Cigna does not cover a drug-eluting device (e.g., Propel™ Steroid-Releasing Implant, Sinu-Foam Spacer) for maintaining postoperative sinus ostial patency following endoscopic sinus surgery because its use is considered experimental, investigational or unproven.

Functional endoscopic sinus surgery (FESS) is typically performed for chronic rhinosinusitis (CRS) unresponsive to medical management. FESS involves the removal of small pieces of bone, polyps and debridement of tissues within the sinus cavity. Postoperative treatment may include saline irrigation, nasal packs, foam dressings, topical steroids, systemic steroids, topical decongestants, oral antibiotics, and/or sinus cavity debridement. A variety of adjunctive devices have been applied to the sinuses during FESS to keep the middle meatus open, with varying degrees of success. These devices have included packing materials, injectable space-filling gels or structured stents. In some instances packing materials have been soaked with a drug but the uncontrolled and inconsistent release of the drug resulted in erratic outcomes. Therefore drug-eluting stents or implants or spacers, have been proposed to help maintain postoperative sinus ostial patency by reducing scarring and adhesions following FESS. A stent/spacer is a device that is placed into a sinus cavity temporarily to keep it open, promote wound healing and relieve an obstruction. Stents/spacers are used temporarily and removed after a period of time (e.g., 14-30 days). Some middle meatal drug-infused spacers have been attempted by the treating surgeon who determines the type and dosage of steroid. There is unknown drug release with these spacers and they are not FDA approved (Intersect ENT, 2016; Parikh, 2014; Catalano, et al., 2011).
Drug-eluting stents (DESs) or implants are surgically inserted scaffolds that are proposed to aid in healing the affected tissue by locally and continuously releasing a loaded drug or saline in a controlled manner for the desired period of time. Some drug-eluting stents are made of a biodegradable material and are absorbed by the body. Commonly used drugs for nasal stents include corticosteroids (e.g., dexamethasone, fluticasone and mometasone) and antibiotics. Proposed advantages of these devices include removing the issues of noncompliance and adequate drug delivery seen with traditional topical medical therapy techniques. However, there is a risk of inducing inflammation from a foreign material and the potential of unintended systemic absorption of medication when an implant is used. The Propel™ (Intersect ENT, Palo Alto, CA), a mometasone-eluting biodegradable implant is an example of a drug-eluting stent. A smaller version of the drug delivery system, Propel™ mini, is also available (Intersect ENT, 2016; Parikh, 2014; Rudmik, 2012; Catalino, et al., 2011).

Outcomes from the published, peer-reviewed literature show varying degrees of success in the use of drug-eluting implants following FESS. Studies primarily report short-term follow-ups and include small patient populations. Data showed variability in the outcomes including maintaining sinus patency. The impact of these foreign materials implanted in the body is unknown. Reported complications include implant blockage and granulation build-up. The effects of the drug released onto the sinus mucosa are unclear. There is insufficient evidence to support the safety and effectiveness of these devices.

US Food and Drug Administration (FDA)
The Relieva Stratus MicoFlow Spacer was FDA 510(k) approved in 2009 as a Class I frontal sinus spacer. The MicroFlow Spacer is indicated “for use as a postoperative spacer to maintain an opening to the frontal sinuses within the first 14 days following surgery”. The device is also approved to prevent obstruction and it maintains its position by a self-retention mechanism. The spacer is a balloon-based device that acts as a reservoir to allow bathing of the ethmoid sinus. A second surgical procedure is needed to remove the device. According to Taulu et al. (2015) the Relieva Stratus has recently been FDA approved for sterile saline. In Europe, the device has a CE Mark approval for use of triamcinolone acetonide.

