BlueCross BlueShield of Alabama

Name of Policy:

Implantable Sinus Stents and Drug-Eluting Implants for Postoperative Use Following Endoscopic Sinus Surgery and for Recurrent Sinus Disease

Policy #: 501
Category: Medical/Surgical

Latest Review Date: May 2018
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *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 that patient's illness, injury or disease.*

Description of Procedure or Service:

Sinus stents are devices that are used postoperatively following endoscopic sinus surgery (ESS). These devices are used to 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.

Chronic Rhinosinusitis

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

Treatment

Endoscopic sinus surgery (ESS) is typically performed in patients with chronic rhinosinusitis unresponsive to conservative treatment. The surgery is associated with improvements in symptoms 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 U.S. 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 that are being treated and the preferences of the treating surgeon. For all procedures, there is a substantial amount of 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 is not certain. Options include saline irrigation, nasal packs, topical steroids, systemic steroids, topical decongestants, oral antibiotics, and/or sinus cavity debridement. There have been a number of randomized controlled trials (RCTs) that have evaluated various treatment options, but all different strategies have not been rigorously evaluated. A systematic review evaluated the evidence for these therapies. The authors of this review 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. 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.

Implantable Sinus Stents
Implantable 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 also have the capability of being infused with medication that can be delivered topically over an extended period of time, and this local delivery of medications may be superior to topical application in the postoperative setting.

Sinus stents are defined as implantable devices that are specifically designed to improve patency and/or deliver local medication. These devices are inserted under endoscopic guidance and are distinguished from sinus packing and variations on packing devices that are routinely employed post sinus surgery.

Foam dressings, such as SinuFoam™, are used as nasal packs for a variety of conditions, including nosebleeds, and have also been used post-ESS. These are considered different types of nasal packing.

Middle meatal spacers are related but separate devices that are intended to maintain sinus patency post-ESS. They are splint-like devices that are inserted directly rather than under endoscopic guidance, and they do not have the capability of delivering local medication.

SINUVA
Placed during a routine physician office visit, Sinuva (mometasone furoate) expands into the sinus cavity and delivers an anti-inflammatory steroid directly to the site of polyp disease for 90 days. Sinuva may be an alternative to surgery and other treatment options for adults who have already had ethmoid sinus surgery. Sinuva is marketed to shrink nasal polyps and reduce nasal obstruction and congestion.

LATERA®
The LATERA Absorbable Nasal Implant is used to support upper and lower lateral cartilage in the nose, reinforcing the nasal wall like traditional cartilage and polymer grafts. Supporting the cartilage in this manner may reduce nasal airway obstruction symptoms and help patients breathe better. This is a new technology for repairing nasal valve collapse. It is a synthetic mesh that is implanted into the nasal sidewall. This implant is being used in place of a cartilage graft in the repair of nasal valve collapse. The technology is delivered inside the nasal wall by ENTs or plastic surgeons.

The LATERA implant is absorbed over a period of ~18 months. Post implantation, a fibrous capsule forms and the integrity of the implant is maintained through 12 months. Tissue encapsulation promotes acute implant stability and enables localized tissue response during the absorption process. Remodeling occurs once the implant is replaced with fibrous collagen construct to provide ongoing support.

Policy:

The use of **implantable nasal/sinus stents or drug-eluting implants does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational** for the following, including, but not limited to:

- postoperative treatment following endoscopic sinus surgery;
- for treatment of recurrent sinonasal polyposis.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature search was performed through December 11, 2017. The following is a summary of the key findings to date.

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 one 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. RCTs 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.

Randomized controlled trials (RCTs) are important in the evaluation of sinus implants as an adjunct to endoscopic sinus surgery to adequately compare implantable stents to 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, as improvement in

symptoms is expected after endoscopic sinus surgery (ESS) and because there are multiple clinical and treatment variables which may confound outcomes.

The most relevant comparison for sinus stents is unclear because there is not a 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 undertreatment in the control group and result in a bias favoring the treatment group. Another concern is for the comparison of efficacy of a drug with the efficacy of a drug delivery system. For example, if a steroid-eluting spacer is compared to 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).

