When a migraine strikes, help your patients

FAST FORWARD TO MIGRAINE RELIEF

With ZOMIG Nasal Spray, migraine relief can start **in as soon as 15 minutes*†**[1]

***The recommended starting dose is 2.5 mg.**[2]

†11.5% of patients using ZOMIG Nasal Spray 5 mg achieved headache response within 15 minutes vs 5.4% for placebo (*P*=.02). The majority of patients had headache relief at 2 hours, which was the primary endpoint.[1]

INDICATION: ZOMIG Nasal Spray is a serotonin $(5\text{-HT})_{1B/1D}$ receptor agonist (triptan) indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years and older.

Limitations of Use: Use ZOMIG Nasal Spray only after a clear diagnosis of migraine has been established. If a patient has no response to ZOMIG Nasal Spray treatment for the first migraine attack, reconsider the diagnosis of migraine before ZOMIG Nasal Spray is administered to treat any subsequent attacks. ZOMIG Nasal Spray is not indicated for the prevention of migraine attacks.
Safety and effectiveness of ZOMIG Nasal Spray have not been established for cluster headache.
ZOMIG Nasal Spray is not recommended in patients with moderate to severe hepatic impairment.

Please see Important Safety Information throughout this piece and Full Prescribing Information.

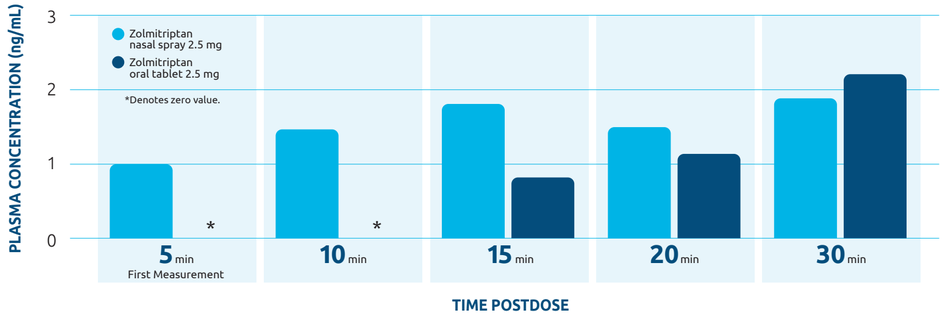
Zomig® Nasal Spray
ZOLMITRIPTAN
2.5 mg
5 mg

ZOLMITRIPTAN NASAL SPRAY DEMONSTRATES BOTH **RAPID AND SUSTAINED ABSORPTION**[2-4]

PHARMACOKINETICS

- **Rapid:** Zolmitriptan nasal spray was detected **in as early as 5 minutes,** and **38% of C_{max}** was reached within **10 minutes** compared with 0% for the oral tablet[2,3]
- **Sustained:** Plasma concentrations of zolmitriptan nasal spray were sustained for **4 to 6 hours**[2]

POSTTREATMENT MEAN PLASMA CONCENTRATIONS[2,3]



Mean plasma concentrations of zolmitriptan up to 30 minutes after single 2.5-mg doses as a nasal spray (at pH 5.0) and as an oral tablet from an open, randomized, 3-period crossover study of 12 healthy volunteers to assess the pharmacokinetics and tolerability of zolmitriptan on 3 separate occasions at least 5 days apart.[3]

Zolmitriptan nasal spray is **initially absorbed in the nasal mucosa,** accounting for **≈70% of drug exposure at 1 hour and 50% at 2 hours.** The remainder of the drug is swallowed and a subsequent **second absorption phase occurs in the GI tract.** Zolmitriptan is metabolized into an *N*-desmethyl metabolite, which is **2 to 6 times more potent** than zolmitriptan in vitro.[2-4]

IMPORTANT SAFETY INFORMATION

Contraindications:

ZOMIG Nasal Spray is contraindicated in patients with: history of coronary artery disease (CAD) or coronary artery vasospasm or other significant underlying cardiovascular disease; Wolff-Parkinson-White Syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders; history of stroke, transient ischemic attack, or hemiplegic or basilar migraine; peripheral vascular disease; ischemic bowel disease;

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

DO YOU HAVE A **COMPLETE TREATMENT PLAN** FOR YOUR PATIENTS?

For over 15 years, ZOMIG Nasal Spray continues to be a solution.