The Propel® implant was approved through the premarket approval application (PMA) process. The implant is intended “for use in patients >18 years of age following ethmoid sinus surgery to maintain patency, thereby reducing the need for post-operative intervention such as surgical adhesion lysis and/or use of oral steroids. The Propel separates mucosal tissues, provides stabilization of the middle turbinate, prevents obstruction by adhesions, and reduces edema.” The implant is manufactured from a synthetic bioabsorbable copolymer, poly(L-lactideco-glycolide) (PLG) and contains 370 μg mometasone furoate (active ingredient), a synthetic corticosteroid with anti-inflammatory activity. The implant is designed to accommodate the size and variability of the post-surgical ethmoid sinus anatomy. The device is dissolvable over a period of several weeks, and thereby does not require removal (FDA, 2011). The Propel Mini was FDA PMA approved in 2012 as a shortened version of the Propel and is indicated for use in a patient ≥ 18 years of age following ethmoid sinus surgery to maintain patency, thereby reducing the need for post-operative intervention such as surgical adhesion lysis and/or use of oral steroids. The Mini also contains 370 μg mometasone furoate (FDA, 2012). In 2016, The Propel Mini FDA indication was expanded to include treatment of the frontal sinus. The Propel Contour Sinus Implant was FDA PMA approved in February 2017 as a supplement to the Propel FDA PMA approval. This device is indicated for use in patients greater than or equal to 18 years of age to maintain patency of the frontal and maxillary sinus ostia following sinus surgery. Per Intersect (2017), the Contour has an hourglass shape and is proposed to conform to sinus ostia, propping the sinuses open while delivering the medication. It is proposed for placement in frontal and maxillary sinuses and, like the other Propel devices, releases 370 μg mometasone furoate.

Sinu Foam (Arthrocare Corp., Austin, TX), is an FDA approved carboxymethylcellulose polysaccharide material that forms a gel when hydrated. The gel is placed within the ethmoid cavity at the completion of an FESS procedure. The dexamethasone Sinu-Foam™ spacer has been evaluated following FESS for CRS without polyps (Parikh, et al., 2014; Rudmik, et al., 2012). The spacer is currently not FDA approved (Rudmik, et al., 2012).

Literature Review
All Devices: In a Cochrane review, Huang et al. (2015) conducted a systematic review of randomized controlled trials (RCTs) to evaluate the effectiveness of steroid-eluting sinus stents for improving symptoms of CRS following functional endoscopic sinus surgery (FESS). The search included all RCTs comparing steroid-eluting sinus stents with non-steroid-eluting sinus stents or nasal packing or no treatment in adult CRS patients.
undergoing FESS. A total of 159 records were retrieved. Twenty-one had the potential to be included given that they had tested sinus stents, spacers and packing materials for patients with CRS undergoing FESS. However, the trials did not meet all of the inclusion criteria. Inclusion criteria included: adult patients with CRS with or without nasal polyps, undergoing FESS. CRS was diagnosed based on the presence of symptoms for 12 weeks, including nasal obstruction, nasal discharge, and either endoscopic signs or CT images showing mucosal changes within the ostiomeatal complex, sinuses, or both. Randomized controlled trials that were a within patient control design were excluded. Studies did not report subjective measurements of sinonasal symptoms. The primary outcome measure was improvement in symptom scores per visual analogue scale or Sino-Nasal Outcome Test-22 (SNOT-22). Secondary outcomes included improvement in quality of life, adverse events, endoscopic score and Lund-Mackay radiographic scores.

Mometasone Furoate (Propel): Smith et al. (2016) conducted a multicenter randomized controlled trial (N=80) to assess the safety and efficacy of the Propel mini steroid-releasing implant following endoscopic sinus surgery (ESS). Each patient was their own control with one side receiving propel and the contralateral side receiving no implant. Subjects were age ≥ 18 years, diagnosed with CRS, scheduled to undergo primary or revision bilateral ESS and had evidence of frontal sinus disease based on computed tomography. The primary outcome measure was the reduction in need for postoperative interventions 30 days post-ESS based on video-endoscopic evaluation by an independent, blinded reviewer. Postoperative intervention was defined as either surgical intervention to debride obstructive adhesions or scar tissue formation in the frontal recess/frontal sinus opening (FSO) and/or oral steroid intervention needed to resolve recurrent inflammation or polypoid edema in the frontal recess/FSO. The implants were removed at day 21 to maintain blinding of the independent reviewer. Following ESS, a 10-day course of antibiotics was required. Intranasal steroid sprays were allowed starting 14 days post-ESS, and oral steroids were prescribed, if warranted, based on the investigator’s discretion. Orally inhaled steroids for control of asthma were prescribed as needed. Patients were encouraged to use saline sprays or irrigation as needed. If oral steroids or surgical intervention was warranted at day 7 or day 21 and received, the grading was revised by the clinical investigator. At the 30-day follow-up, based on clinical investigator judgment, the need for postoperative intervention in the FSO was significantly lower in the implant side vs. the control side (p=0.0070) which remained true when analysis was adjusted for three patients who received postoperative interventions (p=0.0107). The reduction in postoperative interventions remained true at the 90-day follow-up (p=0.0129). Significant differences in favor of the implant group were also seen in oral steroid intervention (p=0.0015), relative reduction (75.0%) in need for surgical intervention (p=0.0225), inflammation scores (p<0.0001), lower number of restenosed or occluded sinuses (p=0.0002), and a greater FSO diameter (p<0.0001). Endoscopic assessments showed that the implant sides had a significantly lower frequency of adhesion and scarring warranting surgical interventions (p=0.0225) and a significant reduction in expanded polypoid edema at day 30 (p=0.0226) by clinical investigators. Five adverse events including headache, left upper eyelid swelling, epistaxis, recurrent chronic sinusitis, and increased sinus pressure were judged by the clinical investigators to have an indeterminate relationship to the implant. Limitations of the study include the small patient population, short-term follow-up and heterogeneity of postoperative treatment regimen. Author-noted limitation includes the intrapatient design which precluded evaluation of the effect of treatment on patient symptoms and other quality-of-life assessments, and removal of the implant at day 21 may have caused additional mucosal trauma hindering normal healing on the treatment sides.