The literature consists of a few, small randomized trials, single-arm case series, and systematic reviews of these studies.

Steroid-Eluting Stents as an Adjunct to Endoscopic Sinus Surgery

Systematic Reviews

A 2015 Cochrane review addressed steroid-eluting sinus stents for improving chronic rhinosinusitis symptoms in individuals undergoing ESS. Study eligibility criteria were RCTs that studied the effects of steroid-eluting sinus stents compared 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 et al (2011) and Marple et al (2012) described above. None of the studies met the authors' inclusion criteria. The authors conclude that there is no evidence from high quality RCTs to demonstrate the benefits of steroid-eluting stents.

A systematic review of early postoperative care following ESS was published in 2011. This review evaluated a number of different postoperative regimens, including stents. The review included one RCT by Cote et al and two nonrandomized studies. Some of the devices included in these studies are considered middle meatal spacers and are outside the scope of this evidence review. The overall level of evidence was judged as B (RCT with limitations). The authors concluded that topical steroids delivered by the "nonstandard" route required further study and that the results of current studies could not be extrapolated to larger populations. Based on this evidence, they did not recommend use of stents but considered them an "option" for postoperative care.

Han et al (2012) performed a meta-analysis of the 2 published RCTs of the Propel™ implant, both of which compared a steroid-eluting stent with a non-steroid-eluting stent. The results of the two RCTs were combined at the patient level, with reanalysis of the endoscopy videos by a panel of three independent ear, nose, and throat experts. The combined results were that the steroid-

eluting device reduced postoperative interventions by 35% (p=0.0008), reduced lysis of adhesions by 51% (p=0.0016), and reduced the need for oral steroids by 46% (p<0.0001).

Randomized Controlled Trials
As noted, there are 2 small RCTs of the steroid eluting sinus implant (PROPEL). Both trials have similar designs and both are sponsored by the manufacturer (Intersect ENT™, Palo Alto, CA.). Both compare an implant that is steroid-eluting versus an identical implant that is not steroid-eluting. Thus these trials test the value of drug delivery via a stent, but do not test the value of a stent itself versus treatment without a stent.

The first RCT of this implant was published in 2011 by Murr et al. A total of 38 patients with refractory chronic rhinosinusitis were included in the efficacy evaluation, and an additional five patients were enrolled for a safety evaluation. An intra-patient control design was used, meaning that each patient received a drug-eluting stent on one side and a non-drug-eluting stent on the other via random assignment. Patients were not permitted to use topical or oral steroids for 30 days following the procedure. A 14-day course of antibiotics was given to all patients. The primary end point was the degree of inflammation recorded on follow-up endoscopy at day 21 postprocedure, as scored by a 100 mm visual analogue scale (VAS). There were also semiquantitative grading performed for polypoid changes, middle turbinate position, and adhesions/synechiae. The clinicians recording the outcomes were the same physicians who were treating the patients**.** One patient withdrew prior to study completion.

The difference in inflammation scores at 21 days was significant in favor of the steroid-eluting group. The estimated difference in scores from graphical representation was approximately 18 units on the 0 to 100 VAS scale. The percent of patients having polypoid changes was 18.4% in the steroid-eluting group versus 36.8% in the non-steroid-eluting group (p=0.039). Adhesions were also significantly less common in the steroid-eluting group (5.3% vs. 21.1%, p=0.03). There were no significant differences in the appearance or position of the middle turbinate.

In 2012, Marple et al published results of the Advance II trial, an RCT of the Propel™ sinus implant for 105 patients with chronic rhinosinusitis refractory to medical management. This trial also used an intra-patient control design with each patient receiving a drug-eluting stent on one side and a non-drug-eluting stent on the other via random assignment. Patients were not permitted to use topical or oral steroids for 30 days following the procedure. A 14-day course of antibiotics was given to all patients. The primary efficacy outcome was reduction in the need for postoperative interventions at day 30 following the procedure. A panel of three independent experts, who were blinded to treatment assignment and clinical information, viewed the endoscopy results and determined whether an intervention was indicated. The primary safety end point was the absence of clinically significant increased ocular pressure through day 90.

