This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

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 succinate) injection, for subcutaneous use
Initial U.S. Approval: 1992

----------INDICATIONS AND USAGE----------

IMITREX is a serotonin ($5\text{-}HT_{1B/1D}$) receptor agonist (triptan) indicated for:

- Acute treatment of migraine with or without aura in adults (1)
- Acute treatment of cluster headache in adults (1)

Limitations of Use:

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

---------- DOSAGE AND ADMINISTRATION ----------

- For subcutaneous use only. (2.1)
- Acute treatment of migraine: 1- to 6-mg Single dose. (2.1)
- Acute treatment of cluster headache: 6-mg Single dose. (2.1)
- Maximum dose in a 24-hour period: 12 mg, Separate doses by at least 1 hour. (2.1)
- Patients receiving doses other than 4 or 6 mg: Use the 6-mg single-dose vial. (2.3)

---------- DOSAGE FORMS AND STRENGTHS ----------

- Injection: 4- and 6-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose Pen (3)
- Injection: 6-mg single-dose vial (3)

----------CONTRAINDICATIONS----------

- Coronary artery disease or coronary 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 $5\text{-}HT_1$ agonist (e.g., another triptan) or of an ergotamine-containing medication (4)
- Ccurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor (4)
- Known hypersensitivity to sumatriptan (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 ischemia and infarction events, 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)
- Increase in blood pressure: Monitor blood pressure. (5.8)
- Anaphylactic/anaphylactoid reactions: Discontinue IMITREX if occurs (5.9)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.10)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (≥5% and > placebo) were injection site reactions, tingling, dizziness/vertigo, warm/hot sensation, burning sensation, feeling of heaviness, pressure sensation, flushing, feeling of tightness, and numbness (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------

- Pregnancy: Based on animal data, may cause fetal harm (8.1)
- Geriatric use: A cardiovascular evaluation is recommended in those who have other cardiovascular risk factors prior to receiving IMITREX. (8.5)

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

Revised: 09/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

IMITREX® Injection is indicated in adults for (1) the acute treatment of migraine, with or without aura, and (2) the acute treatment of cluster headache.

Limitations of Use:

- Use only if a clear diagnosis of migraine or cluster 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.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The maximum single recommended adult dose of IMITREX Injection for the acute treatment of migraine or cluster headache is 6 mg injected subcutaneously. For the treatment of migraine, if side effects are dose limiting, lower doses (1 to 5 mg) may be used *[see Clinical Studies (14.1)]*. For the treatment of cluster headache, the efficacy of lower doses has not been established.

The maximum cumulative dose that may be given in 24 hours is 12 mg, two 6-mg injections separated by at least 1 hour. A second 6-mg dose should only be considered if some response to a first injection was observed.

2.2 Administration Using the IMITREX STATdose Pen®

An autoinjector device (IMITREX STATdose Pen) is available for use with 4- and 6-mg prefilled syringe cartridges. With this device, the needle penetrates approximately 1/4 inch (5 to 6 mm). The injection is intended to be given subcutaneously, and intramuscular or intravascular delivery must be avoided. Instruct patients on the proper use of IMITREX STATdose Pen and direct them to use injection sites with an adequate skin and subcutaneous thickness to accommodate the length of the needle.

2.3 Administration of Doses of IMITREX Other Than 4 or 6 mg

In patients receiving doses other than 4 or 6 mg, use the 6-mg single-dose vial; do not use the IMITREX STATdose Pen. Visually inspect the vial for particulate matter and discoloration before administration. Do not use if particulates and discolorations are noted.