Han et al. (2012) conducted a meta-analysis of two multicenter, randomized controlled trials (n=143) (Murr, et al., 2011 and Marple, et al., 2011). The treatment arm of both studies utilized versions of the Propel implant which were not FDA approved at the time of the studies. Both trials were FDA-regulated trials. Patients served as their own control with subjects receiving the drug-releasing implant on one side and a placebo control implant on the contralateral side. Both studies enrolled patients with similar baseline characteristics and enrolled subjects who were adults (mean age 48) with a diagnosis of CRS with and without polyps who were scheduled to undergo primary or revision FESS with bilateral ethmoidectomy, and were candidates for implants. CRS was defined as inflammation of the mucosa of the nose and paranasal sinuses for at least eight consecutive weeks' duration with presence of bilateral ethmoid disease. All implants were successfully inserted. Significantly fewer adhesions were seen postoperatively in the implant group (4.2% vs. 14.1%) (p=0.0013). The need for postoperative intervention (e.g., lysis of adhesion; need for oral steroid) was 50.8% on control sides compared to 32.8% on treatment sides (p=0.0008). Significantly fewer implant patients required surgical intervention for adhesions (13.2% vs. 29.1%) (p=0.0016) and oral steroids (22.1% vs. 37.25%) (p=0.0023). The rate of frank polyposis was significantly fewer in the implant group as well (19.8% vs. 36.9%) (p<0.0001). Author-noted limitations of the analysis included: some patients could not be evaluated for some of the endpoints when one or both sinus sides was unable to be graded due to inadequate imaging of relevant anatomy or suboptimal video
quality; the required intervention decisions (e.g., oral steroids) were made by the independent panel without consideration of individual clinical factors impacting the patient or recovery process; and since both the sinuses had implants there was no comparison without any implant. Another limitation is the small patient population.

Forwith et al. (2011) conducted a prospective case series (n=50 patients/90 sinuses) of patients with CRS who underwent FESS using bilateral and unilateral drug-eluting implants (Propel). Subjects were adult patients, with or without nasal polyps, scheduled to undergo primary or revision FESS, and in whom placement of the sinus stents was feasible and medically appropriate. Oral and topical steroids were withheld for 60 days postoperatively. Endoscopic follow-ups were performed for up to 60 days and patient questionnaire scores (the Sino-Nasal Outcome Test-22 Questionnaire, Rhinosinusitis Disability Index) were collected for up to six months. Outcomes were assessed by inflammation grading, polyp formation, adhesions, and middle turbinate position. Safety assessment included ocular exams at baseline and 30 days. All devices were successfully implanted. At the one-month follow-up, the prevalence of polyoid edema was 10.0%, significant adhesions were 1.1%, and middle turbinate lateralization was 4.4%. Improved changes from baseline in patient-reported outcomes were statistically significant (p<0.0001). No clinically significant changes from baseline in intraocular pressure occurred. Limitations of the study include the lack of a comparator, the small patient population and the short-term follow-ups.