There were 3 patients lost to follow-up (2.9%), and 9 patients (8.6%) could not be evaluated because the video of the endoscopy could not be graded. Two patients had the device removed within 30 days of placement. Of the remaining patients, the need for postoperative intervention by expert judgment was found in 33.3% of patients in the steroid-eluting arm versus 46.9% in the non-steroid-eluting arm (p=0.028). According to the judgments of the clinical investigators who were treating the patients, intervention was required in 21.9% of the steroid-eluting group and

31.4% of the non-steroid-eluting group (p=0.068). The reduction in interventions was primarily driven by a 52% reduction in lysis of adhesions (p=0.005). The primary safety hypothesis was met, as there were no cases of clinically significant increases in ocular pressure recorded over the 90-day period following the procedure.

Nonrandomized Comparative Studies
The largest nonrandomized study identified was reported by Xu et al in 2015, which evaluated post-ESS synechiae 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 chronic rhinosinusitis with or without nasal polyps and were treated with a sinus spacer. Synechiae related outcomes were unavailable for 10 subjects in the absorbable spacer group (6.8%) and nine subjects in the nonabsorbable spacer group (7.0%) due to lack of 1-month follow up. Rates of synechiae 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).

Noncomparative Studies
In 2014, Matheny et al reported results from a single-arm case series evaluating the use of office-based placement of a mometasone-eluting absorbable stent (PROPEL device) within seven days of ESS including bilateral ethmoidectomy. Eligible patients had chronic rhinosinusitis with or without nasal polyps and were treated by one of three surgeons. The surgical procedure was ESS with complete ethmoidectomy, followed by packing with a chitosan-polyethylene glycol absorbable dressing. At outpatient follow-up scheduled five to seven days post-surgery, patients underwent debridement of the ethmoid cavity with placement of the steroid-eluting stent. Twenty patients who underwent 40 stent placements were included. Complications included acute sinusitis in two patients between two and four weeks post-surgery. Sinuses were evaluated based on video endoscopy by an independent reviewer using a 100-mm VAS and the standardized case report form described by Murr et al. Ethmoid sinus inflammation was reduced from 25.6 at baseline to 18.9 at week for (p=0.034). The mean total SNOT-20 score was reduced (improved) from 42.8 at baseline to 18.4 at week two and 8.9 at week four. The procedure was generally well-tolerated.

The ADVANCE study was a prospective, multicenter single-arm trial of placement of a mometasone-eluting absorbable stent in 50 patients who were scheduled to undergo ESS. As reported by Forwith et al (2011), the end points evaluated on follow-up endoscopies were the degree of inflammation scored on a 100 mm visual analog scale (VAS) and semiquantitative grading for polypoid changes, middle turbinate position, and adhesions. By day 7 post procedure, the inflammation scores were in the “minimal” range and remained there for the rest of the time points. At 1 month, polypoid lesions were present in 10% of patients, adhesions in 1.1%, and middle turbinate lateralization in 4.4%. Scores on the Sino-Nasal Outcome Test-22 and the Rhinosinusitis Disability Index improved significantly in the first month post procedure.

A 2011 case series was published of 23 patients with refractory rhinosinusitis who underwent ESS and were treated postoperatively with the Relieva Stratus Microflow Spacer Device infused with triamcinolone. Over a period of six months, there were significant improvements on

multiple sinus-related outcome measures such as the Sino-Nasal Outcome Test-20 and the Lund-McKay CT (computed tomography) scan scores. There were no significant intraoperative or postoperative complications reported.

Section Summary: Steroid-Eluting Stents as an Adjunct to Endoscopic Sinus Surgery
The most direct evidence relating to the use of steroid-eluting nasal stents as an adjunct to ESS comes from 2 RCTs comparing steroid-eluting stents with a non-steroid-eluting stent. One study used blinded assessors to evaluate post-implantation sinus changes, an important strength, but the trials have other potentials for bias. In addition, to most accurately evaluate the benefit from the Propel device, ensuring that the comparison group is not undertreated (i.e., receives some form of packing, intranasal steroids, and irrigation) is important.