3 DOSAGE FORMS AND STRENGTHS

- Injection: 4- and 6-mg single-dose prefilled syringe cartridges for use with the IMITREX STATdose Pen
- Injection: 6-mg single-dose vial

4 CONTRAINDICATIONS

IMITREX Injection is contraindicated in patients with:

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- 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 or transient ischemic attack (TIA) because these patients are at a higher risk of stroke *[see Warnings and Precautions (5.4)]*.
- History of hemiplegic or basilar migraine.
- 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 (i.e., within 24 hours) use of ergotamine-containing medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine$_1$ (5-HT$_1$) agonist *[see Drug Interactions (7.1, 7.3)]*.
- Concurrent administration of an MAO-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor *[see Drug Interactions (7.2) and Clinical Pharmacology (12.3)]*.
- Known hypersensitivity to sumatriptan *[see Warnings and Precautions (5.9) and Adverse Reactions (6.2)]*.
- 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 Injection 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 Injection. Some of these reactions occurred in patients without known CAD. 5-HT$_1$ agonists, including IMITREX Injection, 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 Injection. If there is evidence of CAD or coronary artery vasospasm, IMITREX Injection is contraindicated. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider administering the first dose of IMITREX Injection in a medically supervised setting and performing an electrocardiogram (ECG) immediately following IMITREX Injection. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of IMITREX Injection.

Evaluate patients with signs or symptoms suggestive of angina following IMITREX Injection for the presence of CAD or Prinzmetal's angina before receiving additional doses of IMITREX Injection.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

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 Injection if these disturbances occur. IMITREX Injection 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

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 IMITREX Injection and are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk. The use of IMITREX Injection is contraindicated in patients shown to have 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 Injection 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 atypical symptoms, exclude other potentially serious neurological conditions. IMITREX Injection is contraindicated in patients with a history of stroke or TIA.

5.5 Other Vasospasm Reactions

5-HT_1 agonists, including IMITREX Injection, 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. Until further evaluation, IMITREX Injection is contraindicated in patients who experience symptoms or signs suggestive of non-coronary vasospasm reaction following the use of any 5-HT_1 agonist.

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, 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

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

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 IMITREX Injection, particularly during coadministration 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 Injection 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 Injection is contraindicated in patients with uncontrolled hypertension.

5.9 Anaphylactic/Anaphylactoid Reactions

Anaphylactic/anaphylactoid reactions have occurred in patients receiving sumatriptan. 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 Injection is contraindicated in patients with prior serious anaphylactic reaction.

5.10 Seizures

Seizures have been reported following administration of sumatriptan. Some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures. There are also reports in patients where no such predisposing factors are apparent. IMITREX Injection should be used with caution in patients with a history of epilepsy or conditions associated with a lowered seizure threshold.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Myocardial ischemia, myocardial infarction, and Prinzmetal's angina *[see Warnings and Precautions (5.1)]*
- Arrhythmias *[see Warnings and Precautions (5.2)]*
- Chest, throat, neck, and/or jaw pain/tightness/pressure *[see Warnings and Precautions (5.3)]*
- Cerebrovascular events *[see Warnings and Precautions (5.4)]*
- Other vasospasm reactions *[see Warnings and Precautions (5.5)]*
- Medication overuse headache *[see Warnings and Precautions (5.6)]*

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- Serotonin syndrome *[see Warnings and Precautions (5.7)]*
- Increase in blood pressure *[see Warnings and Precautions (5.8)]*
- Anaphylactic/anaphylactoid reactions *[see Warnings and Precautions (5.9)]*
- Seizures *[see Warnings and Precautions (5.10)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Migraine Headache: Table 1 lists adverse reactions that occurred in 2 US placebo-controlled clinical trials in migraine subjects *[*Studies 2 and 3, *see Clinical Studies (14.1)]* following either a single 6-mg dose of IMITREX Injection or placebo. Only reactions that occurred at a frequency of 2% or more in groups treated with IMITREX Injection 6 mg and that occurred at a frequency greater than the placebo group are included in Table 1.

