PROPEL® Contour

(mometasone furoate implant, 370 µg)

Instructions For Use

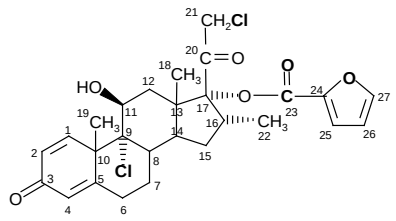
CAREFULLY READ ALL INSTRUCTIONS PRIOR TO USE

STERILE: Sterilized by irradiation. Do not use if the package is open or damaged.
STORAGE: The product should be stored at room temperature (approximately 25º C) with excursions permitted to 15-30º C.
SINGLE USE: Product is supplied sterile and for single use only.

Caution: Federal law (USA) restricts this product to sale by or on the order of a physician.

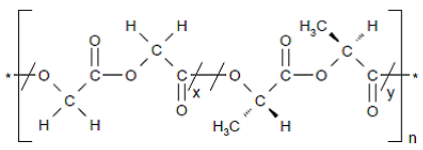
PRODUCT DESCRIPTION
The PROPEL® Contour sinus implant provides sustained release of mometasone furoate via a bioabsorbable sinus implant. A delivery system is provided to insert the implant.

Drug Component Description
The PROPEL Contour sinus implant contains mometasone furoate (active ingredient), a synthetic corticosteroid with anti-inflammatory activity. Mometasone furoate (MF) is a white to off-white powder. The chemical name is 9α,21-dichloro-11β,17α-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2-furoate), with the empirical formula $C_{27}H_{30}Cl_2O_6$, and a molecular weight of 521.43 g/mol. Mometasone furoate is a hydrophobic drug that is practically insoluble in water. Mometasone furoate is stable under aqueous, acidic and oxidative conditions. Mometasone furoate can degrade under extreme basic, thermal and photolytic conditions. The chemical structure is shown below. The drug is embedded in a bioabsorbable polymer matrix containing poly-(DL-lactide-co-glycolide) and polyethylene glycol (inactive ingredients) which provides for gradual release of the drug.



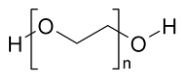
Chemical structure of mometasone furoate

The inactive ingredients on the sinus implant are poly-(DL-lactide-co-glycolide) and polyethylene glycol. Poly-(DL-lactide-co-glycolide) is an amorphous biodegradable polymer. The chemical structure is shown below.



Chemical structure of poly-(DL-lactide-co-glycolide)

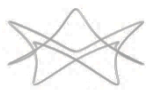
Polyethylene glycol is a hydrophilic polyether compound that is highly flexible. It is non-toxic and non-immunogenic. The chemical structure is shown below.



Chemical structure of polyethylene glycol

Implant Component Description
The PROPEL Contour sinus implant is comprised of a bioabsorbable co-polymer, poly(L-lactide-co-glycolide), PLG.

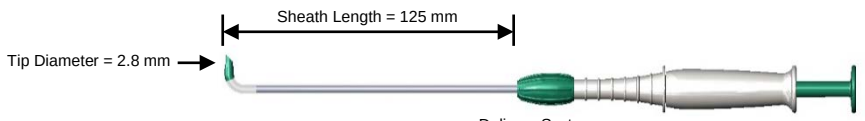
The implant is bioabsorbable and is designed to accommodate the size and variability of the surgically enlarged frontal or maxillary sinus ostium. Once inserted, the implant is designed to be self-retaining against the mucosa of the surgically enlarged sinus ostium in order to maintain sinus patency and deliver drug to the mucosa. The implant should be inserted by a physician under endoscopic visualization. A delivery system is provided to access the frontal or maxillary sinus ostium and deploy the implant. A loading tool and funnel are optional accessories provided to assist in loading of the implant into the delivery system.



Implant

Loading Tool

Funnel



Delivery System

INDICATIONS AND INTENDED USE
The PROPEL Contour sinus implant is intended for use in patients ≥ 18 years of age to maintain patency of the frontal and maxillary sinus ostia following sinus surgery and locally deliver steroids to the sinus mucosa. The PROPEL Contour sinus implant separates/dilates mucosal tissues, prevents obstruction by adhesions/scarring, and reduces edema. The implant reduces the need for post-operative intervention such as surgical adhesion lysis and/or use of oral steroids.