Steroid-Eluting Stents for Recurrent Polyposis
A relatively small body of literature has addressed outcomes after placement of steroid-eluting absorbable sinus stents in the office setting as a planned procedure post-ESS or due to persistent/recurrent nasal polyposis after ESS.

In a randomized, double-blind, placebo-controlled trial, Rudmik et al (2012) evaluated a dexamethasone Sinu-Foam spacer following ESS for CRS without nasal polyposis (CRSsNP). Patients with CRSsNP (n = 36) were enrolled into a double-blind, placebo-controlled trial and randomized into either a treatment arm (dexamethasone Sinu-Foam mixture; n = 18) or placebo arm (Sinu-Foam alone; n = 18). Therapeutic outcomes were evaluated at 1 week, 4 weeks, and 3 months using sino-nasal endoscopy and graded using the Lund-Kennedy scoring system. Post-operative care included nasal saline irrigations and a short course of systemic steroids. All patients completed the study follow-up period. Both study arms experienced significant improvement in endoscopic grading over the study duration ($p < 0.001$). There was no difference in average endoscopic scores between the treatment and placebo groups at 1 week, 4 weeks, and 3 months (all $p > 0.489$). The authors concluded that the findings of this study demonstrated that an off-label drug-eluting MM spacer of dexamethasone and Sinu-Foam did not improve endoscopic outcomes in the early post-operative period following ESS when combined with post-operative saline irrigations and a short course of systemic steroids.

Han et al (2014) reported results of the RESOLVE trial, a sham-controlled RCT evaluating the use of office-based placement of a mometasone-eluting nasal stent for patients with recurrence of nasal polyposis after ESS. Eligible patients 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. Patients and those who administered symptom questionnaires at follow-up visits were blinding to treatment group. The study was powered to detect a between-group difference of at least a 0.6-point change in polyp grade from baseline, and at least a 1.0-point change in nasal obstruction/congestion score. One hundred subjects were randomized to treatment (n=53) or control (n=47). For endoscopically measured outcomes, at 90 days of follow-up the treatment group had a greater reduction in polyp grade compared with the control group (-1.0 vs -0.1; p=0.016) and greater reduction in percent ethmoid obstruction on a 100-mm visual analog scale (VAS; -21.5 mm vs 1.3 mm; p=0.001). For patient-reported outcomes, there were no significant

differences in change in nasal obstruction/congestion score between groups. Compared with controls, fewer treatment-group patients required oral steroids for ethmoid obstruction (11% vs 26%) and fewer treatment-group patients were indicated for sinus surgery at 3 months based on established criteria (47% vs 77%), although statistical comparisons are not reported.

Also in 2014, Lavigne et al reported results from a case series of 12 patients who underwent placement of an investigational mometasone-eluting absorbable stent described as similar to the PROPEL device, but with differences in stent structure to target obstructed sinuses, for recurrent nasal polyposis after ESS. Eligible patients had chronic sinusitis and had undergone bilateral ethmoidectomy more than 90 days before enrollment, but had refractory polyposis on at least one side that was at least Grade 2 on a 0 to 4 point scale. All implants were placed in the office setting. The average SNOT-22 scores (reported as a normalized value with a total possible score that could range from 0-5) changed from 2.19 at baseline to 1.48 at day 7 ($p<0.027$), and continued to demonstrate improvements by the six-month follow-up. The mean bilateral polyp grade (clinician-assessed) improved from 4.5 at baseline to 2.8 at day 7 ($p<0.003$), with continued improvements through 6-month follow-up. No significant adverse events were reported.

