from the implantable stents.

The PROPEL series of sinus stents are bioabsorbable and elute steroids for 30 days. Therefore, outcomes should be assessed within 30 days.

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.

Review of Evidence

The literature consists of randomized trials, single-arm case series, and systematic reviews of these studies. The following is a summary of the key findings to date.

Systematic Reviews

A 2015 Cochrane review addressed steroid-eluting sinus stents for improving chronic rhinosinusitis symptoms in individuals undergoing ESS.(9) Study eligibility criteria were RCTs that compared the effects of steroid-eluting sinus stents with non-steroid-eluting sinus stents, nasal packing, or no treatment in adults with chronic rhinosinusitis who underwent ESS. After an initial search, 21 RCTs were identified, including the RCTs reported by Murr (2011) (10) and Marple (2012) (11) and colleagues (described above). None of the trials met authors' inclusion criteria. Reviewers concluded that there is no evidence from high-quality RCTs to demonstrate the benefits of steroid-eluting stents.

Randomized Controlled Trials

RCTs are shown in Tables 1 and 2. There are four RCTs of the PROPEL, PROPEL mini, and PROPEL Contour steroid-eluting sinus stents, all sponsored by the device manufacturer (Intersect ENT). These trials used an intrapatient control design, with each patient receiving a drug-eluting stent on 1 side and a non-drug-eluting stent or medical treatment on the other via random assignment.

The 2 trials of PROPEL for the ethmoid sinus had similar designs.(10,11) Both compared an implant that is steroid-eluting with an identical non-steroid-eluting implant. Thus, these trials tested the value of drug delivery via a stent but did not test the value of a stent itself vs treatment without a stent. The primary efficacy outcome in Murr et al was degree of inflammation rated by the treating physician.(10) In Marple et al the primary outcome was reduction in the need for postoperative interventions at day 30 post-procedure.(11) A panel of three independent experts, blinded to treatment assignment and clinical information, viewed the endoscopic results and determined whether an intervention was indicated. The need for postoperative intervention by expert judgment was found in 33.3% of patients in the steroid-eluting arm and in 46.9% in the non-steroid-eluting arm ($p=0.028$). The reduction in interventions was primarily driven by a 52% reduction in lysis of adhesions ($p=0.005$). The primary safety hypothesis was met, because there were no cases of clinically significant increases in ocular pressure recorded over the 90-day period post-procedure.

The RCTs by Smith et al (2016) and Luong et al (2017), implanted either a PROPEL Mini Sinus Implant or a PROPEL Contour Sinus Implant in the frontal sinus with a control of surgery alone on the contralateral side.(12,13) The primary outcome was the need for post-operative intervention (eg, surgery or steroids) determined by an independent blinded physician. Both trials showed a reduction in the need for additional surgical intervention by approximately 22%, with no adverse effects of treatment. The number needed to treat was 4.7 to prevent 1 patient from undergoing postoperative intervention.(13) No stent-related adverse events were noted.

Table 1. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Participants	Interventions	
				Active	Comparator
Murr et al (2011) ¹⁰	U.S.	4	38 patients with refractory CRS	Unilateral PROPEL steroid-eluting stent in the ethmoid sinus	Non drug-eluting stent on the other contralateral side
Marple et al (2012) ¹¹ ADVANCE II	U.S.	11	105 patients with refractory CRS	Unilateral PROPEL steroid-eluting stent in the ethmoid sinus	Non-drug-eluting stent on the contralateral side
Smith et al (2016) ¹²	U.S.	11	80 patients with CRS who were scheduled to undergo primary or revision bilateral frontal sinusotomy	Unilateral PROPEL Mini Sinus Implant in the frontal sinus	Surgery alone on the contralateral side
Luong et al (2017) ¹³	U.S.	12	80 patients with CRS who were scheduled to undergo primary or revision bilateral frontal sinusotomy	Unilateral PROPEL Contour Sinus Implant in the frontal sinus	Surgery alone on the contralateral side