Table 1. Adverse Reactions Reported by at Least 2% of Subjects and at a Greater Frequency Than Placebo in 2 Placebo-Controlled Migraine Clinical Trials (Studies 2 and 3)[a]

	Percent of Subjects Reporting	
Adverse Reaction	IMITREX Injection 6 mg Subcutaneous (n = 547)	Placebo (n = 370)
Atypical sensations	42	9
Tingling	14	3
Warm/hot sensation	11	4
Burning sensation	7	<1
Feeling of heaviness	7	1
Pressure sensation	7	2
Feeling of tightness	5	<1
Numbness	5	2
Feeling strange	2	<1
Tight feeling in head	2	<1
Cardiovascular		
Flushing	7	2
Chest discomfort	5	1
Tightness in chest	3	<1
Pressure in chest	2	<1
Ear, nose, and throat		
Throat discomfort	3	<1
Discomfort: nasal cavity/sinuses	2	<1
Injection site reaction[b]	59	24

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Miscellaneous		
Jaw discomfort	2	0
Musculoskeletal		
Weakness	5	<1
Neck pain/stiffness	5	<1
Myalgia	2	<1
Neurological		
Dizziness/vertigo	12	4
Drowsiness/sedation	3	2
Headache	2	<1
Skin		
Sweating	2	1

[a] The sum of the percentages cited is greater than 100% because subjects may have experienced more than 1 type of adverse reaction. Only reactions that occurred at a frequency of 2% or more in groups treated with IMITREX Injection and occurred at a frequency greater than the placebo groups are included.

[b] Includes injection site pain, stinging/burning, swelling, erythema, bruising, bleeding.

The incidence of adverse reactions in controlled clinical trials was not affected by gender or age of the subjects. There were insufficient data to assess the impact of race on the incidence of adverse reactions.

Cluster Headache: In the controlled clinical trials assessing the efficacy of IMITREX Injection as a treatment for cluster headache *[*Studies 4 and 5, *see Clinical Studies (14.2)]*, no new significant adverse reactions were detected that had not already been identified in trials of IMITREX in subjects with migraine.

Overall, the frequency of adverse reactions reported in the trials of cluster headache was generally lower than in the migraine trials. Exceptions include reports of paresthesia (5% IMITREX, 0% placebo), nausea and vomiting (4% IMITREX, 0% placebo), and bronchospasm (1% IMITREX, 0% placebo).

Other Adverse Reactions: In the paragraphs that follow, the frequencies of less commonly reported adverse reactions are presented. Reaction frequencies were calculated as the number of subjects reporting a reaction divided by the total number of subjects (N = 6,218) exposed to subcutaneous IMITREX Injection. All reported reactions are included except those already listed in the previous table. Reactions are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent are defined as those occurring in at least 1/100 subjects, infrequent are those occurring in 1/100 to 1/1,000 subjects, and rare are those occurring in fewer than 1/1,000 subjects.

Cardiovascular: Infrequent were hypertension, hypotension, bradycardia, tachycardia, palpitations, and syncope. Rare was arrhythmia.

Gastrointestinal: Frequent was abdominal discomfort.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Musculoskeletal: Frequent were muscle cramps.

Neurological: Frequent was anxiety. Infrequent were mental confusion, euphoria, agitation, tremor. Rare were myoclonia, sleep disturbance, and dystonia.

Respiratory: Infrequent was dyspnea.

Skin: Infrequent were erythema, pruritus, and skin rashes.

Miscellaneous: Infrequent was "serotonin agonist effect".

Adverse Events Observed With Other Formulations of IMITREX: The following adverse events occurred in clinical trials with IMITREX® Tablets and IMITREX® Nasal Spray. Because the reports include events observed in open and uncontrolled trials, the role of IMITREX in their causation cannot be reliably determined. All reported events are included except those already listed, those too general to be informative, and those not reasonably associated with the use of the drug.

Cardiovascular: Angina, cerebrovascular lesion, heart block, peripheral cyanosis, phlebitis, thrombosis.

Gastrointestinal: Abdominal distention and colitis.

Neurological: Convulsions, hallucinations, syncope, suicide, and twitching.

Miscellaneous: Edema, hypersensitivity, swelling of extremities, and swelling of face.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of IMITREX Tablets, IMITREX Nasal Spray, and IMITREX Injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These reactions have been chosen for inclusion due to either their seriousness, frequency of reporting, or causal connection to IMITREX or a combination of these factors.