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Ow et al (2014) reported plasma mometasone and cortisol concentrations for 5 patients with recurrent polyposis after bilateral total ethmoidectomy who underwent placement of the same investigational device described by Lavigne et al. Plasma mometasone concentrations were in the undetectable range in 26 of 32 samples at 3, 7, 14, 21, and 30 days postimplant and undetectable in all samples at 21 and 30 days postimplant.

Forwith et al (2016) reported results from a randomized, controlled, blinded study with 100 chronic rhinosinusitis with nasal polyp's patients who failed medical treatment and were considered candidates for revision ESS. Treated patients (n=57) underwent in-office implant placement. Control patients (n=43) underwent a sham procedure. Endoscopic grading at 3 months by clinicians was corroborated by an independent review of randomized videoendoscopies by a panel of 3 sinus surgeons. Six-month follow-up included endoscopic grading and patient-reported outcomes. At 6 months, treated patients experienced significant improvement in Nasal Obstruction Symptom Evaluation (NOSE) score ($p = 0.021$) and >2-fold improvement in mean nasal obstruction/congestion score (-1.06 ± 1.4 vs -0.44 ± 1.4; $p = 0.124$).

Endoscopically, treated patients experienced significant reduction in ethmoid sinus obstruction ($p < 0.001$) and bilateral polyp grade ($p = 0.018$) compared to controls. Panel review confirmed a significant reduction in ethmoid sinus obstruction ($p = 0.010$) and 2-fold improvement in bilateral polyp grade ($p = 0.099$), which reached statistical significance ($p = 0.049$) in a subset of 67 patients with baseline polyp burden ≥ 2 bilaterally. At 6 months, control patients were at 3.6 times higher risk of remaining indicated for ESS than treated patients.

Smith et al (2016) published a randomized controlled trial assessing the safety and efficacy of steroid eluting implants when placed in the frontal sinus opening following endoscopic sinus surgery in patients with chronic rhinosinusitis. Eighty adult ($\geq$ 18 years) CRS patients who underwent successful bilateral frontal sinusotomy were randomized to receive a steroid-releasing implant in one FSO, whereas the contralateral control side received no implant. All patients received standard postoperative care. Endoscopic evaluations recorded at 30-days post-endoscopic sinus surgery (ESS) were graded real time by clinical investigators and by an independent, blinded sinus surgeon to assess the need for postoperative interventions in the FSO. Implants were successfully placed in all 80 frontal sinuses, resulting in 100% implant delivery success. At 30-days post-ESS, steroid-releasing implants provided a statistically significant ($P = 0.0070$) reduction in the need for postoperative interventions compared to surgery alone by an independent reviewer, representing 38% relative reduction. Clinical investigators reported statistically significant reduction in this measure at 30 days ($P < 0.0001$) and 90 days ($P = 0.0129$). Clinical investigators also reported a 55.6% reduction in the need for oral steroid interventions ($P = 0.0015$), 75% reduction in the need for surgical interventions ($P = 0.0225$), 16.7% reduction in inflammation score, 54.3% reduction in restenosis rate ($P = 0.0002$), and 32.2% greater diameter of FSO ($P < 0.0001$) on treated sides compared to control at 30 days. No implant-related adverse events were reported.

Section Summary: Steroid-Eluting Stents for Recurrent Polyposis

One RCT was identified evaluating the use of steroid-eluting nasal stents for recurrent/persistent nasal polyposis after ESS, which demonstrated improvements in polyp grade and ethmoid obstruction. Strengths of this trial include the use of a sham control and adequate power for its primary outcome. However, the trial is at high risk of bias due to unblinded outcome assessment. Although avoidance of repeat ESS and oral steroids may be a relevant outcome for this indication, it would be important for decisions about repeat ESS or other treatments to be standardized and prespecified or be made by a clinician blinded to treatment group. Sinus stents may prove to have a role in nasal polyposis; however, additional positive results from well-designed RCTs are needed to confirm the results of the single available RCT.