Hayes Inc. published two Prognosis Overview reports (2016) for bioabsorbable steroid-releasing sinus implants including Propel, Propel Mini and the Propel Contour. Regarding Propel and Propel Mini, Hayes concluded that there is insufficient evidence to draw firm conclusion on whether the Propel implants improve clinical outcomes following ESS compared to conventional postoperative regimens. Available studies preclude firm conclusions on the clinical benefits of these devices relative to standard postoperative ESS treatment. The Propel Contour (formerly called Nova Implant) is scheduled to be marketed in the US in the second quarter of 2017. Currently, there are no published studies supporting the safety and efficacy of the Propel Contour. According to Hayes, the Relieve Stratus MicroFlow Spacer (Acclarent Inc.) is no longer marketed in the US.

Mometasone Furoate (Resolve): Investigational studies have been conducted for a new steroid-eluting implant (Resolve) that contains 1350 μg of mometasone furoate which is released over a 90-day period (Intersect ENT, Palo Alto, CA). This device is not currently FDA approved. Forwith et al. (2016) reported outcomes of the Han et al. (2014) randomized controlled trial (n=100) on the steroid-eluting sinus implant for in-office treatment of recurrent ethmoid sinus obstruction after ESS. Three sinus surgeons (the panel) graded the baseline and three-month video-endoscopies in order to independently corroborate the findings reported by the clinical investigators. Implants were removed at day 60 to ensure the panel was blinded to the treatment assignment. Six-month clinical outcomes were also reported. The original study was a multi-center randomized controlled trial that assessed the safety and efficacy of office-based steroid-eluting sinus implant. The control group (n=43) underwent sham procedure. Patients, age ≥ 18 years, had CRS and were candidates for revision ESS based on recurrent symptoms and bilateral polyposis (minimum grade 2 on one side). Within six months of study enrollment, the polyposis had been treated with ongoing topical intranasal steroid irrigation or spray and repeated courses of treatment with oral steroids and/or sinus steroid irrigations. Patients were required to use topical steroid sprays up to the time of the baseline in-office procedure. Following the implant both groups were required to take mometasone furoate nasal spray (Nasonex®; 100 μg nostril once daily) and encouraged to use saline sprays or irrigations, as needed. Patients were permitted to continue regimens of orally-inhaled steroids and sinus-related medical therapy (e.g., immunotherapy, leukotriene antagonists) during the 90-day follow-up. Antibiotic were used as needed for sinus infection. Follow-up occurred for six months. At six months, the study group experienced a significantly greater reduction in bilateral polyp grade (p=0.018) and percent ethmoid obstruction on 100-mm visual analog scale (p=0.001) compared to the control group according to clinical investigator judgment. These results were corroborated by the independent panel at three months. The study group reported a significant improvement in the Nasal Obstruction Symptom Evaluation (NOSE) score (p=0.021) and a two-fold reduction in nasal obstruction and congestion score (p=0.124; not statistically significant). Also, at six months 31% (16/52) of the study group patients were no longer indicated for repeat ESS vs. 11% (5/46) of controls. Adverse events included sinusitis, upper respiratory tract infection, epistaxis, nasopharyngitis, asthma, headache, and presyncope and were similar between the two groups. An Author-noted limitation is the fact that the clinical investigators performing endoscopic grading were not blinded to the treatment assignment. Also, the study entry criteria required patients to be surgical revision candidates while concurrently allowing for one sinus side to have only grade 1 polyposis which may have resulted in enrollment of patients with less opportunity for improvement from baseline. Other limitations are the small patient population and short-term follow-up. This device is not been FDA approved.
Han et al. (2014) conducted a multicenter, randomized controlled trial (n=100) to evaluate the safety and efficacy of a bioabsorbable steroid-eluting implant with 1350 μg of mometasone furoate (Intersect ENT, Menlo Park, CA). Subjects were age 18 years or older, had CRS and had undergone bilateral total ethmoidectomy more than three months earlier. Patients were randomized to the implant group or to the placebo group following FESS and underwent in-office bilateral implants. Three months post procedure, compared to the control group, the implant group experienced a significant reduction in bilateral polyg grade (p=0.0269), and ethmoid sinus obstruction (p=0.0001), and a 2-fold improvement in the mean nasal obstruction/congestion score. Also, 53% of treated patients compared to 23% of controls were no longer indicated for repeat FESS. The mean percentages of implants remaining at days 30, 45, and 60 were 92.5, 86.5, and 56.7, respectively. All implant remnants remaining at 60 days were removed. A total of 34 (64%) patients in the implant group and 35 (75%) in the control group experienced an adverse event including: sinusitis, nasopharyngitis, epistaxis, headache, upper respiratory infection and nasal congestion. No patient experienced a significant increase in intraocular pressure or any type of cataract. According to the authors limitations of the study included: there was not a defined medical treatment regimen prior to enrollment; there was no control over patient prior treatment regimens and compliance; clinical investigators performing endoscopic grading were not blinded to the treatment (implant vs. placebo); and the study entry criteria required patients to be surgical revision candidates while concurrently allowing for one sinus side to have only grade one polyposis which may have impacted the outcomes and lessened the opportunity of generalizing these outcomes to other patients. Another limitation is the small patient population. This device is not been FDA approved.

