

(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 25° C) with excursions permitted to 15-30° C.
SINGLE USE: Product is supplied sterile and for single use only.

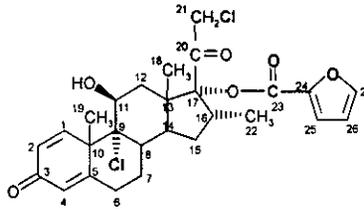
Caution: Federal law (USA) restricts this product to sale by or on the order of a physician.

PRODUCT DESCRIPTION

The Propel sinus implant provides sustained release of mometasone furoate via a bioabsorbable sinus implant. A delivery system is provided to insert the implant.

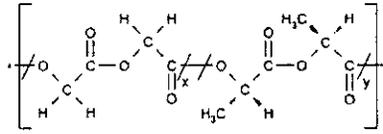
Drug Component Description

The Propel™ sinus implant contains mometasone furoate (active ingredient), a synthetic corticosteroid with anti-inflammatory activity. Mometasone furoate is a white to off-white powder. The chemical name is 9 α ,21-dichloro-11 β ,17 α -dihydroxy-16 α -methylpregna-1,4-diene-3,20-dione 17-(2-furoate), with the empirical formula C₂₇H₃₀Cl₂O₆, 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. MF 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.



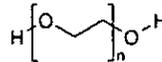
Chemical structure of mometasone furoate

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.

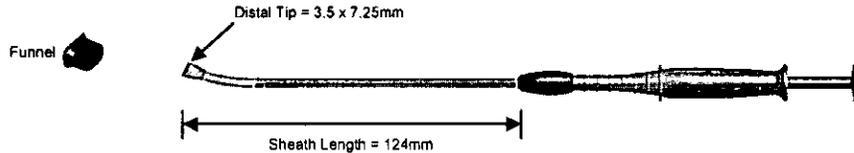
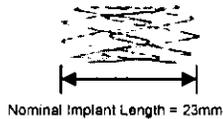


Chemical structure of polyethylene glycol

Implant Component Description

The Propel implant is comprised of a synthetic bioabsorbable co-polymer, poly(L-lactide-co-glycolide), PLG.

The implant is bioabsorbable and is designed to accommodate the size and variability of the post-surgical ethmoid sinus anatomy. Once inserted, the implant is designed to be self-retaining against the mucosa of the surgically enlarged sinus in order to maintain sinus patency and deliver drug to the mucosa. The Propel implant should be inserted by a physician under endoscopic visualization. A delivery system is provided to access the ethmoid sinus and insert the implant.



INDICATIONS AND INTENDED USE

The Propel sinus implant is intended for use in patients \geq 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 sinus implant separates mucosal tissues, provides stabilization of the middle turbinate, prevents obstruction by adhesions, and reduces edema.

CONTRAINDICATION:

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

WARNINGS

- The Propel 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).

35

(mometasone furoate implant, 370 µg)

Instructions For Use

- 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: Following bilateral drug-eluting 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 sinus implant. The Propel 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 Propel implant should be used only if the potential benefits justify the potential risk.

DOSAGE AND ADMINISTRATION

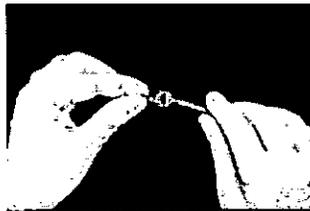
Each Propel implant contains 370µg of mometasone furoate which is gradually released over time.

DIRECTIONS FOR USE

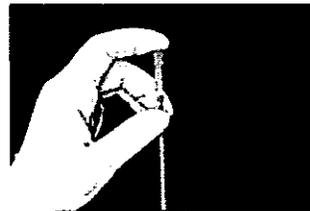
1. Remove the implant and delivery system from its protective packaging using sterile technique. Inspect for any obvious damage.
2. The implant must be compressed and loaded into the tip of the delivery system prior to use.
 - a. Gently slide implant off its holder.
 - b. Grasp the implant between the fingers of both hands and gently compress the implant.
 - c. Insert compressed implant into the funnel attached to the distal tip of the delivery system.
 - d. Gently push the implant into the funnel (as far as possible) using a fingertip.
 - e. 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.
 - f. The implant may be compressed and loaded into the delivery system tip up to two times.



