2.6 Removal Instructions

The implant is placed from the delivery system into the ethmoid sinus utilizing standard surgical instruments. The implant is designed to be unmodified by the physician. The implant is not intended to be compressed and loaded into the delivery system more than twice. The implant must be placed under endoscopic visualization.

2.6.1 Indications and Usage

2.6.2 Dosage and Administration

2.7 Health Care Provider Training

2.8 Repeat Administration

3 Placement of SINEVA Sinus Implant

4 Repeat Administration

5 Placement of SINEVA Sinus Implant

6 Placement of SINEVA Sinus Implant

7 Ocular Effects

8 Ocular Effects

9 Indications and Usage

10 IMPLANT

11 Local Effects

12 CONTRAINDICATIONS

13 IMPLANT

14 IMPLANT

15 Implant Preparation

16 IMPLANT

17 PATIENT COUNSELING

18 PATIENT COUNSELING

19 PATIENT COUNSELING

20 CONTRAINDICATIONS

21 IMPLANT

22 IMPLANT

23 IMPLANT

24 IMPLANT

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**6 ADVERSE REACTIONS**

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Local effects including epistaxis, irritation, infection, or perforation
- Catarrh and glucagona (see Warnings and Precautions, 5.4)
- Hypersensitivity Reactions (see Warnings and Precautions, 5.3)

**Drum Interactions**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of another drug may not be directly comparable to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of the SINUVA Sinus Implant was evaluated and demonstrated in 400 patients in 2 controlled, randomized, parallel-group, single-dose studies. In Study 1, 131 patients were assigned to the control group and underwent a sham procedure consisting of advancement of the Delivery System with the SINUVA Sinus Implant followed by removal without deployment. The implants were removed by Day 90. All patients were required to use mometasone furoate nasal spray once daily (200 mcg of mometasone furoate) from Day 90 through 6 months. Studies demonstrated in 400 patients in 2 controlled, randomized, parallel-group, single-dose studies. In Study 1, 131 patients were assigned to the control group and underwent a sham procedure consisting of advancement of the Delivery System with the SINUVA Sinus Implant followed by removal without deployment. The implants were removed by Day 90. All patients were required to use mometasone furoate nasal spray once daily (200 mcg of mometasone furoate) from Day 90 through 6 months.

**Table 1: Adverse Reactions with > 1% Incidence and More than 20% Greater than Placebo in Controlled Clinical Trials with SINUVA Sinus Implant**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (%)</th>
<th>SINUVA Sinus Implant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety Trough Day 90</td>
<td>(N=164)</td>
<td>(N=164)</td>
</tr>
<tr>
<td><strong>Allergic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal Obstruction/Congestion</td>
<td>3.7</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Systemic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized pruritus</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Ocular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epiphora</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Neurological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Cutaneous</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Hypersensitivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**7 DRUG INTERACTIONS**

Formal drug-drug interaction studies have not been conducted with the SINUVA Sinus Implant. An evaluation of the concurrent administration of the SINUVA Sinus Implant and other commonly used nasal drug products was not associated with any unusual adverse reactions.

**7.1 Inhibitors of Cytochrome P450 3A4**

Co-administration with macrolide antibiotics, in particular CYP 3A4 inhibitors, may increase the plasma concentrations of mometasone furoate.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

There are no randomized clinical studies of SINUVA Sinus Implant in pregnancy. However, mometasone furoate is a racemic mixture of the two enantiomers with the active component being the right enantiomer. In vitro and in vivo species may vary widely in their metabolism of drugs. For example, studies have shown that mometasone furoate is primarily metabolized by CYP 3A4 and extensively metabolized in the liver of all species that have been studied. Multiple metabolites.

Studies have shown that mometasone furoate is primarily metabolized by CYP 3A4 and extensively metabolized in the liver of all species that have been studied. Multiple metabolites.

In vitro studies have confirmed the primary role of CYP 3A4 in the metabolism of this compound; however, no major metabolites were identified.

**Excretion**

Following intranasal dosing, the terminal half-life was reported to be 3 hours.