A 2016 Hayes Prognosis Overview stated that the Resolve is an investigational, second-generation, bioabsorbable steroid releasing sinus implant in development by Intersect the manufacturer of the Propel devices. The device is proposed for placement in the ethmoid sinuses and releases mometasone furoate (1350 μg) directly into the sinus lining over approximately 90 days to reduce inflammation. Resolve is described as having an arched design with a rounded tip, with more radial strength to dilate narrowed sinuses over a longer period of time and remain within the cavity as obstructive tissue recedes. The device is not FDA approved and is still investigational.

Relieva Stratus MicroFlow Spacer: Studies are primarily in the form of case series with small patient populations (n=23) and short-term follow-ups (six months) (Catalano, et al., 2011).

Sinu-Foam Spacer: Rudmik et al. (2012) conducted a randomized controlled trial (n=36) to evaluate the safety and efficacy of the off-label use of dexamethasone Sinu-Foam spacer following FESS for CRS without nasal polyposis. Subjects were age 18 years or older who had failed medical management (i.e., nasal saline irrigations, topical nasal steroids spray for three months, course of systemic steroids with a broad spectrum oral antibiotic), were eligible for minimum bilateral FESS procedure consisting of maxillary antrostomy and ethmoidectomy; and were able to adhere to the follow-up schedule. Patients were randomized to the treatment arm (n=18) or the placebo control arm (n=18). Follow-ups occurred for up to three months and included sinonasal endoscopy and Lund-Kennedy scoring. Postoperatively, patients were treated with nasal saline irrigations and systemic steroids. Both groups showed significant improvement in endoscopic grading (p<0.001) following FESS, but there was no significant difference between the groups (p>0.489). Sinu-Foam did not improve outcomes following FESS.

Professional Societies/Organizations

American Rhinologic Society (ARS): The ARS position statement (2016) on drug-elution implants stated that studies investigation drug-eluting implants have demonstrated improvement in outcomes by reducing inflammation, decreasing scarring and middle turbinate laterization and limiting the need for oral steroids. ARS “feels strongly that drug-eluting implants are not investigational and should be available to our patients, when selected by the physician, in order to maximize outcomes”.

American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS): In a position statement regarding FDA-approved biomaterials, AAO-HNS (2015) stated that these materials can be utilized in sinonasal procedures to improve patient outcomes and reduce complications. These devices include implants, stents, and packing materials and have functions including, but not limited to, local drug delivery, stenting, and hemostasis. According to AAO-HNS FDA-approved biomaterials for rhinologic application are not investigational, and the final decision regarding use of these biomaterials should be determined by the treating physician, factoring in best available scientific evidence, surgeon experience, the clinical situation, and individual patient preference.
Use Outside of the US
The Relieva Stratus MicoFlow Spacer has a CE Mark approval for use in Europe and includes the delivery of triamcinolone acetonide.

In an interventional procedure guidance (2016), the National Institute for Health and Care Excellence (NICE), United Kingdom, stated that current evidence on the safety of corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery raises no major concerns but the evidence for efficacy is limited. Reported improvement of sinus patency is short term and there is inadequate evidence on patient reported outcomes and quality of life. The procedure should only be used with special arrangements for clinical governance, consent, and audit or research.

Summary
Drug-eluting devices (e.g., Propel, Sinu-Foam Spacer) have been proposed for use following FESS to aid in maintaining ostial patency, prevent adhesions, control bleeding and/or for the administration of topical medications. However, there is insufficient evidence in the published peer-reviewed literature to support the safety and effectiveness of these devices. There are a limited number of published studies investigating these devices. Studies primarily report short-term follow-ups and include small patient populations. Data showed variability in the outcomes including maintenance of sinus patency. The impact of these foreign materials implanted in the body is unknown.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
    2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Experimental/Investigational/Unproven/Not Covered:

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References


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