IMITREX- sumatriptan spray
GlaxoSmithKline LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use IMITREX safely and effectively. See full prescribing information for IMITREX.
IMITREX (sumatriptan) Nasal Spray
Initial U.S. Approval: 1992

INDICATIONS AND USAGE

IMITREX is a serotonin (5-$HT_{1B/1D}$) receptor agonist (triptan) indicated for acute treatment of migraine with or without aura in adults. (1)

Limitations of Use:

- Use only if a clear diagnosis of migraine headache has been established. (1)
- Not indicated for the prophylactic therapy of migraine attacks. (1)
- Not indicated for the treatment of cluster headache. (1)

DOSAGE AND ADMINISTRATION

- Single dose of 5 mg, 10 mg, or 20 mg of nasal spray. (2)
- A second dose should only be considered if some response to the first dose was observed. Separate doses by at least 2 hours. (2)
- Maximum dose in a 24-hour period: 40 mg. (2)

DOSAGE FORMS AND STRENGTHS

Nasal spray: 5 mg and 20 mg (3, 16)

CONTRAINDICATIONS

- History of coronary artery disease or coronary artery vasospasm. (4)
- 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-HT1 agonist (e.g., another triptan) or of an ergotamine-containing medication. (4)
- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor. (4)
- Hypersensitivity to IMITREX (angioedema and anaphylaxis seen). (4)
- Severe hepatic impairment. (4)

WARNINGS AND PRECAUTIONS

- Myocardial ischemia/infarction and Prinzmetal's angina: Perform cardiac evaluation in patients with multiple cardiovascular risk factors. (5.1)
- Arrhythmias: Discontinue IMITREX 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 IMITREX if occurs. (5.4)
- Gastrointestinal ischemic reactions and peripheral vasospastic reactions: Discontinue IMITREX if occurs. (5.5)
- Medication overuse headache: Detoxification may be necessary. (5.6)
- Serotonin syndrome: Discontinue IMITREX if occurs. (5.7)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.11)

ADVERSE REACTIONS

Most common adverse reactions (≥1% and >placebo) were burning sensation, disorder/discomfort of nasal cavity/sinuses,

FDA-1088 or www.fda.gov/medwatch.

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: 11/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

Limitations of Use:

- Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with IMITREX, reconsider the diagnosis of migraine before IMITREX is administered to treat any subsequent attacks.
- IMITREX is not indicated for the prevention of migraine attacks.
- Safety and effectiveness of IMITREX Nasal Spray have not been established for cluster headache.

2 DOSAGE AND ADMINISTRATION

The recommended adult dose of IMITREX Nasal Spray for the acute treatment of migraine is 5 mg, 10 mg, or 20 mg. The 20-mg dose may provide a greater effect than the 5-mg and 10-mg doses, but may have a greater risk of adverse reactions *[see Clinical Studies (14)]*.

The 5-mg and 20-mg doses are given as a single spray in 1 nostril. The 10-mg dose may be achieved by the administration of a single 5-mg dose in each nostril.

If the migraine has not resolved by 2 hours after taking IMITREX Nasal Spray, or returns after a transient improvement, 1 additional dose may be administered at least 2 hours after the first dose. The maximum daily dose is 40 mg in a 24-hour period.

The safety of treating an average of more than 4 headaches in a 30-day period has not been established.

3 DOSAGE FORMS AND STRENGTHS

Unit dose nasal spray devices containing 5 mg or 20 mg sumatriptan.

4 CONTRAINDICATIONS

IMITREX Nasal Spray is contraindicated in patients with:

- Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or documented silent ischemia) 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 a higher risk of stroke *[see Warnings and Precautions (5.4)]*
- Peripheral vascular disease *[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 ergotamine-containing medications or ergot-type medications

[see Drug Interactions (7.1, 7.3)]

- Concurrent administration of a monoamine oxidase (MAO)-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor *[see Drug Interactions (7.2) and Clinical Pharmacology (12.3)]*
- Hypersensitivity to IMITREX (angioedema and anaphylaxis seen) *[see Warnings and Precautions (5.10)]*
- Severe hepatic impairment *[see Clinical Pharmacology (12.3)]*

5 WARNINGS AND PRECAUTIONS

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

The use of IMITREX Nasal Spray is contraindicated in patients with ischemic or vasospastic CAD. There have been rare reports of serious cardiac adverse reactions, including acute myocardial infarction, occurring within a few hours following administration of IMITREX Nasal Spray. Some of these reactions occurred in patients without known CAD. IMITREX Nasal Spray may cause coronary artery vasospasm (Prinzmetal's angina), even in patients without a history of CAD.

Perform a cardiovascular evaluation in triptan-naive patients who have multiple cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to receiving IMITREX Nasal Spray. If there is evidence of CAD or coronary artery vasospasm, IMITREX Nasal Spray is contraindicated. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider administering the first dose of IMITREX Nasal Spray in a medically supervised setting and performing an electrocardiogram (ECG) immediately following administration of IMITREX Nasal Spray. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of IMITREX Nasal Spray.

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 IMITREX Nasal Spray if these disturbances occur. IMITREX Nasal Spray is contraindicated in patients with Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.

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

Sensations of tightness, pain, pressure, and heaviness in the precordium, throat, neck, and jaw may occur after treatment with IMITREX Nasal Spray and are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk. The use of IMITREX Nasal Spray is contraindicated in patients with CAD and those with Prinzmetal's variant angina.

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. Also, patients with migraine may be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, TIA). Discontinue IMITREX Nasal Spray if a cerebrovascular event occurs.

Before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms, exclude other potentially serious neurological conditions. IMITREX Nasal Spray is contraindicated in patients with a history of stroke or TIA.

IMITREX Nasal Spray 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 non-coronary vasospasm reaction following the use of any 5-HT_1 agonist, rule out a vasospastic reaction before using additional IMITREX Nasal Spray.

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 combination of these 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 IMITREX Nasal Spray, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors *[see Drug Interactions (7.4)]*. 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 occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. Discontinue IMITREX Nasal Spray if serotonin syndrome is suspected.

5.8 Increase in Blood Pressure

Significant elevation in blood pressure, including hypertensive crisis with acute impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT_1 agonists, including patients without a history of hypertension. Monitor blood pressure in patients treated with IMITREX. IMITREX Nasal Spray is contraindicated in patients with uncontrolled hypertension.

5.9 Local Irritation

Local irritative symptoms such as burning, numbness, paresthesia, discharge, and pain or soreness were reported in approximately 5% of patients in controlled clinical trials and were noted to be severe in about 1%. The symptoms were transient and generally resolved in less than 2 hours. Limited examinations of the nose and throat did not reveal any clinically noticeable injury in these patients. The consequences of extended and repeated use of Imitrex Nasal Spray on the nasal and/or respiratory mucosa have not been systematically evaluated in patients.

5.10 Anaphylactic/Anaphylactoid Reactions

Anaphylactic/anaphylactoid reactions have occurred in patients receiving IMITREX. Such reactions can be life threatening or fatal. In general, anaphylactic reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens. IMITREX Nasal Spray is contraindicated in patients with a history of hypersensitivity reaction to IMITREX.

5.11 Seizures

Seizures have been reported following administration of IMITREX. Some have occurred in patients

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