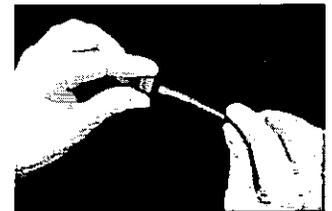
Step 2b



Step 2c



Step 2d



3. For adequate visualization, ensure hemostasis in operated sinus cavities prior to insertion. Advance the Delivery System into the sinus cavity using endoscopic visualization. To insert the implant:
 - a. Ensure that the Delivery System is oriented so the distal tip is curved superiorly toward the posterior roof of the sinus cavity
 - b. Align the proximal end of the implant with the anterior edge of the middle turbinate.
 - c. Insert the implant by depressing the plunger while simultaneously withdrawing the delivery system.
4. Confirm final placement by endoscopic visualization. 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.
- 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 efficacy and safety of the Propel sinus implant, when used in adult patients with chronic sinusitis undergoing functional endoscopic sinus surgery (FESS) have been studied in three prospective clinical trials conducted in the United States and totaling 205 patients. The principal safety and efficacy information is derived from the ADVANCE II clinical trial and is supported by the ADVANCE clinical trial and CONSENSUS II pilot study. In all three studies, implant placement occurred following ethmoidectomy. Implants were successfully placed in a total of 400 sinuses in the 205 patients. Of the 400 implants, 16 (4%) were removed and replaced immediately after deployment due to sub-optimal apposition, crossed struts or inadvertent removal, and 3 (0.8%) were damaged during preparation. In these 3 cases, a new implant was used successfully.

The ADVANCE II study was a prospective randomized, double-blind, concurrently controlled study that enrolled 105 patients at 11 study centers. The study utilized an intra-patient control design to assess the safety and efficacy of the Propel sinus implant compared to the non-drug control version of the implant. The primary efficacy endpoint was the reduction in need for post-operative interventions at day 30, determined from video-endoscopies reviewed by a panel of independent blinded sinus surgeons. Post-operative intervention was a composite endpoint that included surgical intervention required to separate an adhesion and/or oral steroid intervention to resolve recurrent ethmoid sinus inflammation, edema and/or polyp recurrence. Additional efficacy endpoints were determined by endoscopic grading done by clinical investigators at the study centers.

The primary safety endpoint was ocular safety defined as absence of clinically significant sustained elevation (≥ 10 mm Hg) in intraocular pressure through Day 90. Ocular examinations also included assessment of changes in or development of lens opacities.

The Propel implant delivery success rate was 100%. The primary efficacy endpoint was met demonstrating a statistically significant reduction in the need for post-operative interventions at day 30 ($p=0.0280$). There were no clinically significant increases in intraocular pressure and no clinically significant changes from baseline in lens opacities.

(mometasone furoate implant, 370 µg)
Instructions For Use

	N	Treatment	Control	Difference / p-value* (Ctrl - Tx)
Number of patients in ITT population		105	105	
PRIMARY EFFICACY RESULTS[§]	Evaluable	N (%)	N (%)	
Post-Operative Intervention	96	32 (33.3%)	45 (46.9%)	13 (13.5%) / 0.0280
PRIMARY SAFETY RESULTS				
Clinically Significant Elevation in IOP**	105	0 (0.0%)	0 (0.0%)	p < 0.0001
95% CI***		0.0000, 0.0352	0.0000, 0.0352	
SECONDARY EFFICACY RESULTS[§]	Evaluable	N (%)	N (%)	
Frank Polyposis (Grades 2 and 3) [§]	85	16 (18.8%)	29 (34.1%)	13 (15.3%) / 0.0023
SECONDARY EFFICACY RESULTS[§]	Evaluable	N (%)	N (%)	
Frank Polyposis (Grades 2 and 3)	104	4 (3.8%)	8 (7.7%)	4 (3.9%) / 0.3437
Middle Turbinate Lateralization	105	2 (1.9%)	7 (6.7%)	5 (4.8%) / 0.1250
Significant Adhesions	104	5 (4.8%)	13 (12.5%)	8 (7.7%) / 0.0386