CONTRAINDICATIONS:
The use of the PROPEL Contour sinus implant is contraindicated in the following patients:
- Patients with suspected or confirmed hypersensitivity and/ or intolerance to mometasone furoate.
- Patients with a known hypersensitivity and/ or intolerance to lactide, glycolide or caprolactone copolymers.

WARNINGS
- The PROPEL Contour sinus implant is designed for single patient use only. Do not reprocess or reuse.
- Do not use if the package is open or damaged.

PRECAUTIONS
- Special care should be taken to avoid bending, twisting or damaging the implant.
- The implant is not designed to be modified by the physician.
- The implant is not intended to be compressed and loaded into the delivery system more than two times.
- The implant must be placed under endoscopic visualization.
- The implant exhibits no antimicrobial properties.
- Foreign body reaction may occur as is possible with most surgical adjuncts.
- In rare instances, the physiochemical condition associated with sinus surgery, both with and without sinus implants or packing, may present a risk of toxic shock syndrome (TSS).
- Pediatric Use: The safety and effectiveness of the implant in pediatric patients have not been established.
- Pregnancy and Nursing Females: The safety and effectiveness of the implant in pregnant or nursing females have not been established.

DRUG INFORMATION

MECHANISM OF ACTION: Corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation. The precise mechanism behind the anti-inflammatory properties of the eluted mometasone furoate is not known.

PHARMACOKINETICS: The PROPEL Sinus Implant underwent pharmacokinetic testing. Following bilateral drug-eluting PROPEL implant placement after sinus surgery for chronic sinusitis and subsequent weekly morning blood sampling for 4 weeks in 5 adult patients, plasma mometasone furoate concentrations were not quantifiable at any time point. Mean cortisol concentrations were within normal limits.

DRUG INTERACTIONS
No drug-drug interaction studies have been conducted with the implant.

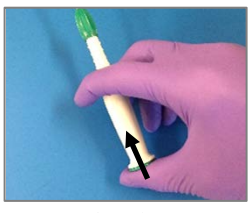
CARCINOGENICITY, GENOTOXICITY AND REPRODUCTIVE TOXICITY
No long term studies in animals have been performed to evaluate the carcinogenic potential of the implant.

PREGNANCY
There have been no controlled studies in pregnant women using the PROPEL Contour sinus implant. The PROPEL Contour sinus implant should be used during pregnancy only if the potential benefits justify the potential risk.

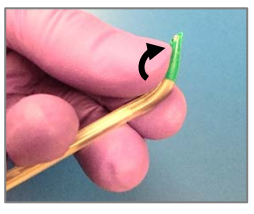
LACTATION
It is not known if mometasone furoate is excreted in human milk. Because other corticosteroids are excreted in human milk, the implant should be used only if the potential benefits justify the potential risk.

DOSAGE AND ADMINISTRATION
Each PROPEL Contour sinus implant contains 370 µg of mometasone furoate which is gradually released over time.

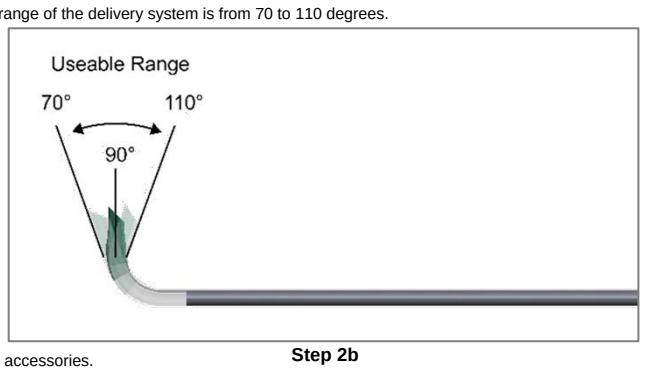
DIRECTIONS FOR USE
1. Remove the implant and delivery system from its protective packaging using sterile technique. Inspect for any obvious damage.
2. Prepare the delivery system.
   a. Depress and hold the plunger.
   b. Using your fingers, gently bend the tip of the applicator to the desired angle while supporting the tubing with your fingers. The useable range of the delivery system is from 70 to 110 degrees.
      Note: It may be necessary to bend the tip past the desired angle to achieve the appropriate angle.
   c. Release the plunger.