Blood: Hemolytic anemia, pancytopenia, thrombocytopenia.

Ear, Nose, and Throat: Deafness.

Eye: Ischemic optic neuropathy, retinal artery occlusion, retinal vein thrombosis.

Neurological: Central nervous system vasculitis, cerebrovascular accident, serotonin syndrome, subarachnoid hemorrhage.

Non-Site Specific: Angioedema, cyanosis, temporal arteritis.

Skin: Exacerbation of sunburn, hypersensitivity reactions (allergic vasculitis, erythema, pruritus, rash, shortness of breath, urticaria), photosensitivity. Following subcutaneous administration of IMITREX, pain, redness, stinging, induration, swelling, contusion, subcutaneous bleeding, and, on rare occasions, lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) have been reported.

Urogenital: Acute renal failure.

7 DRUG INTERACTIONS

7.1 Ergot-Containing Drugs

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine or methysergide) and IMITREX Injection within 24 hours of each other is contraindicated.

7.2 Monoamine Oxidase-A Inhibitors

MAO-A inhibitors increase systemic exposure by 2-fold. Therefore, the use of IMITREX Injection in patients receiving MAO-A inhibitors is contraindicated *[see Clinical Pharmacology (12.3)]*.

7.3 Other 5-HT_1 Agonists

Because their vasospastic effects may be additive, coadministration of IMITREX Injection and other 5-HT_1 agonists (e.g., triptans) within 24 hours of each other is contraindicated.

7.4 Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome

Cases of serotonin syndrome have been reported during coadministration of triptans and SSRIs, or SNRIs, SNRIs, TCAs, and MAO inhibitors *[see Warnings and Precautions (5.7)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: There are no adequate and well-controlled trials of IMITREX Injection in pregnant women. IMITREX Injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

When sumatriptan was administered intravenously to pregnant rabbits daily throughout the period of organogenesis, embryolethality was observed at doses at or close to those producing maternal toxicity. These doses were less than the maximum recommended human dose (MRHD) of 12 mg/day on a mg/m^2 basis. Oral administration of sumatriptan to rabbits during organogenesis was associated with increased incidences of fetal vascular and skeletal abnormalities. The highest no-effect dose for these effects was 15 mg/kg/day. The intravenous administration of sumatriptan to pregnant rats throughout organogenesis at doses that are approximately 10 times the MRHD on a mg/m^2 basis, did not produce evidence of embryolethality. The subcutaneous administration of sumatriptan to pregnant rats prior to and throughout pregnancy did not produce evidence of embryolethality or teratogenicity.

8.3 Nursing Mothers

It is not known whether sumatriptan is excreted in human breast milk following subcutaneous administration. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from IMITREX, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Safety and effectiveness of IMITREX Injection in pediatric patients under 18 years of age have not been established; therefore, IMITREX Injection is not recommended for use in patients under 18 years of age.

Two controlled clinical trials evaluated IMITREX Nasal Spray (5 to 20 mg) in 1,248 adolescent migraineurs aged 12 to 17 years who treated a single attack. The trials did not establish the efficacy of IMITREX Nasal Spray compared with placebo in the treatment of migraine in adolescents. Adverse reactions observed in these clinical trials were similar in nature to those reported in clinical trials in adults.

Five controlled clinical trials (2 single-attack trials, 3 multiple-attack trials) evaluating oral IMITREX (25 to 100 mg) in pediatric subjects aged 12 to 17 years enrolled a total of 701 adolescent migraineurs. These trials did not establish the efficacy of oral IMITREX compared with placebo in the treatment of migraine in adolescents. Adverse reactions observed in these clinical trials were similar in nature to those reported in clinical trials in adults. The frequency of all adverse reactions in these subjects appeared to be both dose- and age-dependent, with younger subjects reporting reactions more commonly than older adolescents.