EVEN IF PATIENTS TAKE PREVENTIVE MEDICATION, MIGRAINES CAN HAPPEN ANYTIME[5,6]

- As part of a complete treatment plan, patients should also have medication for breakthrough migraines

A NON-ORAL ROUTE OF ADMINISTRATION MAY BE BENEFICIAL

- Some patients may have difficulty swallowing oral medications[7]

- Nausea and vomiting can make it difficult to keep oral medication down[7,8]
  - **73%** of adult patients and **86.3%** of adolescent patients report nausea[9,10]
  - **29%** of adult patients and **47.7%** of adolescent patients report vomiting[9,10]

- Migraine-associated gastric stasis can retard drug absorption[7,8,11]
  - During a migraine, gastric emptying has been shown to significantly slow down (27 minutes to half empty for non-migraineurs vs 49 minutes for migraineurs [*P*<.05])[12]

IMPORTANT SAFETY INFORMATION (continued)

Contraindications (continued):

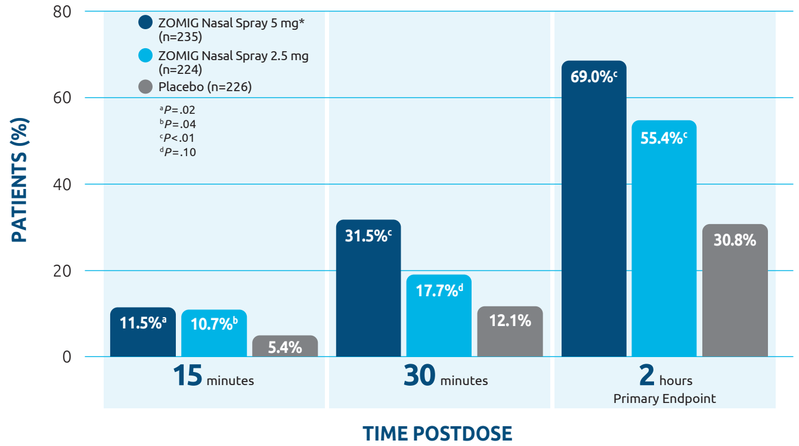
uncontrolled hypertension; recent (within 24 hours) use of another 5-HT$_1$ agonist (eg, another triptan), or ergot-type medication; current or recent (past 2 weeks) use of monoamine oxidase (MAO)-A inhibitor; known hypersensitivity to ZOMIG, ZOMIG-ZMT, or ZOMIG Nasal Spray

Zomig® Nasal Spray
ZOLMITRIPTAN 2.5 mg 5 mg

FAST MIGRAINE RELIEF **IN AS SOON AS 15 MINUTES** FOR SOME ADULTS[1]

MIGRAINE HEADACHE RESPONSE:

Reduction in headache severity from moderate or severe pain to mild or no pain[1]



Relief in as soon as

Efficacy was unaffected by[2]

- Migraine upon awakening
- Relationship to menses
- Migraine with nausea
- Migraine with aura
- Gender, age, or weight

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.[2]**

From a multicenter, randomized, double-blind, double-dummy, placebo-controlled study of ZOMIG Nasal Spray 5 mg (n=235) and 2.5 mg (n=224) vs placebo (n=226) for the acute treatment of moderate or severe migraines in adults. **Primary endpoint was headache response at 2 hours. Secondary endpoints included measurements at 15 minutes, 30 minutes, 45 minutes, 1 hour, and 4 hours.[1]**

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions:

- Myocardial ischemia, myocardial infarction, and Prinzmetal's Angina: Perform a cardiovascular evaluation in triptan-naïve patients who have multiple cardiovascular risk factors and if satisfactory, consider administrating the first ZOMIG Nasal Spray dose in a medically supervised setting

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

A SINGLE SPRAY **MAY BE ALL THE MAJORITY OF ADULTS NEED[7]**

A single spray for

Nearly 70% of adult patients using ZOMIG Nasal Spray 5 mg* **DID NOT** need to use a second dose or additional medications **within 24 hours** vs 27.8% with placebo†[7]

- **67.7%** with ZOMIG Nasal Spray 5 mg
- **60.7%** with ZOMIG Nasal Spray 2.5 mg

From a multicenter, randomized, double-blind, double-dummy, placebo-controlled study of ZOMIG Nasal Spray 5 mg (n=235) and 2.5 mg (n=224) vs placebo (n=226) for the acute treatment of moderate or severe migraines in adults. **Primary endpoint was headache response at 2 hours. Secondary endpoints included the use of rescue medication.[1,7]**

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.[2]**

†Includes both patients who had a headache response at 2 hours and those who had no response to the initial dose. The trial protocol did not allow remedication within 4 hours postdose. *P*≤.0001 for all comparisons with placebo.[7]

