

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ZOMIG Nasal Spray safely and effectively. See full prescribing information for ZOMIG Nasal Spray.

### ZOMIG (zolmitriptan) nasal spray

INITIAL US APPROVAL: 1997

#### RECENT MAJOR CHANGES

Dosage and Administration, Dosing Information (2.1, 2.2, 2.3) 09/2013  
Warnings And Precautions, Medication Overuse Headache (5.6) 09/2013

#### INDICATIONS AND USAGE

ZOMIG Nasal Spray is a serotonin (5-HT<sub>1B/1D</sub>) receptor agonist (triptan) indicated for the acute treatment of migraine with or without aura in adults (1)

#### Limitations of Use:

- Use only after a clear diagnosis of migraine has been established (1)
- Not intended for the prophylactic therapy of migraine (1)
- Not indicated for the treatment of cluster headache (1)
- Not recommended in patients with moderate to severe hepatic impairment (1)

#### DOSAGE AND ADMINISTRATION

- Recommended starting dose: 2.5 mg. (2.1)
- Maximum single dose: 5 mg (2.1)
- May repeat dose after 2 hours if needed; not to exceed 10 mg in any 24-hour period (2.1)

#### DOSAGE FORMS AND STRENGTHS

Nasal Spray: 2.5 mg, and 5 mg (3)

#### CONTRAINDICATIONS

- History of ischemic heart disease or coronary artery vasospasm (4)
- Symptomatic Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders (4)
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine (4)
- Peripheral Vascular Disease (4)
- Ischemic bowel disease (4)
- Uncontrolled hypertension (4)

- Recent (within 24 hours) use of another 5-HT<sub>1</sub> agonist (e.g., another triptan) or of an ergot-type medication (4)
- MAO-A inhibitor used in past 2 weeks (4)
- Hypersensitivity to ZOMIG (4)

#### WARNINGS AND PRECAUTIONS

- *Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina:* Perform cardiac evaluation in patients with multiple cardiovascular risk factors (5.1)
- *Arrhythmias:* Discontinue dosing if occurs (5.2)
- *Chest/throat/neck/jaw pain, tightness, pressure, or heaviness:* Generally not associated with myocardial ischemia; evaluate for coronary artery disease in patients at high risk (5.3)
- *Cerebral hemorrhage, subarachnoid hemorrhage, and stroke:* Discontinue dosing if occurs (5.4)
- *Gastrointestinal ischemic events, peripheral vasospastic reactions:* Discontinue dosing if occurs (5.5)
- *Medication Overuse Headache:* Detoxification may be necessary (5.6)
- *Serotonin syndrome:* Discontinue dosing if occurs (5.7, 7.5)
- *Increase in blood pressure:* very rarely associated with significant events (5.8)

#### ADVERSE REACTIONS

- The most common adverse reactions (≥ 5% and > placebo) were unusual taste, paresthesia, dizziness, and hyperesthesia (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Impax Pharmaceuticals at 1-877-994-6729 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

#### DRUG INTERACTIONS

- If co-administered with cimetidine: Maximum single dose of 2.5 mg, not to exceed 5 mg in any 24-hour period (2.3, 7.4)

#### USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm.(8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 09/2013

## FULL PRESCRIBING INFORMATION: CONTENTS\*

1	INDICATIONS AND USAGE	7.4	Cimetidine
2	DOSAGE AND ADMINISTRATION	7.5	Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome
	2.1 Dosing Information	8	USE IN SPECIFIC POPULATIONS
	2.2 Dosing in Patients with Hepatic Impairment	8.1	Pregnancy
	2.3 Dosing in Patients taking Cimetidine	8.3	Nursing Mothers
3	DOSAGE FORMS AND STRENGTHS	8.4	Pediatric Use
4	CONTRAINDICATIONS	8.5	Geriatric Use
5	WARNINGS AND PRECAUTIONS	8.6	Patients With Hepatic Impairment
	5.1 Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina	10	OVERDOSAGE
	5.2 Arrhythmias	11	DESCRIPTION
	5.3 Chest, Throat, Neck, and/or Jaw Pain/Tightness/Pressure	12	CLINICAL PHARMACOLOGY
	5.4 Cerebrovascular Events	12.1	Mechanism of Action
	5.5 Other Vasospasm Reactions	12.3	Pharmacokinetics
	5.6 Medication Overuse Headache	13	NONCLINICAL TOXICOLOGY
	5.7 Serotonin Syndrome	13.1	Carcinogenesis, Mutagenesis, Impairment of Fertility
	5.8 Increase in Blood Pressure	14	CLINICAL STUDIES
6	ADVERSE REACTIONS	16	HOW SUPPLIED/STORAGE AND HANDLING
	6.1 Clinical Trials Experience	17	PATIENT COUNSELING INFORMATION
	6.2 Postmarketing Experience		FDA-APPROVED PATIENT LABELING
7	DRUG INTERACTIONS		
	7.1 Ergot-containing drugs		
	7.2 MAO-A Inhibitors		
	7.3 5-HT <sub>1B/1D</sub> agonists		