ADVANCE II: a prospective, randomized study assessing safety and efficacy of bioabsorbable steroid-releasing sinus implants; CRS: chronic rhinosinusitis; RCT: randomized controlled trial

Table 2. Summary of Key RCT Results

Study	Primary Outcome Measure	Polypoid Changes	Adhesions/scarring	Implant-Related Adverse Events
Murr et al (2011)¹⁰	Degree of Inflammation at 21 Days Post-Procedure (100 mm VAS)			
N	37	37		
PROPEL steroid-eluting Stent		18.4%	5.3%	
Non-steroid-eluting stent		36.8%	21.1%	
Diff	18 points			
p-value	NR	0.039	0.03	
Marple et al (2012)¹¹	Need for Post-Operative Intervention Determined by 3 Independent Reviewers			
N	91			
PROPEL steroid-eluting Stent	33.3%			
Non-steroid-eluting stent	46.9%			
Diff	13.6%			
p-value	0.028			
Smith et al (2016)¹²	Need for Post-Operative Intervention at 30 Days (Independent Reviewer) n (%)	Need for Post-Operative Intervention at 90 Days		Occlusion/Restenosis Rate at Day 30

N	67 (adequate video for independent review)	79		
PROPEL mini-sinus steroid-eluting stent	26 (38.8%)		16 (21.1%)	None
SOC without a stent	42 (62.7%)		35 (46.1%)	
p-value	0.007	0.013	0.023	<0.001
Luong et al (2017)¹³	<i>Need for Post-Operative Intervention at 30 Days (Independent Reviewer) n (%)</i>	<i>Need for Surgical Intervention at 30 Days (Independent Reviewer) n (%)</i>	<i>Occlusion/Restenosis Rate at Day 30</i>	
N	61	58	69	
PROPEL	7 (11.5)	4 (6.9)	16 (23.2)	
Contour steroid-eluting stent				
SOC without a stent	20 (32.8)	15 (25.9)	28 (40.6)	
Diff (95% CI)	21.3% (35.1% to 7.6%)	19.0% (32.8% to 5.1)	-17.4% (-28.6% to -6.1%)	
NNT	4.7			
Summary	Range 13.6% to 23.9%			

CI: confidence interval; Diff: difference; NNT: number needed to treat; NR: not reported; RCT: randomized controlled trial; SOC: standard of care; VAS: visual analog scale.

Limitations in relevance and in design and conduct are shown in Tables 3 and 4. The primary limitation for the studies by Murr et al (2011) and Marple et al (2012) on the PROPEL implant in the ethmoid sinus was whether the comparator had received the optimal treatment in terms of packing, intranasal steroids, and irrigation. For the studies by Smith et al (2016) and Luong et al (2017), there was a high percentage of patients who were not able to be evaluated due to video quality.

Table 3. Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Murr et al (2011) ¹⁰		3. The comparator may not have received the optimal treatment (some form of packing, intranasal steroids, and irrigation)			
Marple et al (2012) ¹¹		3. The comparator may not have received the optimal treatment (some form of packing, intranasal steroids, and irrigation)			
Smith et al (2016) ¹²					
Luong et al (2017) ¹³					

The evidence gaps 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. 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. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

^e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Limitations

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Powers ^e	Statistical ^f
Murr et al (2011) ¹⁰		3. Outcome assessed by treating physician				
Marple et al (2012) ¹¹						
Smith et al (2016) ¹²			2. Incomplete reporting of secondary outcomes	1. 12 (17%) patients did not have independent review at 30 days due to suboptimal video quality.		
Luong et al (2017)				1. 19 (24%) patients did not have independent review at 30 days due to suboptimal video quality.		

The evidence gaps 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.

Nonrandomized Comparative Studies

The largest nonrandomized study identified was reported by Xu et al (2016).⁽¹⁴⁾ It evaluated post-ESS synechia formation among 146 patients (252 nasal cavities) treated with a steroid-eluting absorbable spacer and 128 patients (233 nasal cavities) treated with a nonabsorbable spacer. Eligible patients included those who underwent ESS (at minimum, maxillary antrostomy and anterior ethmoidectomy) for CRS with or without nasal polyps and were treated with a sinus spacer. Rates of synechia formation at 1 month postoperatively did not differ significantly between groups (5 [2.0%] nasal cavities in the absorbable stent group vs 13 [5.6%] nasal cavities in the nonabsorbable spacer group).