**Special Populations**

The effects of renal impairment, hepatic impairment, age, or gender on mometasone furoate pharmacokinetics have not been adequately investigated.

**Drug-Drug Interaction**

Formal drug-drug interaction studies have not been conducted with the SINUVA Sinus Implant.

**14 CLINICAL STUDIES**

The efficacy and the safety of the SINUVA Sinus Implant was evaluated in 480 patients, 18 years of age and older, with bilateral polyp grade, compared to the control group.

**15 NONCLINICAL TOXICOLOGY**

**15.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

In 2-year carcinogenicity study in Syrian Hamster eye cell assay, mometasone furoate demonstrated no statistically significant increase of tumors at inhalation doses up to 47 mcg/m3 (approximately 44 times the MRHD on an AUC basis [see Data]). In a 19-month carcinogenicity study in Swiss CD1 mice, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 47 mcg/m3 (approximately 9 times the MRHD on an AUC basis).

Mometasone furoate increased chromosomal aberrations in K562 cells at concentrations from single digit to approximately 10 times the MRHD. Mometasone furoate produced no statistically significant increase in the incidence of tumors at inhalation doses up to 47 mcg/m3 (approximately 9 times the MRHD on an AUC basis).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 3% and 1% to 2%, respectively.

**Adverse Data**

In an embryological development study with pregnant mice dosed once daily with mometasone furoate, the incidence of tumors was not statistically significantly different from the control group. Mometasone furoate produced no statistically significant increase in the incidence of tumors at inhalation doses up to 47 mcg/m3 (approximately 9 times the MRHD on an AUC basis).

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of another drug may not be directly comparable to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

**16 HOW SUPPLIED AND STORAGE**

One SINUVA Sinus Implant kit consists of 1 assembly unit for use with a SINUVA Sinus Implant Inside Crimper and one disposable Delivery System (inactive ingredients) which provides for gradual release of the drug. The SINUVA Sinus Implant is packaged in a tray, which is then sealed in a foil pouch and placed in the product carton. The SINUVA Sinus Implant is provided sterile.

**17 CLINICAL PHARMACOLOGY**

**17.1 Mechanism of Action**

Mometasone furoate is a corticosteroid demonstrating potent anti-inflammatory activity. The precise mechanism of corticosteroid action on inflammation is not known.

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, eosinocins, leukotrienes, and cytokines) involved in inflammation.

**17.2 Pharmacokinetics**

The effects of the SINUVA Sinus Implant on adrenal function have not been evaluated in clinical studies.

**17.3 Pharmacokinematics**

One pharmacokinetics study was conducted with the SINUVA Sinus Implant. The reported peak plasma concentration of mometasone furoate at 30 min post-dose from oral administration of mometasone furoate dry powder inhalation formulation as per CLINICAL PHARMACOLOGY (12.3). Therefore, mometasone furoate is not eliminated via the systemic route of elimination following bilateral placement of the SINUVA Sinus Implant.

Baseline blood samples were taken before the procedure, and on Days 3, 7, 14, 21 and 30 to assess systemic concentrations of mometasone furoate in plasma. No evidence of systemic concentrations from five subjects had measurable mometasone furoate plasma concentrations from Days 3 to Day 14. All the measured concentrations were within 0.25-fold of the lower limit of quantitation (LOQ). 30 pg/mL. No PK samples had measurable mometasone furoate plasma concentrations after Day 14.

**Table 2: Co-Primary Efficacy Results with the SINUVA Sinus Implant (Study 2)**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Treatment</th>
<th>Mean</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial, Viral, or Parasitic Infections; or Ocular Herpes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nasal Obstruction/Congestion Score</strong></td>
<td>SINUVA Sinus Implant</td>
<td>3.1</td>
<td>0.8 to 5.4</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>3.9</td>
<td>2.7 to 5.0</td>
<td></td>
</tr>
</tbody>
</table>

**18 CONCLUSION**

The SINUVA Sinus Implant is a self-expanding, biodegradable, drug eluting implant provided with a crimper and a single-use delivery system. The SINUVA Sinus Implant is an amorphous biodegradable polymer.