\*Sections or subsections omitted from the full prescribing information are not listed.

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

ZOMIG Nasal Spray is indicated for the acute treatment of migraine with or without aura in adults.

#### **Limitations of Use**

- Only use ZOMIG if a clear diagnosis of migraine has been established. If a patient has no response to ZOMIG treatment for the first migraine attack, reconsider the diagnosis of migraine before ZOMIG is administered to treat any subsequent attacks.
- ZOMIG is not indicated for the prevention of migraine attacks.
- Safety and effectiveness of ZOMIG have not been established for cluster headache.
- Not recommended in patients with moderate or severe hepatic impairment [*see Dosage and Administration (2.2)*].

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Dosing Information

The recommended starting dose for ZOMIG nasal spray is 2.5 mg. As the individual response to ZOMIG Nasal spray may vary, the dose should be adjusted on an individual basis. The maximum recommended single dose of ZOMIG is 5 mg.

In controlled clinical trials, a greater proportion of patients had headache response following a 2.5 mg or 5 mg dose than following a 1 mg dose. There was little added benefit from the 5 mg dose compared to the 2.5 mg dose, but adverse reactions were more frequent with the 5 mg dose.

If the migraine has not resolved by 2 hours after taking ZOMIG, or returns after a transient improvement, another dose may be administered at least 2 hours after the previous dose.

The maximum daily dose should not exceed 10 mg in any 24-hour period.

The safety of ZOMIG in the treatment of an average of more than four headaches in a 30-day period has not been established.

## 2.2 Dosing in Patients with Hepatic Impairment

ZOMIG nasal spray is not recommended in patients with moderate to severe hepatic impairment because of increased zolmitriptan blood levels in these patients and elevation of blood pressure in some of these patients. The recommended dosage of ZOMIG nasal spray in patients with mild hepatic impairment is the same as for patients with normal hepatic function [see *Dosage and Administration (2.1)*, *Warnings and Precautions (5.8)*, *Use in Specific Populations (8.6)* and *Clinical Pharmacology (12.3)*].

## 2.3 Dosing in Patients taking Cimetidine

If ZOMIG is co-administered with cimetidine, limit the maximum single dose of ZOMIG to 2.5 mg, not to exceed 5 mg in any 24-hour period [see *Drug Interactions (7.4)* and *Clinical Pharmacology (12.3)*].

## 3 DOSAGE FORMS AND STRENGTHS

Nasal Spray 2.5 mg and 5 mg.

## 4 CONTRAINDICATIONS

ZOMIG is contraindicated in patients with:

- Ischemic coronary artery disease (angina pectoris, history of myocardial infarction, or documented silent ischemia), other significant underlying cardiovascular disease, or coronary artery vasospasm including Prinzmetal's angina [see *Warnings and Precautions (5.1)*]
- Wolff-Parkinson-White Syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders [see *Warnings and Precautions (5.2)*]
- History of stroke, transient ischemic attack (TIA) or history of hemiplegic or basilar migraine because these patients are at higher risk of stroke [see *Warnings and Precautions (5.4)*]
- Peripheral vascular disease (PVD) [see *Warnings and Precautions (5.5)*]
- Ischemic bowel disease [see *Warnings and Precautions (5.5)*]
- Uncontrolled hypertension [see *Warnings and Precautions (5.8)*]
- Recent use (i.e., within 24 hours) of another 5-HT<sub>1</sub> agonist, ergotamine-containing medication, or ergot-type medication (such as dihydroergotamine or methysergide) [see *Drug Interactions (7.1, 7.3)*]
- Concurrent administration of an MAO-A inhibitor or recent discontinuation of a MAO-A inhibitor (that is within 2 weeks) [see *Drug Interactions (7.2)* and *Clinical Pharmacology (12.3)*]
- Known hypersensitivity to ZOMIG (angioedema and anaphylaxis seen) [see *Adverse Reactions (6.2)*]

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina

ZOMIG is contraindicated in patients with ischemic or vasospastic coronary artery disease (CAD). There have been rare reports of serious cardiac adverse reactions, including acute myocardial infarction, occurring within a few hours following administration of ZOMIG. Some of these reactions occurred in patients without known CAD. 5-HT<sub>1</sub> agonists including ZOMIG may cause coronary artery vasospasm (Prinzmetal's Angina), even in patients without a history of CAD.