Postmarketing experience documents that serious adverse reactions have occurred in the pediatric population after use of subcutaneous, oral, and/or intranasal IMITREX. These reports include reactions similar in nature to those reported rarely in adults, including stroke, visual loss, and death. A myocardial infarction has been reported in a 14-year-old male following the use of oral IMITREX; clinical signs occurred within 1 day of drug administration. Since clinical data to determine the frequency of serious adverse reactions in pediatric patients who might receive subcutaneous, oral, or intranasal IMITREX are not presently available, the use of IMITREX in patients under 18 years of age is not recommended.

8.5 Geriatric Use

Clinical trials of IMITREX Injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

A cardiovascular evaluation is recommended for geriatric patients who have other cardiovascular risk factors (e.g., diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to receiving IMITREX Injection *[see Warnings and Precautions (5.1)]*.

10 OVERDOSAGE

No gross overdoses in clinical practice have been reported. Coronary vasospasm was observed after intravenous administration of IMITREX Injection *[see Contraindications (4)]*. Overdoses would be expected from animal data (dogs at 0.1 g/kg, rats at 2 g/kg) to possibly cause convulsions, tremor, inactivity, erythema of the extremities, reduced respiratory rate,

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

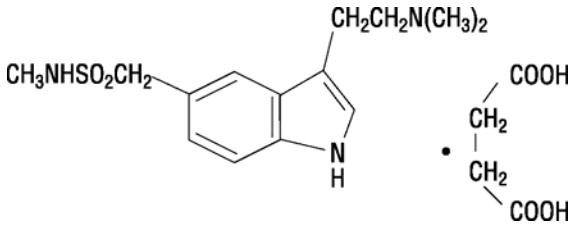
cyanosis, ataxia, mydriasis, injection site reactions (desquamation, hair loss, and scab formation), and paralysis.

The elimination half-life of sumatriptan is about 2 hours *[see Clinical Pharmacology (12.3)]*, and therefore monitoring of patients after overdose with IMITREX Injection should continue for at least 10 hours or while symptoms or signs persist.

It is unknown what effect hemodialysis or peritoneal dialysis has on the serum concentrations of sumatriptan.

11 DESCRIPTION

IMITREX Injection contains sumatriptan succinate, a selective 5-$HT_{1B/1D}$ receptor agonist. Sumatriptan succinate is chemically designated as 3-[2-(dimethylamino)ethyl]-N-methyl-indole-5-methanesulfonamide succinate (1:1), and it has the following structure:



The empirical formula is $C_{14}H_{21}N_3O_2S \bullet C_4H_6O_4$, representing a molecular weight of 413.5. Sumatriptan succinate is a white to off-white powder that is readily soluble in water and in saline.

IMITREX Injection is a clear, colorless to pale yellow, sterile, nonpyrogenic solution for subcutaneous injection. Each 0.5 mL of IMITREX Injection 8 mg/mL solution contains 4 mg of sumatriptan (base) as the succinate salt and 3.8 mg of sodium chloride, USP in Water for Injection, USP. Each 0.5 mL of IMITREX Injection 12 mg/mL solution contains 6 mg of sumatriptan (base) as the succinate salt and 3.5 mg of sodium chloride, USP in Water for Injection, USP. The pH range of both solutions is approximately 4.2 to 5.3. The osmolality of both injections is 291 mOsmol.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Sumatriptan binds with high affinity to human cloned 5-$HT_{1B/1D}$ receptors. IMITREX presumably exerts its therapeutic effects in the treatment of migraine headache by binding to 5-$HT_{1B/1D}$ receptors located on intracranial blood vessels and sensory nerves of the trigeminal system.

Current theories proposed to explain the etiology of migraine headache suggest that symptoms are due to local cranial vasodilatation and/or to the release of sensory neuropeptides (including substance P and calcitonin gene-related peptide) through nerve endings in the trigeminal system. The therapeutic activity of IMITREX for the treatment of migraine and cluster headaches is thought to be due to the agonist effects at the 5-$HT_{1B/1D}$ receptors on

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

intracranial blood vessels (including the arterio-venous anastomoses) and sensory nerves of the trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory neuropeptide release.