Step 2a

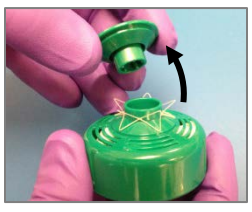


Step 2b

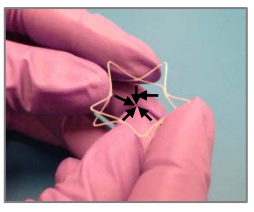


Step 2b

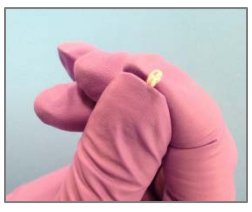
3. The implant must be compressed and loaded into the tip of the delivery system prior to use.
   Note: The compressed implant may be loaded directly into the tip of the delivery system or with the use of the optional funnel and loading tool accessories.
   a. For implant loading with the use of the funnel, place the funnel onto the tip of the delivery system.
   b. Carefully remove the top of the implant holder, being careful not to grasp or dislodge the implant.
   c. Gently lift the implant off of the base of the implant holder.
   d. Grasp the implant between the fingers of both hands and gently compress the implant.
   e. Insert compressed implant into either the attached funnel (if applicable) or directly into to the distal tip of the delivery system.
   f. If the funnel is attached, use the loading tool to push the implant past the opening of the funnel. If the funnel is not attached, continue to push the compressed implant directly into the delivery system until it is flush with the distal tip.
   g. If the funnel is attached, carefully remove the funnel, taking care not to dislodge the implant from the tip of the delivery system. If the implant begins to withdraw from the tip during funnel removal, replace the funnel and gently squeeze the tip of the delivery system to hold implant in place.
   h. The implant may be compressed and loaded into the delivery system tip up to two times.
      CAUTION: Do not leave the implant in the crimped state for more than three minutes prior to placement.



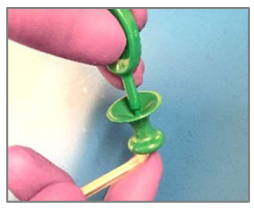
Step 3b



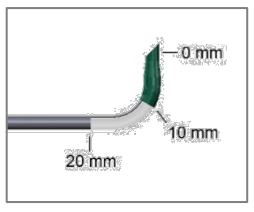
Step 3d



Step 3f



Step 3g



Step 5b

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4. For adequate visualization, ensure hemostasis in operated sinus ostia and/or cavities prior to insertion. Advance the delivery system into the sinus cavity using endoscopic visualization.
5. To insert the implant in the sinus ostium:
   a. Ensure the delivery system is oriented so the distal tip is curved appropriately for the targeted patient anatomy and advance the distal tip of the delivery system into the sinus ostium.
   b. Note: The markings (shown above) on the distal end of the delivery system may be used to aid in placement (for reference only).
   c. Deploy the implant halfway by depressing the plunger until the distal edge of the coiled pusher aligns with the green to clear transition. At this point, the implant is approximately halfway deployed.
   d. Slightly withdraw the delivery system to visualize the waist of the implant (which is denoted by the strut crossing-points).
   e. Align the waist of the implant with the ostium.
   f. While keeping the waist of the implant aligned with the ostium, continue withdrawing the delivery system from the sinus ostium while simultaneously continuing to depress the plunger.
   g. Visualize the waist of the implant and ensure it is aligned with the ostium before completely depressing the plunger and fully deploying the implant.
6. Confirm final placement by endoscopic visualization. Confirm the waist of the implant is aligned with the sinus ostium. Confirm the implant is well apposed to the tissue to maximize drug delivery. To adjust the position of the implant, use standard surgical instruments.

POST-OPERATIVE CARE

- As part of routine post-operative care, frequent use of saline sprays, rinses or irrigations is recommended to keep the implant moist.
- Routine debridement may be performed as part of the usual post-operative care.
- The implant may be removed at the discretion of the physician by use of suction, forceps or other surgical instruments.

CLINICAL TRIALS

The safety and efficacy of the PROPEL Contour sinus implant when placed in the maxillary sinus ostia (MSO) and frontal sinus ostia (FSO) following endoscopic sinus surgery (ESS) in patients with chronic sinusitis was assessed in 2 prospective clinical trials conducted in the United States.