IMPORTANT SAFETY INFORMATION (continued)

- Arrhythmias: Discontinue ZOMIG Nasal Spray if these occur
- Sensations of tightness, pain, pressure in the chest, and heaviness in the precordium, throat, neck, and jaw commonly occur after treatment with 5-HT_1 agonists like ZOMIG Nasal Spray and are usually non-cardiac in origin. Perform a cardiac evaluation if these patients are at cardiac risk
- Cerebrovascular events: Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT_1 agonists, some resulting in fatalities. Discontinue ZOMIG Nasal Spray if any of these events occur

Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN

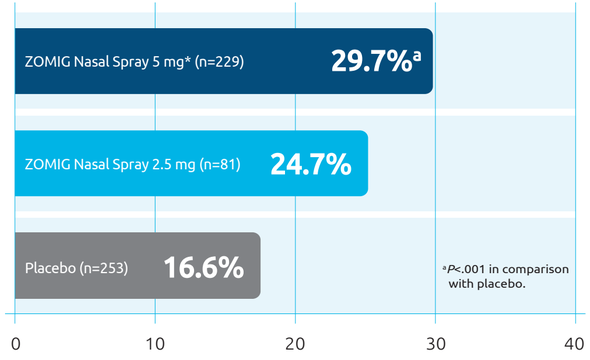
PAIN FREE IS POSSIBLE **FOR SOME ADOLESCENTS**[1]

The first and only nasal spray approved for adolescent migraine patients (ages 12-17 years).[13]

PLACEBO CHALLENGE:

A 30-day placebo challenge run-in period was implemented. Patients treated a single migraine with 1 dose of single-blind placebo. Only patients who demonstrated a lack of response to placebo during the run-in period were randomized.[2]

PAIN FREE: Reduction in headache pain from severe or moderate pain to no pain[1]



PATIENTS WITH NO HEADACHE PAIN AT 2 HOURS POSTTREATMENT (%)[1]

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.**[2]

From a multicenter, randomized, double-blind, parallel-group, placebo-controlled study of ZOMIG Nasal Spray 5 mg (n=229) and 2.5 mg (n=81) vs placebo (n=253) for the acute treatment of moderate or severe migraines in pediatric patients (ages 12-17 years). **Primary endpoint was no headache pain at 2 hours.**[1]

IMPORTANT SAFETY INFORMATION (continued)

- ZOMIG Nasal Spray may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction, splenic infarction, and Raynaud's syndrome. Discontinue ZOMIG Nasal Spray if any of these events occur

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

A SINGLE SPRAY **MAY BE ALL MOST ADOLESCENTS NEED**[1]

A single spray for

Nearly 80% of adolescent patients using ZOMIG Nasal Spray 5 mg* **DID NOT** need to use a second dose or additional medications **within 24 hours** vs 68.4% for placebo (*P*=.004)[1]

- **79.7%** with ZOMIG Nasal Spray 5 mg
- **77.8%** with ZOMIG Nasal Spray 2.5 mg

From a multicenter, randomized, double-blind, parallel-group, placebo-controlled study of ZOMIG Nasal Spray 5 mg (n=229) and 2.5 mg (n=81) vs placebo (n=253) for the acute treatment of moderate or severe migraines in pediatric patients (ages 12-17 years). **Primary endpoint was no headache pain at 2 hours. Secondary endpoints included the use of rescue medication and the ability to perform normal activities.**[1]

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.**[2]

GETTING BACK TO NORMAL ACTIVITIES COULD BE A SPRAY AWAY

At 4 hours, **71%** of patients returned to normal activities using either ZOMIG Nasal Spray 5 mg (*P*=.002) or 2.5 mg (*P*=.028) vs 57% for placebo.[1]

IMPORTANT SAFETY INFORMATION (continued)

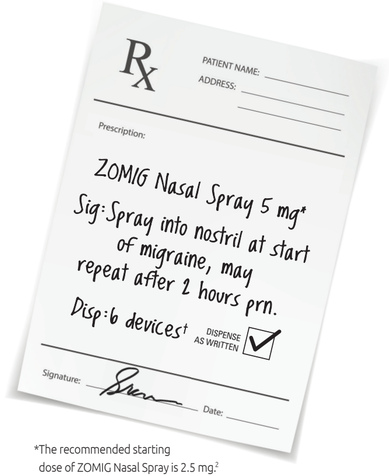
- Transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT_1 agonists
- Overuse of acute migraine drugs may lead to exacerbation of headache. Detoxification may be necessary

Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN

RECOMMENDED DOSING **FOR PATIENTS 12 AND OLDER**[2]