Summary of Evidence

For individuals who have chronic rhinosinusitis who have undergone endoscopic sinus surgery (ESS) who receive implantable steroid-eluting sinus stents, the evidence includes randomized controlled trials (RCTs), a number of observational studies, and systematic reviews of these studies. Relevant outcomes include symptoms, change in disease status, morbid events, and treatment-related morbidity. The most direct evidence comes from RCTs comparing steroid-eluting sinus stents with non-steroid-eluting stents, both of which showed some benefit with steroid-eluting stents. However, the studies have some limitations, include risk of bias. In addition, because of the comparison group used, these trials primarily evaluate the efficacy of

topical steroids when delivered by an implanted device, but do not evaluate the efficacy of the device versus standard care. 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 one RCT and one single-arm study. Relevant outcomes include symptoms, change in disease status, morbid events, and treatment-related morbidity. The most direct evidence comes from the available RCT, which compared steroid eluting stents plus topical steroids with steroids alone for individuals with recurrent polyposis after ESS. This trial had a high risk of bias due to unblinded outcome assessment. Although avoidance of repeat ESS and oral steroids may be a relevant outcome for this indication, it would be important for decisions about repeat ESS or other treatments to be standardized and prespecified or be made by a clinician blinded to treatment group. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Key Words:

Implantable sinus stents, implantable sinus spacers, PROPEL™, Relieva Stratus™ MicroFlow spacer, Mometasone furoate sinus implant, Sinuva (mometasone furoate), Sinu-Foam spacer, Latera

Approved by Governing Bodies:

The PROPEL™ system (Intersect ENT, Palo Alto, CA) was granted U.S. Food and Drug Administration (FDA) approval under the premarketing approval (PMA) process in August 2011. 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 that is 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 is dissolvable over a period of several weeks, and therefore does not require removal. In September 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.

The Relieva Stratus™ MicroFlow spacer is a balloon-based device that acts as a spacer and medication delivery system which was cleared for marketing under the 510(k) process in October 2011. It is indicated for use as a postoperative spacer to maintain an opening to the sinuses within the first 14 days postoperatively. It is placed via a catheter under endoscopic guidance. This device is temporary and requires manual removal after 30 days, with implantation

of a new device if needed. It is approved for infusion with saline, but not for use with other medications such as steroids. This device is no longer marketed in the U.S.

The SINUVA™ (mometasone furoate) implant is NDA approved (209310) by the FDA, for the treatment of nasal polyps in patients > 18 years of age (18 years of age and older), who have had ethmoid sinus surgery. SINUVA™ is intended as an alternative to sinus surgery in patients with recurrent polyp disease. The SINUVA Sinus Implant is loaded into a Delivery System and placed in the ethmoid sinus under endoscopic visualization. The SINUVA Sinus Implant is made from bioabsorbable polymers designed to gradually soften over time. The SINUVA Sinus Implant may be left in the sinus to gradually release the corticosteroid over 90 days. The SINUVA Sinus Implant can be removed at day 90 or earlier at the physician's discretion using standard surgical instruments.

Sinu-Foam™ is a Food and Drug Administration (FDA)-approved mixture, which is commonly mixed with saline and gently placed in the ethmoid cavity following FESS. A dexamethasone Sinu-Foam spacer has been studied to examine if it could promote wound healing of the nasal and sinus mucosa by reducing the inflammation associated with CRS. However, its clinical utility remains a debate since it does not improve endoscopic outcomes in the early post-operative period following FESS.

LATERA®
LATERA (Spirox/Stryker) received 510(k) FDA approval in June 2016. The LATERA Absorbable Nasal Implant is used to support upper and lower lateral cartilage in the nose, reinforcing the nasal wall like traditional cartilage and polymer grafts. The LATERA implant is absorbed over a period of ~18 months. Post implantation, a fibrous capsule forms and the integrity of the implant is maintained through 12 months. Tissue encapsulation promotes acute implant stability and enables localized tissue response during the absorption process.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply.
FEP: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

CPT Codes:

0406T	Nasal endoscopy, surgical, ethmoid sinus, placement of drug eluting implant;
0407T	; with biopsy, polypectomy or debridement
30999	Unlisted procedure, Nose

HCPCS Codes:

J3490	Unclassified Drugs
S1090	Mometasone furoate sinus implant, 370 micrograms

Previous Coding:

Prior to January 1, 2016, there was not a specific CPT code.