Section Summary: Steroid-Eluting Implants as an Adjunct to ESS

The most direct evidence relating to use of steroid-eluting nasal stents as an adjunct to ESS comes from four RCTs comparing steroid-eluting stents with either a non-steroid-eluting stent or medical management. The need for post-operative intervention at 30 days was reduced by 14% to 24%, translating to a number needed to treat of 4.7 or more. Three trials used blinded assessors to evaluate postimplantation sinus changes, an important strength, but the trials had potentials for bias. To most accurately evaluate the benefit from PROPEL devices it is important to ensure that the comparison group is not undertreated (ie, receives some form of packing, intranasal steroids, and irrigation).

Steroid-Eluting Implants for Recurrent Polyposis

Clinical Context and Therapy Purpose

The purpose of steroid-eluting stents in patients who have recurrent polyposis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of steroid-eluting stents improve the net health outcome in patients with recurrent polyposis?

The following PICOs were used to select literature to inform this review.

Populations

The relevant population of interest are patients with recurrent polyposis after ESS.

Interventions

The therapy being considered is steroid-eluting stent (eg, SINUVA).

This implant is bioresorbable and softens over time but needs to be removed by 90 days.

Comparators

A sham treatment may be used to determine whether active treatment reduces the need for ESS.

Outcomes

The general outcomes of interest are symptoms, anatomic outcomes, and need for additional ESS. These outcomes may be measured by the nasal obstruction/congestion score change (scale 0–3), polyp grade change (scale 0 to 8), ethmoid sinus obstruction change (scale 0–100), and the percentage of patients still indicated for repeat sinus surgery.

A beneficial outcome would be an improvement in symptoms and reduction in repeat ESS.

A harmful outcome would be adverse events from the implant.

The steroid-eluting stents are kept in place for up to 90 days. Relevant outcomes would be measured at 90 days to evaluate the short-term effects of the treatment and at 1 or 2 years to evaluate the durability of this treatment.

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.

Review of Evidence

Two sham-controlled RCTs RESOLVE (A Randomized, Controlled, Blinded Study of Bioabsorbable Steroid-eluting Sinus Implants for in-office Treatment of Recurrent Sinonasal Polyposis) and RESOLVE II (A Phase 3 Trial of Mometasone Furoate Sinus Implants for Chronic Sinusitis with Recurrent Nasal Polyps) with a total of 400 patients have addressed outcomes after placement of steroid-eluting absorbable sinus stents in the office setting due to recurrent or persistent nasal polyposis after ESS (see Tables 5 and 6).^(15,16, 17)

In RESOLVE, For endoscopically measured outcomes, at 90 days of follow-up, the treatment group had a greater reduction in polyp grade than the control group (-1.0 vs -0.1; $p=0.016$) and a greater reduction in percent ethmoid obstruction on a 100-mm VAS (-21.5 mm vs 1.3 mm; $p=0.001$), both respectively. For patient-reported outcomes, there were no significant differences in change in nasal obstruction/congestion scores between groups. Six-month outcomes from RESOLVE were reported by Forwith et al in 2016. Differences in polyp grade and ethmoid obstruction scores remained significantly improved in the intervention group at 6 months, but the difference between groups in patient-reported symptom scores was not statistically significant at 6 months (See Table 6).⁽¹⁷⁾ In RESOLVE II the implant group showed significant reductions in nasal congestion, polyp grade, and ethmoid obstruction at 90 days compared to sham controls. Out of 200 patients treated with the implant, 39% were indicated for sinus surgery at 3 months compared to 63.3% of controls ($p<0.001$).