The EXCEED study was a prospective, single-arm, open-label, feasibility trial designed to assess the performance, safety and initial signals of efficacy of the PROPEL Contour sinus implant placement in the frontal and maxillary sinuses in patients with chronic sinusitis following ESS in the office and operating room settings. Fifteen of 16 patients enrolled at 2 study sites were eligible to participate. The EXCEED study results showed an overall implant delivery success rate of 97.8% (100% in frontal sinuses; 95.2% in maxillary sinuses), demonstrating that the primary performance endpoint was met. No serious unanticipated AEs were reported; therefore, the study met the primary safety endpoint. In addition, no AEs were related to placement of the PROPEL Contour sinus implant. Observed endoscopic improvements at Day 90 included a 46.8% increase in ostial patency, a 75.0% reduction in polypoid edema, a 19% reduction in grade 2 and 3 adhesion/scarring, and a 38.1 mm decrease in inflammation score. The mean SNOT-22 score at Day 90 showed a treatment effect size of 1.09, representing a large health benefit. None of the patients required oral steroids for sinus obstruction, and only 2 received surgical interventions (i.e., polypectomy; removal of left frontal scar) through the duration of the study.

The PROGRESS study was a prospective, randomized, blinded, controlled study that enrolled 80 patients across 12 study centers. The study utilized an intra-patient control design to assess the safety and efficacy of the PROPEL Contour sinus implant when placed following surgery on 1 sinus side compared to surgery alone on the contralateral side. The primary efficacy endpoint was the reduction in need for post-operative interventions at Day 30, as determined by an independent, blinded, sinus surgeon based on video-endoscopy review. Post-operative intervention was a composite endpoint that included surgical intervention required to debride obstructive adhesions or scar tissue formation (grade 2 or 3) in the frontal sinus ostia (FSO), and/or oral steroid intervention warranted to resolve recurrent inflammation or polypoid edema in the frontal recess/FSO. Secondary efficacy endpoints of frequency and severity of adhesion/scarring, polypoid edema and inflammation were determined endoscopically by an independent reviewer and clinical investigators at the study centers. The safety measures of adverse events and serious adverse events were recorded throughout the 90-day follow-up period.

The PROGRESS study demonstrated that PROPEL Contour sinus implant placement in the FSO was successful (100% implant delivery), safe, and effective in significantly reducing the need for post-operative interventions in the FSO at Day 30 (p=0.0023), as judged by an independent blinded reviewer (see table below). Holm's step-down procedure used to control for family-wise type I error rate on 6 prespecified secondary efficacy endpoints showed statistically significant reductions in the need for postoperative interventions (p=0.0039), need for surgical interventions (p=0.0156), degree of inflammation (p=0.0005), and rate of occlusion/restenosis (p<0.0001) as observed by clinical investigators at Day 30. Through Day 90, the rate of occlusion/restenosis was significantly (p=0.0055) lower on the treatment compared to the control sides, representing a relative reduction of 42.9%.

	Treatment (Tx) (n=80)	Control (Ctrl) (n=80)	p-value
PRIMARY EFFICACY RESULTS[a,¥]			
Need for Post-Operative Interventions, N (%)	7 (11.5%) (n=61)[§]	20 (32.8%) (n=61)[§]	0.0023
SECONDARY EFFICACY RESULTS[b,ł]			
Need for Post-Operative interventions, N (%)	12 (16.0%) (n=75)[§]	25 (33.3%) (n=75)[§]	0.0039
Need for Surgical Interventions, N (%)	3 (4.0%) (n=75)[§]	11 (14.7%) (n=75)[§]	0.0156
Inflammation (100-VAS, mm), Mean (SD)	23.1 (24.23) (n=79)[§]	35.6 (31.12) (n=77)[§]	0.0005
Occlusion/Restenosis, N (%)	10 (13.3%) (n=75)[§]	27 (36.0%) (n=75)[§]	<0.0001