References:

1. Berlucchi M, Castelnuovo P, Vincenzi A et al. Endoscopic outcomes of resorbable nasal packing after functional endoscopic sinus surgery: a multicenter prospective randomized controlled study. Eur Arch Otorhinolaryngol 2009; 266(6):839-45.
2. Catalona PJ TM, Weiss R, Rimash T. The MicroFlow Spacer: a drug-eluting stent for the ethmoid sinus. Indian J Otolaryngol Head Neck Surg 2011; 63(3):258.
3. Cote DW, Wright ED. Triamcinolone-impregnated nasal dressing following endoscopic sinus surgery: a randomized, double-blind, placebo-controlled study. Laryngoscope 2010; 120(6):1269-73.
4. Forwith KD, Chandra RK, Yun PT et al. ADVANCE: a multisite trial of bioabsorbable steroid-eluting sinus implants. Laryngoscope 2011; 121(11):2473-80.
5. Forwith KD, Han JK, Stolovitzky JP, et al. RESOLVE: bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis after sinus surgery: 6-month outcomes from a randomized, controlled, blinded study. Int Forum Allergy Rhinol. 2016; 6: 573-581.
6. Food & Drug Administration, Office of Criminal Investigations. July 22, 2016: Medical Device Manufacturer Acclarent Inc. to Pay $18 Million to Settle False Claims Act Allegations. 2016; https://www.fda.gov/iceci/criminalinvestigations/ucm512838.htm. Accessed January 18, 2018.
7. Freeman SR, Sivayoham ES, Jepson K et al. A preliminary randomised controlled trial evaluating the efficacy of saline douching following endoscopic sinus surgery. Clin Otolaryngol 2008; 33(5):462-5.
8. Han J, Forwith K, Brown W, et al. A Randomized, Controlled, Blinded, Multi-Center Study with Bioabsorbable Steroid-Eluting Sinus Implant for In-Office Treatment of Recurrent Sinonasal Polyposis: 3-Month Safety and Efficacy American Rhinologic Society (ARS at AAO) -- 60th Annual Meeting; September 20, 2014. 2014; Orlando, Florida.
9. Han JK, Forwith KD, Smith TL, et al. RESOLVE: a randomized, controlled, blinded study of bioabsorbable steroid-eluting sinus implants for in-office treatment of recurrent sinonasal polyposis. Int Forum Allergy Rhinol. Nov 2014; 4(11):861-870.
10. Han JK, Marple BF, Smith TL. Effect of steroid-releasing sinus implants on postoperative medical and surgical interventions: an efficacy meta-analysis. Int Forum Allergy Rhinol 2012; 2(4):271-9.
11. https://www.sinuva.com/. Accessed February 09, 2018.