Table 5. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Han et al (2014) ¹⁵	U.S.	18	2013-2014	100 patients with recurrent nasal polyposis after ESS who had chronic rhinosinusitis, had undergone prior bilateral total ethmoidectomy more than 3 months earlier, had endoscopically confirmed recurrent bilateral ethmoid sinus obstruction due to polyposis that was refractory to medical therapy, and were considered candidates for repeat surgery based on the judgment of the surgeon and patient.	53 patients who received office-based placement of a mometasone eluting nasal stent	47 patients who received sham treatment
Forwith et al (2016) ¹⁷ RESOLVE						
Kern et al (2018) ¹⁶ RESOLVE II	US	34	2014-2016	300 adults with refractory chronic rhinosinusitis with nasal polyps who were candidates for repeat surgery. To be indicated for repeat ESS, a patient had to: (1) be using intranasal corticosteroid daily ; (2) receive at least 1 course of high-dose steroid therapy or refused such therapy due to side effects within the past 1 year; (3) continue to have moderate-to-severe symptoms of nasal obstruction/congestion ; and (4) have endoscopic evidence of bilateral ethmoid sinus obstruction due to polyposis .	201 patients Who received a SINUVA(TM) Mometasone eluting bioabsorbable nasal stent	99 patients who received sham treatment consisting of insertion and removal of implants

RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis; RESOLVE II: a phase 3 trial of mometasone furoate sinus implants for chronic sinusitis with recurrent nasal polyps; ESS: endoscopic sinus surgery; RCT: randomized controlled trial.

Table 6. Summary of Key RCT Results

Study	Nasal obstruction/congestion score change (scale 0–3) at 90 days	Nasal obstruction/congestion score change (scale 0–3) at 6 months	Change in Polyp Grade at 90 Days (scale 0 to 8)	Change in Polyp Grade at 6 Months (scale 0 to 8)	Reduction in Ethmoid Obstruction (scale 100) at 90 Days	Reduction in Ethmoid Obstruction (scale 100) at 6 months	Patients Indicated for Sinus Surgery at 3 months n (%)
Han et al. (2014); Forwith et al (2016)^{15,17}; RESOLVE							
Drug-eluting nasal implant		-1.06	-1.0	-.071	-21.5 mm	-17.1 mm	47%
Sham		-0.44	-0.1	0.02	1.3 mm	-5.6 mm	77%
P-value		.124	.016	.018	.001	.010	NR
Kern et al. (2018)¹⁶; RESOLVE II							
Drug-eluting nasal implant mean (SD)	-0.80 (0.73)		-0.56 (1.06)		-11.3 (18.1)		78/200 (39.0%)
Sham mean (SD)	-0.56 (0.62)		-0.15 (0.91)		-1.9 (14.4)		62/98 (63.3%)
Diff or OR (95% CI)	-0.23 (-0.39 to -0.06)		-0.35 (-0.60 to -0.09)		-7.96 (-12.10 to		2.69 (1.63 to 4.44)

P-value	.007	.007	-3.83) <.001	<.001
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RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis;
RESOLVE II: a phase 3 trial of mometasone furoate sinus implants for chronic sinusitis with recurrent nasal polyps; CI: confidence interval; Diff: difference; NR: not reported; OR: odds ratio; RCT: randomized controlled trial; SD: standard deviation.

Limitations in relevance and design and conduct are shown in Tables 7 and 8. A major limitation of RESOLVE II was the short duration of follow-up to determine the durability of the treatment. In addition, there is a potential for bias since outcomes were evaluated by the treating physician.

Table 7. Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Han et al (2014) ¹⁵ Forwith et al (2016) ¹⁷ RESOLVE					1. The 6-month follow-up is insufficient to evaluate the durability of this treatment.
Kern et al (2018) ¹⁶ RESOLVE II					1. The 90 day follow-up is insufficient to evaluate the durability of this treatment.

RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis; RESOLVE II: a phase 3 trial of mometasone furoate sinus implants for chronic sinusitis with recurrent nasal polyps. The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations 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. 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. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Limitations

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Power ^e	Statistical ^f
Han et al. (2014); Forwith et al (2016) ^{15,17} ; RESOLVE		3. Outcomes were assessed by the treating physician				3. Statistics were not reported for some outcome measures.

RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis;

RESOLVE II: a phase 3 trial of mometasone furoate sinus implants for chronic sinusitis with recurrent nasal polyps.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations 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.^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: Steroid-Eluting Implants for Recurrent Polyposis

Two RCTs evaluated the use of steroid-eluting nasal stents for recurrent or persistent nasal polyposis after ESS, which demonstrated improvements in polyp grade and ethmoid obstruction. Strengths of this trial included use of a sham control and adequate power for its primary outcome. However, the trial had a high risk of bias due to unblinded outcome assessment. Although avoidance of repeat ESS and oral steroids may be relevant outcomes for this indication, it would be more important if decisions about repeat ESS or other treatments were standardized and, in the trial setting, if decisions were prespecified or made by a clinician blinded to treatment group.

Summary of Evidence

For individuals who have chronic rhinosinusitis who have undergone ESS who receive implantable steroid-eluting sinus stents, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, and treatment-related morbidity. The most direct evidence relating to use of steroid-eluting nasal stents as an adjunct to ESS comes from 4 RCTs comparing steroid-eluting stents with either a non-steroid-eluting stent or medical management. The need for post-operative intervention at 30 days was reduced by 14% to 24%, translating to a number needed to treat of 4.7 or more. Three trials used blinded assessors to evaluate postimplantation sinus changes, an important strength, but the trials had potentials for bias. To most accurately evaluate the benefit from PROPEL devices it is important to ensure that the comparison group is not undertreated (ie, receives some form of packing, intranasal steroids, and irrigation). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have recurrent sinonasal polyposis who have undergone endoscopic sinus surgery who receive implantable steroid-eluting sinus stents, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, and treatment-related morbidity. Two RCTs were identified evaluating the use of steroid-eluting nasal stents for recurrent or persistent nasal polyposis after ESS, which demonstrated improvements in polyp grade and ethmoid obstruction. Strengths of these trials included use of a sham control and adequate power for its primary outcome. However, the trials had a high risk of bias due to unblinded outcome assessment. Although avoidance of repeat ESS and oral steroids may be relevant outcomes for this indication, it would be more important if decisions about repeat ESS or other treatments were standardized and, in the trial setting, if decisions were prespecified or made by a clinician blinded to treatment group. Sinus stents may prove to have a role in nasal polyposis; however, further follow-up is needed to evaluate the durability of the results. The evidence is insufficient to determine the effects of the technology on health outcomes.

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.

BCBSA received input from 1 physician specialty society and 4 academic medical centers while this policy was under review in 2012. Input overall was mixed, without consensus among respondents. Some reviewers expressed support for use of these devices after endoscopic sinus surgery. Reviewers who supported use cited the randomized controlled trials(RCTs) reviewed in this review as the main source of evidence. Other reviewers did not support use in

general following endoscopic sinus surgery, arguing that a subset of patients may benefit, but there was no consensus on which populations this subgroup would include.

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.

No guidelines or statements were identified.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 9.

Table 9. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03943121	The Effects of Steroid-eluting Stent Implant for the Treatment of Patients Undergoing Sinus Surgery for Eosinophilic Chronic Rhinosinusitis With Nasal Polyps	40	Oct 2021
NCT03607175	Randomized Clinical Control Trial Comparing the Effects of a Steroid Eluting Implant Versus Triamcinolone-impregnated Carboxymethylcellulose Foam on the Postoperative Clinic Experience in Patients That Underwent Functional Endoscopic Surgery for Nasal Polyposis	30	Dec 2022
Unpublished			
NCT02668302 ^a	The PIO II Study: A Randomized, Controlled, Blinded Trial to Evaluate the Safety and Efficacy of In-office Placement of a Steroid-eluting Sinus Implant Post-ethmoidectomy	40	Nov 2016 (completed)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

Government Regulations

There is no national or local coverage determination on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- N/A

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 6/14/22, the date the research was completed.

Medical Policy History

Policy Effective Date	Comments
1/1/2022	Medical policy established
11/1/2022	Routine maintenance

Next Review Date: 3rd Qtr, 2023