[¥]All eighty patients returned for the Day 30 visit and had their endoscopy recorded for grading by independent reviewer; however, data were considered missing if the independent reviewer could not grade a video due to sub-optimal video quality or inadequate imaging of the relevant anatomy. Inadequate imaging of the relevant anatomy can occur when presence of significant edema or an adhesion prevents access into the frontal sinus. Since the planned statistical test (McNemar's test of correlated proportions) requires patients with an observed pair of outcomes, 19 patients could not be included in the test. McNemar's exact binomial test was employed to obtain the 2-sided p-value at alpha level of 0.05 for the primary efficacy endpoint and other categorical efficacy endpoints; T-tests were performed for all continuous efficacy data on the side-to-side difference in scores
[ł]p-values adjusted using a Holm's step-down method to control for familywise type I error
[a] Determined at Day 30 by the independent reviewer based on video-endoscopy review
[b] Determined at Day 30 by clinical investigators
[§] Number of patients with evaluable sinuses
SD=Standard Deviation, VAS=Visual Analog Scale

ADVERSE EVENTS

OBSERVED ADVERSE EVENTS

PROPEL Contour sinus implant is a drug-releasing sinus implant that is smaller in size than the PROPEL Mini, to accommodate the size and variability of the enlarged sinus ostium. Two prospective clinical trials (EXCEED and PROGRESS) conducted in the United States studied 95 patients and 125 PROPEL Contour sinus implants. In the EXCEED study, no implant-related serious adverse events were reported, resulting in a 0% incidence rate of implant-related adverse events. No patients withdrew due to an adverse event, and no deaths occurred.

In the Nova cohort (with PROPEL Contour) of the PROGRESS study with 80 patients, no implant-related serious adverse events or adverse events were observed, resulting in a 0% overall incidence rate of implant-related adverse events. Three adverse events (headache, epistaxis, acute sinusitis) were judged by clinical investigators as having an indeterminate relationship to the implant. All three events resolved without sequelae. No patients withdrew due to an adverse event and no deaths occurred. Adverse events (regardless of relationship to implant), which were reported in ≥ 2% of patients in the PROGRESS study are summarized in the table below.

Adverse Events (n=80) – PROGRESS study (Nova Cohort)	
Adverse Event Type	**Patients Reporting (%)**
Acute Sinusitis	20.0
Asthma	7.5
Headache	6.3
Chronic Sinusitis	5.0
Upper Respiratory Tract Infection	5.0
Fungal Sinusitis	2.5

Adverse Events (n=80) – PROGRESS study (Nova Cohort)	
Adverse Event Type	**Patients Reporting (%)**
Nasopharyngitis	2.5
Nausea	2.5
Neck Pain	2.5
Sinus Headache	2.5
Streptococcal Pharyngitis	2.5

POTENTIAL ADVERSE EVENTS

Risks associated with the use of the PROPEL Contour sinus implant are anticipated to be similar to those experienced by patients who undergo placement of sinus implants or packing. Risks potentially associated with use of the PROPEL Contour sinus implant may include, but not be limited to the following.

- Premature displacement of implant or implant fragments
- Swallowing of implant or implant fragments
- Pain/pressure/headache due to the adherence of crusting to, or presence of the implant
- Aspiration of small implant fragments
- Foreign body response, including formation of granulation tissue

Risks potentially associated with intranasal mometasone furoate may include, but not be limited to the following.

- Nasal irritation
- Hypersensitivity reaction
- Intranasal bleeding (epistaxis)
- Localized infection (bacterial, fungal or viral) in the nose or pharynx
- Nasal burning
- Nasal dryness
- Susceptibility to secondary infections due to bacteria, fungi or viruses
- Glaucoma/elevation of intraocular pressure
- Cataracts/change in lens opacities
- Headache
- Pharyngitis

Risks potentially associated with steroids may include, but not be limited to the following.

- Alteration of the HPA axis including growth suppression
- Immunosuppression
- Hypersensitivity reactions
- Headache
- Epistaxis
- Coughing
- Vomiting
- Candidiasis
- Glaucoma/elevation in intraocular pressure
- Cataracts/changes in lens opacities
- Arthralgia
- Myalgia

There may be other potential adverse effects that may occur which are currently unforeseen.

Symbols Used on Product Labeling					
REF:	Reference Number		Use By		Single Use
LOT	Lot Number		Read Instructions Prior to Use	STERILE R	Sterilized using Irradiation
15°C 30°C	Room Temperature				

Product Information Disclosure

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