12. Huang Z, Hwang P, Sun Y, et al. Steroid-eluting sinus stents for improving symptoms in chronic rhinosinusitis patients undergoing functional endoscopic sinus surgery. Cochrane Database Syst Rev. 2015; 6:CD010436.
13. https://www.sinuva.com
14. www.spiroxmed.com/latera/
15. Lavigne F, Miller SK, Gould AR, et al. Steroid-eluting sinus implant for in-office treatment of recurrent nasal polyposis: a prospective, multicenter study. Int Forum Allergy Rhinol. May 2014; 4(5):381-389.
16. Lee JM, Grewal A. Middle meatal spacers for the prevention of synechiae following endoscopic sinus surgery: a systematic review and meta-analysis of randomized controlled trials. Int Forum Allergy Rhinol 2012; 2(6): 477-486.
17. Marple BF, Smith TL, Han JK et al. Advance II: a prospective, randomized study assessing safety and efficacy of bioabsorbable steroid-releasing sinus implants. Otolaryngol. Head Neck Surg. 2012; 146(6):1004-11.
18. Matheny KE, Carter KB, Jr., Tseng EY, et al. Safety, feasibility, and efficacy of placement of steroid-eluting bioabsorbable sinus implants in the office setting: a prospective case series. Int Forum Allergy Rhinol. Sep 15 2014.
19. Murr AH, Smith TL, Hwang PH et al. Safety and efficacy of a novel bioabsorbable, steroid-eluting sinus stent. Int Forum Allergy Rhinol 2011; 1(1):23-32.
20. Ow R, Groppo E, Clutter D, et al.
21. Steroid-eluting sinus implant for in-office treatment of recurrent polyposis: a pharmacokinetic study. Int Forum Allergy Rhinol. Sep 25 2014.
22. Rudmik L, Mace J, Mechor B. Effect of a dexamethasone Sinu-Foam™ middle meatal spacer on endoscopic sinus surgery outcomes: A randomized, double-blind, placebo-controlled trial. Int Forum Allergy Rhinol. 2012; 2(3):248-251.
23. Rotenberg BW, Zhang I, Arra I et al. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: a double-blinded, randomized controlled trial. Laryngoscope 2011; 121(12):2702-5.
24. Rudmik L MJ, Mechor B. Effect of a dexamethasone SinuFoam middle meatal spacer on endoscopic sinus surgery outcomes: A randomized, double-blind, placebo-controlled trial. Int Forum Allergy Rhinol. 2012 May-Jun; 2(3):248-51.
25. Rudmik L, Soler ZM, Orlandi RR et al. Early postoperative care following endoscopic sinus surgery: an evidence-based review with recommendations. Int Forum Allergy Rhinol 2011; 1(6):417-30.
26. Sedaghat AR. Chronic rhinosinusitis. Am Fam Physician. Oct 15 2017; 96(8):500-506.
27. Smith TL, Singh A, Luong A, Ow RA, Shotts SD, Sautter NB, Han JK, Stamaugh J, Raman A. Randomized controlled trial of a bioabsorbable steroid-releasing implant in the frontal sinus opening. Laryngoscope. 2016; 126:2659-2664.
28. Xu JJ, Busato GM, McKnight C, et al. Absorbable steroid-impregnated spacer after endoscopic sinus surgery to reduce synechiae formation. Ann Otol Rhinol Laryngol. Sep 21 2015.

Policy History:

Medical Policy Panel, July 2012
Medical Policy Group, July 2012 **(2)** New policy

Medical Policy Administration Committee, July 2012
Available for comment July 26 through September 4, 2012
Medical Policy Panel, November 2013
Medical Policy Group, January 2014 **(2):** No change to policy statement. "Spacer" removed from title and body of policy. Key Points, Approved by Governing Bodies, Key Words, References updated with results of literature search through September 2013.
Medical Policy Panel, November 2014
Medical Policy Group, November 2014 **(5):** Updates to Description, Key Points and References. No Policy change.
Medical Policy Group, November 2015: 2016 Annual Coding Update. Added CPT codes 0406T and0407T to Current Coding; also added a Previous Coding section.
Medical Policy Panel, February 2016
Medical Policy Group, February 2016 (**2):** 2016 Updates to Title, Description, Key Points, and References; policy statement updated to include "and for treatment of recurrent sinonasal polyposis- no change in coverage- policy remains investigational.
Medical Policy Panel, February 2017
Medical Policy Group, March 2017 **(6)**: Updates to Key Points. No change to policy statement.
Medical Policy Group, February 2018 (**6**): Updated Governing Bodies, Key Words and References to include Sinuva. No change to policy intent.
Medical Policy Group, February 2018 **(6)**: Clarified policy title and statement to include "drug-eluting implants". Updated policy with Sinu-Foam™ to Key Points, Coding and Governing Bodies. No change to policy intent.
Medical Policy Panel, February 2018
Medical Policy Group, March 2018 **(6)**: Updates to Description, Key Points and References.
Medical Policy Group, May 2018 **(6):** Updates to Description, Governing Bodies, Coding and References to include Sinuva and LATERA; added "nasal" to policy statement, Latera already investigational per DORS.