All patients returned for the Day 30 visit and had their endoscopy recorded for grading by independent panel; however, data were considered missing if the panel 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 ethmoid sinus. Since the planned statistical test (McNemar's test of correlated proportions) requires subjects with an observed pair of outcomes, 9 subjects could not be included in the test. Evaluable subjects were those with gradable sinuses on both sides. **Intraocular pressure ***Exact 2-sided confidence intervals are calculated by the method of Clopper and Pearson. [§]By independent panel at Day 30 [§]By on site clinical investigators at Day 30

*McNemar's test was employed to obtain the 2-sided p-value at alpha level of 0.05 for all efficacy endpoints; an exact version was used for endpoints with <20 discordant pairs; an exact binomial test was employed to obtain the 1-sided p-value at alpha level of 0.025 for the primary safety endpoint.

The ADVANCE study was a single-cohort, open-label trial that enrolled 50 patients with either unilateral or bilateral ethmoid sinus disease at 7 study centers. Follow-up assessments included endoscopic examination and scoring through 2 months, with patient symptom scoring done through 6 months (Sinonasal Outcomes Test 22 (SNOT22), Rhinosinusitis Disability Index (RSDI) and a total nasal symptom scoring instrument (TNSS)). Outlier examinations consisted of IOP measurement and dilated slit-lamp examination for lens opacities at baseline and day 30. The implant delivery success rate was 100%. The observed rate of polypoid tissue formation of any grade at 30 days was 10.0%, adhesions 1.1%; and middle turbinate lateralization 4.4%. There were no clinically significant changes from baseline in lens opacities or IOP. The mean changes from baseline to Day 60 and 6 months in total RSDI score were -36.2 and -29.7, respectively (p<0.0001). For the SNOT 22, the changes were -1.9 and -1.7, respectively (p<0.0001). All changes from baseline in RSDI, SNOT 22 and TNSS were statistically significant (p≤0.0002).

The CONSENSUS II pilot study was a randomized, double-blind, concurrently controlled feasibility trial that enrolled 50 patients at 4 study centers. A total of 43 patients received the 23 mm Propel sinus implant and 7 patients received a shorter version. The study utilized an intra-patient control design to assess the safety and efficacy of the drug-eluting Propel sinus implant compared to the non-drug eluting control version of the implant. Thirty eight patients were enrolled in this group and received the 23 mm implants. The other group of patients (n=5) received bilateral drug-eluting implants to assess systemic safety (described in Drug Information section). The implant delivery success rate was 100%. The drug-eluting implant provided a statistically significant reduction in ethmoid sinus inflammation, scored using a 100 mm visual analog scale, compared to the control implant at day 21 (p=0.0032). Statistically significant reductions in inflammation were also observed at days 30 and 45 (p≤0.0022). The drug-eluting implant reduced the frequency of middle turbinate lateralization, significant adhesion occurrence, and polypoid tissue formation through day 30, compared to the control implant.