Recommended Starting Dose	Maximum Recommended Single Dose	Subsequent Dose	Maximum Daily Dose
2.5 mg	**5 mg**	May repeat after 2 hours if headache returns	Should not exceed 10 mg in any 24-hour period

- Each ZOMIG Nasal Spray single-unit device delivers either a 2.5-mg or a 5-mg dose of zolmitriptan[2]
- The safety of treating more than 4 headaches with ZOMIG Nasal Spray in a 30-day period has not been established[2]
- If ZOMIG Nasal Spray is co-administered with cimetidine, limit the maximum single dose of ZOMIG Nasal Spray to 2.5 mg, not to exceed 5 mg in any 24-hour period[2]



*The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.[2]
†Note: Six devices come in each box of ZOMIG Nasal Spray. Quantity limits may apply.

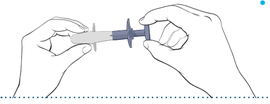
IMPORTANT SAFETY INFORMATION (continued)

- Serotonin syndrome may occur with triptans, including ZOMIG Nasal Spray, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and MAO inhibitors. Discontinue ZOMIG Nasal Spray if serotonin syndrome is suspected
- Increase in blood pressure

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

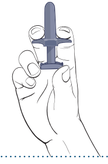
STRAIGHTFORWARD **ADMINISTRATION**[2]

READY



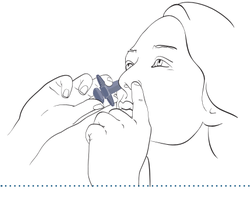
- Blow nose gently before use
- Remove the protective cap

SET



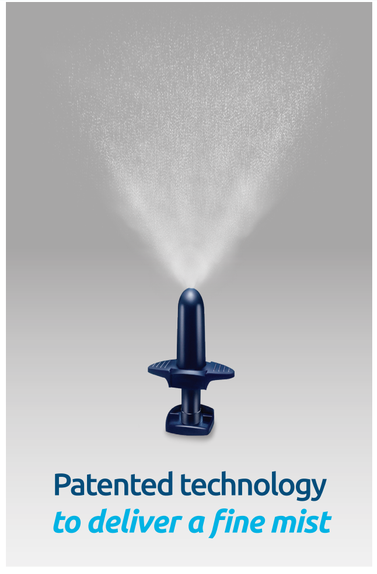
- Hold device as shown
- With the head upright, gently close 1 nostril with the index finger and breathe out through the mouth

SPRAY



- Put the tip of the sprayer device into the other nostril as far as feels comfortable, and tilt the head back slightly
- Breathe in slowly and gently through the nose, and, at the same time, press the plunger firmly with the thumb
- Keep the head slightly tilted back, remove the tip from the nose, and breathe gently through the mouth for 5 to 10 seconds

Note: There is only 1 dose in the nasal sprayer. Patients should not try to prime the nasal sprayer or press the plunger until they have put the tip into the nostril, or they will lose the dose.



Patented technology
to deliver a fine mist

Patients should read all of the instructions for use provided under the patient information section in the Full Prescribing Information before using ZOMIG Nasal Spray for the first time.

Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN

ADVERSE REACTIONS **IN ADULTS**[2]

(≥2% in the ZOMIG Nasal Spray groups and > placebo)

Of 460 adult patients, the discontinuation rates due to adverse reactions were[1,2]

- 1.3% using ZOMIG Nasal Spray 5 mg
- 0% using ZOMIG Nasal Spray 2.5 mg
- 0.4% in the placebo group

- Unusual taste was typically mild in severity, transient, and resolved spontaneously[2,7]

Body System Adverse Reaction	Placebo (n=226)	ZOMIG Nasal Spray 2.5 mg (n=224)	ZOMIG Nasal Spray 5 mg (n=236)
Atypical sensations			
Hyperesthesia	0%	1%	5%
Paresthesia	6%	5%	10%
Warm sensation	2%	4%	0%
Ear/nose/throat			
Disorder or discomfort of the nasal cavity	2%	1%	3%
Pain and pressure sensations			
Pain location specified	1%	2%	4%
Throat pain	1%	4%	4%
Throat tightness	1%	<1%	2%
Digestive			
Dry mouth	<1%	3%	2%
Nausea	1%	1%	4%
Neurological			
Dizziness	4%	6%	3%
Somnolence	2%	1%	4%
Other			
Unusual taste	3%	17%	21%
Asthenia	1%	3%	3%

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

ADVERSE REACTIONS **IN ADOLESCENTS***[2]

(≥2% in the ZOMIG Nasal Spray groups and > placebo)