Perform a cardiovascular evaluation in triptan-naïve patients who have multiple cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to receiving ZOMIG. Do not administer ZOMIG if there is evidence of CAD or coronary artery vasospasm [see *Contraindications (4)*]. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider administering the first ZOMIG dose in a medically-supervised setting and performing an electrocardiogram (ECG) immediately following ZOMIG administration. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of ZOMIG.

### 5.2 Arrhythmias

Life-threatening disturbances of cardiac rhythm including ventricular tachycardia and ventricular fibrillation leading to death have been reported within a few hours following the administration of 5-HT<sub>1</sub> agonists. Discontinue ZOMIG if these disturbances occur. Patients with Wolff-Parkinson-White Syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders should not receive ZOMIG [see *Contraindications (4)*].

### 5.3 Chest, Throat, Neck and/or Jaw Pain/Tightness/Pressure

As with other 5-HT<sub>1</sub> agonists, sensations of tightness, pain, pressure, and heaviness in the precordium, throat, neck, and jaw commonly occur after treatment with ZOMIG and is usually non-cardiac in origin. However, if a cardiac origin is suspected, patients should be evaluated. Patients shown to have CAD and those with Prinzmetal's variant angina should not receive 5-HT<sub>1</sub> agonists [see *Contraindications (4)*].

### 5.4 Cerebrovascular Events

Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT<sub>1</sub> agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the 5-HT<sub>1</sub> agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. Discontinue ZOMIG if a cerebrovascular event occurs.

As with other acute migraine therapies, before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with symptoms atypical for migraine, other potentially serious neurological conditions should be excluded. ZOMIG should not be administered to patients with a history of stroke or transient ischemic attack [see *Contraindications (4)*].

## 5.5 Other Vasospasm Reactions

5-HT<sub>1</sub> agonists, including ZOMIG, may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction (presenting with abdominal pain and bloody diarrhea), splenic infarction, and Raynaud's syndrome. In patients who experience symptoms or signs suggestive of vasospasm reaction following the use of any 5-HT<sub>1</sub> agonist, the suspected vasospasm reaction should be ruled out before receiving additional ZOMIG doses [see *Contraindications (4)*].

Reports of transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT<sub>1</sub> agonists. Since visual disorders may be part of a migraine attack, a causal relationship between these events and the use of 5-HT<sub>1</sub> agonists have not been clearly established.

## 5.6 Medication Overuse Headache

Overuse of acute migraine drugs (e.g. ergotamine, triptans, opioids, or a combination of drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). Medication overuse headache may present as migraine-like daily headaches, or as a marked increase in frequency of migraine attacks. Detoxification of patients, including withdrawal of the overused drugs, and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

## 5.7 Serotonin Syndrome

Serotonin syndrome may occur with triptans, including ZOMIG, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors [see *Drug Interactions (7.5)*]. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually rapidly occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. ZOMIG treatment should be discontinued if serotonin syndrome is suspected [see *Drug Interactions (7.5)* and *Patient Counseling Information (17)*].

## 5.8 Increase in Blood Pressure

Significant elevations in systemic blood pressure have been reported in patients treated with 5-HT<sub>1</sub> agonists including patients without a history of hypertension. Very rarely these increases in blood pressure have been associated with significant clinical events. In healthy subjects treated with 5 mg of ZOMIG oral tablet, an increase of 1 and 5 mm Hg in the systolic and diastolic blood pressure, respectively, was seen. In a study of patients with moderate to severe liver impairment, 7 of 27 patients experienced 20 to 80 mm Hg elevations in systolic and/or diastolic blood pressure after a dose of 10 mg of ZOMIG oral tablet. As with all triptans, blood pressure should be monitored in ZOMIG-treated patients. ZOMIG is contraindicated in patients with uncontrolled hypertension [see *Contraindications (4)*].

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.