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)1B/1D 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_1 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

----------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

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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_1 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_1 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 administrating 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_1 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_1 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_1 agonists *[see Contraindications (4)]*.

5.4 Cerebrovascular Events

Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT_1 agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the 5-HT_1 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_1 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_1 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_1 agonists. Since visual disorders may be part of a migraine attack, a causal relationship between these events and the use of 5-HT_1 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_1 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)]*.

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