ADVERSE EVENTS

OBSERVED ADVERSE EVENTS

In three prospective clinical trials conducted in the United States and including 205 patients, a total of 400 sinus implants were studied. Of these 400 implants, 250 were drug-eluting (243 were the 23 mm Propel sinus implant and 7 were a shorter version containing 220 µg of MF, available only in the pilot trial) and 150 were non-eluting control implants (143 were the 23 mm length implants and 7 were a shorter version available only in the pilot trial). The overall incidence rate of product-related adverse events on a by-patient count was 1.5%; three patients had product related adverse events. One event was a headache with nasal burning and two were recurrent sinusitis. All three events resolved without sequelae. No patients withdrew due to an adverse event and no deaths occurred in any of the three trials.

Adverse events (regardless of relationship to implant) reported in ≥2% of patients across all three trials are displayed in the table below.

Adverse Events From All Three Clinical Trials (n=205)	
Adverse Event Type	Percent of Patients Reporting
Sinusitis	32.2
Headache	5.4
Epistaxis	2.0
Bronchitis	2.0

Note: Events were tabulated through day 60 in the feasibility trial and ADVANCE trial, and through day 90 in the ADVANCE II trial.

POTENTIAL ADVERSE EVENTS

Risks associated with the use of the Propel sinus implant are anticipated to be similar to those experienced by patients who undergo placement of sinus implants or packing. The risks potentially associated with use of the Propel implant are:

- Premature displacement of implant or small implant fragments out the nares
- Swallowing implant or implant fragments
- Adherence of crusting to the implant, resulting in or contributing to sensations of pain/pressure/headache
- Aspiration of small implant fragments (not observed in clinical trials)
- Foreign body response, including formation of granulation tissue

Potential risks or side effects associated with intranasal mometasone furoate include:

- nasal irritation
- hypersensitivity reaction
- intranasal bleeding
- 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

Potential risks or general side effects associated with steroids:

- alteration of the HPA axis including growth suppression
- immunosuppression
- hypersensitivity reactions
- headache

Propel™
(mometasone furoate implant, 370 µg)
Instructions For Use

- epistaxis
- coughing
- vomiting
- candidiasis
- glaucoma/elevation in intraocular pressure
- cataracts/changes in lens opacities
- arthralgia
- myalgia

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

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

Product Information Disclosure

Intersect ENT, Inc. has exercised reasonable care in the manufacture of this product. Intersect ENT, Inc. excludes all warranties, whether expressed or implied, by operation of law or otherwise, including but not limited to, any implied warranties of merchantability or fitness, since handling and storage of this product, as well as factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond Intersect ENT, Inc.'s control, directly affect this product and the results obtained from its use. Intersect ENT, Inc. shall not be liable for any incidental or consequential loss, damage or expense, directly or indirectly arising from the use of this product. Intersect ENT, Inc. neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this product.

Use of this product in a method may be covered by one or more of U.S. Patent Nos. 7,544,192, 7,662,141, 7,662,142, 7,713,255, 7,951,130, 7,951,131, and 7,951,133. Other United States and Non-United States Patents Pending.

2011 © Intersect ENT, Inc. All rights reserved. INTERSECT ENT™ and PROPEL™ are trademarks of Intersect ENT, Inc.

Attachment 2: Draft Product Label, PN 00124 Rev. D

(Not actual size)

Propel™ (mometasone furoate implant, 370 µg)

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

Contents Include:

- One sinus implant (nominal length: 23 mm)
- One delivery system

REF: Reference Number	TBD
LOT Lot Number	YMMDDXXX-001
 Use By	YYYY-MM-DD

Read Instructions Prior to Use

Sterilized Using Radiation

Store at Room Temperature (15-30° C)

For Single Use Only

Contents are **STERILE** in unopened and undamaged package.



1049 Elwell Court
Palo Alto, CA 94303
Customer Service 1-866-531-6004
CustomerService@intersectENT.com 00124 Rev D

Attachment 3: Draft Product End Label, PN 00221 Rev. B

(Not actual size)

Propel™ (mometasone furoate implant, 370 µg)



REF:	TBD
LOT	YMMDDXXX-01
	YYYY-MM-DD

00221 Rev. B

40