Adverse Reaction	Placebo (n=437)	ZOMIG Nasal Spray 2.5 mg (n=81)	ZOMIG Nasal Spray 5 mg (n=431)
Unusual taste	2%	6%	10%
Nasal discomfort	1%	3%	3%
Dizziness	1%	0%	2%
Oropharyngeal pain	2%	0%	2%
Nausea	1%	1%	2%

*The safety of ZOMIG Nasal Spray in the acute treatment of migraine in adolescent patients ages 12 to 17 years was established in 2 placebo-controlled studies.[2]

No serious adverse events or adverse events leading to discontinuation were reported.[9]

- The adverse reaction profile was similar across both genders[2]
- Safety and effectiveness of ZOMIG Nasal Spray in pediatric patients younger than 12 years of age have not been established[2]

IMPORTANT SAFETY INFORMATION (continued)

Use in Specific Populations

- Pregnancy: Based on animal data, ZOMIG Nasal Spray may cause fetal harm
- Lactation: There are no data on the presence of zolmitriptan or its metabolites in human milk, effects on milk production, or on the breastfed infant
- Pediatrics: Safety and effectiveness of ZOMIG Nasal Spray in patients <12 years of age have not been established

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Specialty, a division of Amneal Pharmaceuticals LLC at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. Data on file, Impax Laboratories, LLC. **2.** ZOMIG Nasal Spray [package insert]. **3.** Yates R, Nairn K, Dixon R, Seaber E. *J Clin Pharmacol.* 2002;42(11):1237-1243. **4.** Kågedal M, Zingmark PH, Hedlund C, Yates R. *Am J Drug Deliv.* 2005;3(2):133-140. **5.** Migraine. Office on Women's Health. https://www.womenshealth.gov/a-z-topics/migraine. Updated April 1, 2019. Accessed May 31, 2019. **6.** Diamond S, Wenzel R. *CNS Drugs.* 2002;16(6):385-403. **7.** Charlesworth BR, Dowson AJ, Purdy A, Becker WJ, Boes-Hansen S, Färkkilä M. *CNS Drugs.* 2003;17(9):653-667. **8.** Yates R, Sörensen J, Bergström M, et al. *Cephalalgia.* 2005;25(12):1103-1109. **9.** Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. *Headache.* 2001;41(7):646-657. **10.** Winner P, Farkas V, Štillová H, et al; TEENZ Study Group. *Headache.* 2016;56(7):1107-1119. **11.** Newman LC. *Headache.* 2013;53(suppl 1): 11-16. **12.** Yalcin H, Okuyucu EE, Ucar E, Duman T, Yilmazer S. *J Intern Med.* 2012;42(4):455-459. **13.** FDA approves ZOMIG® (zolmitriptan) Nasal Spray for migraine in pediatric patients (ages 12-17) [press release]. Hayward, CA: PR Newswire; June 16, 2015.

Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN

HELP YOUR PATIENTS FAST FORWARD TO MIGRAINE RELIEF **WITH ZOMIG NASAL SPRAY**

- Migraine relief in as soon as **15 minutes** for some adult patients (11.5% using the 5-mg* dose vs 5.4% for placebo; *P*=.02)[1]

Migraine relief at **2 hours** (primary endpoint):

- **69.0%** of adult patients achieved headache response† using the 5-mg dose[1]
- **29.7%** of adolescent patients had no headache pain‡ using the 5-mg dose[1]

- Nearly **70%** of adult patients§[7] and nearly **80%** of adolescent patients‖[1] using the 5-mg dose **DID NOT** need to use a second dose or additional medications **within 24 hours**

Eligible patients may save on their ZOMIG Nasal Spray prescription. Visit ZOMIGSavings.com for Terms, Conditions, and Eligibility Criteria.

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.**[2]

†Primary endpoint (*P*<.01 vs placebo [30.8%]).[1]

‡Primary endpoint (*P*<.001 vs placebo [16.6%]).[1]

§Secondary endpoint (*P*≤.0001 vs placebo [27.8%]).[7]

‖Secondary endpoint (*P*=.004 vs placebo [68.4%]).[1]

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

The most common adverse reactions (≥5% and > placebo) were:

- Adults: unusual taste, paresthesia, dizziness, and hyperesthesia
- Pediatrics: unusual taste

Drug Interactions

- Cimetidine: If co-administered, limit the maximum single dose of ZOMIG Nasal Spray to 2.5 mg, not to exceed 5 mg in any 24-hour period

Please see additional Important Safety Information throughout this piece and Full Prescribing Information.

amneal

Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN