ARE YOUR PATIENTS **WAITING FOR RELIEF?**

"If I can't keep my medication down, how can it *help my migraine?*"

– *Nicole, 31-year-old financial analyst*

Nausea and/or vomiting frequently accompany her migraines, compromising oral medication effectiveness

Experiences 4 to 5 migraines per month

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 additional Important Safety Information throughout this piece and accompanying Full Prescribing Information.

Zomig® Nasal Spray
ZOLMITRIPTAN 2.5 mg 5 mg

NON-ORAL OPTIONS MAY BE BETTER FOR MIGRAINE PATIENTS

MIGRAINE PATIENTS FREQUENTLY SUFFER FROM NAUSEA AND VOMITING[1]

NAUSEA

- Reported by **73% of adults**[1]
  - Experienced by ≈50% of patients during more than half of their migraines[2]
- Can cause patients to **delay or avoid** taking oral medication[2]

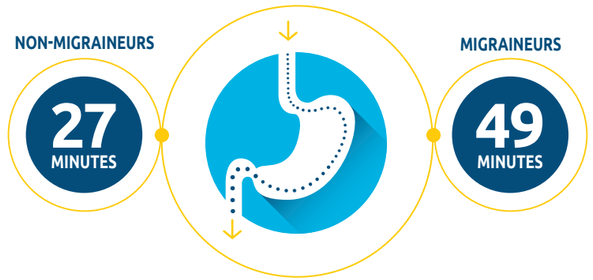
VOMITING

- Reported by **29% of adults**[1]
- Can result in **lost doses**[2]

THIS MAY BE DUE TO GASTRIC STASIS, WHICH SLOWS DIGESTION IN MIGRAINE PATIENTS[3]

Slowed gastric emptying

- Occurs both **ictally and interictally**[4]
- Is significant during a migraine, which **delays drug absorption**[3,5-7]
  - Non-migraineurs: 27 minutes to half emptying[5]
  - Migraineurs: 49 minutes to half emptying ($P<.05$)[5]



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; 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

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
- 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

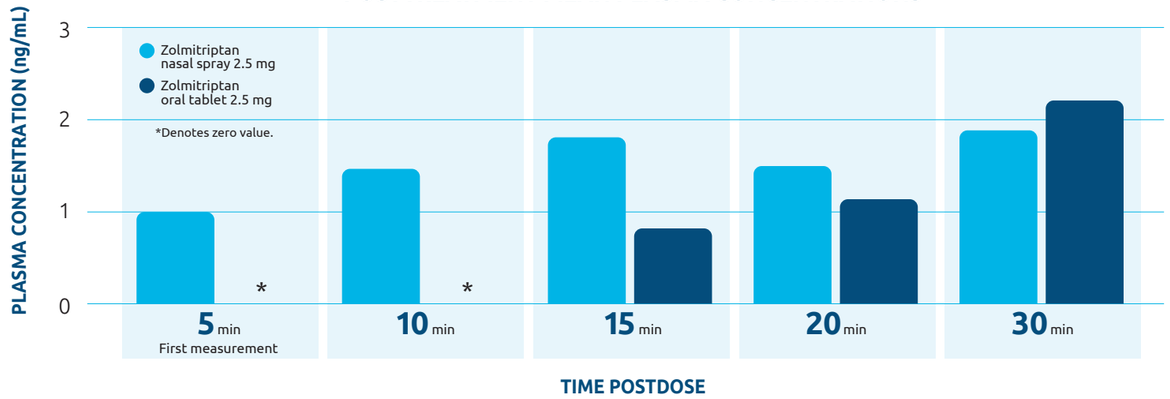
WHY CHOOSE A NASAL SPRAY FOR NICOLE'S MIGRAINES?

PHARMACOKINETICS

THE UNIQUE PHARMACOKINETICS OF ZOLMITRIPTAN NASAL SPRAY CREATE BOTH RAPID AND SUSTAINED ABSORPTION[8-10]

- **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[8,9]
- **Sustained:** Plasma concentrations of zolmitriptan nasal spray were sustained for **4 to 6 hours**[8]

POSTTREATMENT MEAN PLASMA CONCENTRATIONS[8,9]



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.[9]

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.[8-10]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (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
- 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
- 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

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Zomig® Nasal Spray 2.5 mg 5 mg
ZOLMITRIPTAN

ZOMIG NASAL SPRAY MAY PROVIDE FAST RELIEF, EVEN FOR PATIENTS LIKE NICOLE[11]

RELIEF WITH LESS DELAY

11.5% of ZOMIG Nasal Spray 5 mg* patients achieved headache response within **15 minutes** vs 5.4% with placebo (*P*=.02)[11]

RELIEF WITH CONFIDENCE

The majority of patients had headache relief at 2 hours (primary endpoint)[12]

- **Nearly 70%** did not need a second 5-mg dose or additional medication **within 24 hours†[12]**
  - **67.7%** with the 5-mg dose
  - **60.7%** with the 2.5-mg dose
  - **27.8%** with placebo
- **Efficacy was unaffected by** migraine with nausea or aura; migraine upon awakening; relationship to menses; or gender, age, or weight[8]

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 and the use of rescue medication.[11,12]**

***The recommended starting dose of ZOMIG Nasal Spray is 2.5 mg.[8]**

†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.[12]

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

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

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

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. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. *Headache.* 2001;41(7):646-657. **2.** Newman LC. *Headache.* 2013;53(suppl 1):11-16. **3.** Aurora SK, Papapetropoulos S, Kori SH, Kedar A, Abell TL. *Cephalalgia.* 2013;33(6):408-415. **4.** Aurora SK, Kori SH, Barrodale P, Mcdonald SA, Haseley D. *Headache.* 2006;46(1):57-63. **5.** Yalcin H, Okuyucu EE, Ucar E, Duman T, Yilmazer S. *Intern Med J.* 2012;42(4):455-459. **6.** Thomsen LL, Dixon R, Lassen LH, et al. *Cephalalgia.* 1996;16(4):270-275. **7.** Parkman HP. *Headache.* 2013;53(suppl 1):4-10. **8.** ZOMIG Nasal Spray [package insert]. **9.** Yates R, Nairn K, Dixon R, Seaber E. *J Clin Pharmacol.* 2002;42(11):1237-1243. **10.** Kågedal M, Zingmark PH, Hedlund C, Yates R. *Am J Drug Deliv.* 2005;3(2):133-140. **11.** Data on file, Impax Laboratories, LLC. **12.** Charlesworth BR, Dowson AJ, Purdy A, Becker WJ, Boes-Hansen S, Färkkilä M. *CNS Drugs.* 2003;17(9):653-667.

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