12.2 Pharmacodynamics

Blood Pressure: Significant elevation in blood pressure, including hypertensive crisis, has been reported in patients with and without a history of hypertension *[see Warnings and Precautions (5.8)]*.

Peripheral (Small) Arteries: In healthy volunteers (N = 18), a trial evaluating the effects of sumatriptan on peripheral (small vessel) arterial reactivity failed to detect a clinically significant increase in peripheral resistance.

Heart Rate: Transient increases in blood pressure observed in some subjects in clinical trials carried out during sumatriptan's development as a treatment for migraine were not accompanied by any clinically significant changes in heart rate.

12.3 Pharmacokinetics

Absorption and Bioavailability: The bioavailability of sumatriptan via subcutaneous site injection to 18 healthy male subjects was 97% ± 16% of that obtained following intravenous injection.

After a single 6-mg subcutaneous manual injection into the deltoid area of the arm in 18 healthy males (age: 24 ± 6 years, weight: 70 kg), the maximum serum concentration (C_{max}) of sumatriptan was (mean ± standard deviation) 74 ± 15 ng/mL and the time to peak concentration (T_{max}) was 12 minutes after injection (range: 5 to 20 minutes). In this trial, the same dose injected subcutaneously in the thigh gave a C_{max} of 61 ± 15 ng/mL by manual injection versus 52 ± 15 ng/mL by autoinjector techniques. The T_{max} or amount absorbed was not significantly altered by either the site or technique of injection.

Distribution: Protein binding, determined by equilibrium dialysis over the concentration range of 10 to 1,000 ng/mL, is low, approximately 14% to 21%. The effect of sumatriptan on the protein binding of other drugs has not been evaluated.

Following a 6-mg subcutaneous injection into the deltoid area of the arm in 9 males (mean age: 33 years, mean weight: 77 kg) the volume of distribution central compartment of sumatriptan was 50 ± 8 liters and the distribution half-life was 15 ± 2 minutes.

Metabolism: In vitro studies with human microsomes suggest that sumatriptan is metabolized by MAO, predominantly the A isoenzyme. Most of a radiolabeled dose of sumatriptan excreted in the urine is the major metabolite indole acetic acid (IAA) or the IAA glucuronide, both of which are inactive.

Elimination: After a single 6-mg subcutaneous dose, 22% ± 4% was excreted in the urine as unchanged sumatriptan and 38% ± 7% as the IAA metabolite.

Following a 6-mg subcutaneous injection into the deltoid area of the arm, the systemic clearance of sumatriptan was 1,194 ± 149 mL/min and the terminal half-life was 115 ± 19 minutes.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Special Populations: *Age:* The pharmacokinetics of sumatriptan in the elderly (mean age: 72 years, 2 males and 4 females) and in subjects with migraine (mean age: 38 years, 25 males and 155 females) were similar to that in healthy male subjects (mean age: 30 years).

Renal Impairment: The effect of renal impairment on the pharmacokinetics of sumatriptan has not been examined.

Hepatic Impairment: The effect of mild to moderate hepatic disease on the pharmacokinetics of subcutaneously administered sumatriptan has been evaluated. There were no significant differences in the pharmacokinetics of subcutaneously administered sumatriptan in moderately hepatically impaired subjects compared with healthy controls. The pharmacokinetics of subcutaneously administered sumatriptan in patients with severe hepatic impairment has not been studied. The use of IMITREX Injection in this population is contraindicated *[see Contraindications (4)]*.

Race: The systemic clearance and C_{max} of sumatriptan were similar in black (n = 34) and Caucasian (n = 38) healthy male subjects.

Drug Interaction Studies: *Monoamine Oxidase-A Inhibitors:* In a trial of 14 healthy females, pretreatment with an MAO-A inhibitor decreased the clearance of sumatriptan, resulting in a 2-fold increase in the area under the sumatriptan plasma concentration-time curve (AUC), corresponding to a 40% increase in elimination half-life.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: In carcinogenicity studies, rats and mice were given sumatriptan by oral gavage. Mice were dosed for 78 weeks and rats were dosed for 104 weeks. Average exposures achieved in mice receiving the highest dose were approximately 110 times the exposure attained in humans after the maximum recommended single dose of 6 mg. The highest dose to rats was approximately 260 times the maximum single dose of 6 mg on a mg/m^2 basis. There was no evidence of an increase in tumors in either species related to sumatriptan administration.

Mutagenesis: Sumatriptan was not mutagenic in the presence or absence of metabolic activation when tested in 2 gene mutation assays (the Ames test and the in vitro mammalian Chinese hamster V79/HGPRT assay). It was not clastogenic in 2 cytogenetics assays (the in vitro human lymphocyte assay and the in vivo rat micronucleus assay).

Impairment of Fertility: A fertility study (Segment I) by the subcutaneous route, during which male and female rats were dosed daily with sumatriptan prior to and throughout the mating period, has shown no evidence of impaired fertility at doses equivalent to approximately 100 times the maximum recommended single human dose of 6 mg on a mg/m^2 basis. However, following oral administration, a treatment-related decrease in fertility, secondary to a decrease in mating, was seen for rats treated with 50 and 500 mg/kg/day. The no-effect dose for this finding was approximately 8 times the maximum recommended single human dose of 6 mg on a mg/m^2

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

basis. It is not clear whether the problem is associated with the treatment of males or females or both.

13.2 Animal Toxicology and/or Pharmacology

Corneal Opacities: Dogs receiving oral sumatriptan developed corneal opacities and defects in the corneal epithelium. Corneal opacities were seen at the lowest dosage tested, 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and no-effect doses were not established; however, the relative exposure at the lowest dose tested was approximately 5 times the human exposure after a 100-mg oral dose or 3 times the human exposure after a 6-mg subcutaneous dose.

Melanin Binding: In rats with a single subcutaneous dose (0.5 mg/kg) of radiolabeled sumatriptan, the elimination half-life of radioactivity from the eye was 15 days, suggesting that sumatriptan and its metabolites bind to the melanin of the eye. The clinical significance of this binding is unknown.

14 CLINICAL STUDIES

14.1 Migraine

In controlled clinical trials enrolling more than 1,000 subjects during migraine attacks who were experiencing moderate or severe pain and 1 or more of the symptoms enumerated in Table 3, onset of relief began as early as 10 minutes following a 6-mg IMITREX Injection. Lower doses of IMITREX Injection may also prove effective, although the proportion of subjects obtaining adequate relief was decreased and the latency to that relief is greater with lower doses.

In Study 1, 6 different doses of IMITREX Injection (n = 30 each group) were compared with placebo (n = 62), in a single-attack, parallel-group design, the dose response relationship was found to be as shown in Table 2.

Table 2. Proportion of Subjects With Migraine Relief and Incidence of Adverse Events by Time and by IMITREX Dose in Study 1

Dose of IMITREX Injection	Percent Subjects With Relief[a]				Adverse Events Incidence (%)
	at 10 Minutes	at 30 Minutes	at 1 Hour	at 2 Hours	
Placebo	5	15	24	21	55
1 mg	10	40	43	40	63
2 mg	7	23	57	43	63
3 mg	17	47	57	60	77
4 mg	13	37	50	57	80
6 mg	10	63	73	70	83
8 mg	23	57	80	83	93

[a] Relief is defined as the reduction of moderate or severe pain to no or mild pain after dosing without use of rescue medication.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

In 2 randomized, placebo-controlled clinical trials of IMITREX Injection 6 mg in 1,104 subjects with moderate or severe migraine pain (Studies 2 and 3), the onset of relief was less than 10 minutes. Headache relief, as defined by a reduction in pain from severe or moderately severe to mild or no headache, was achieved in 70% of the subjects within 1 hour of a single 6-mg subcutaneous dose of IMITREX Injection. Approximately 82% and 65% of subjects treated with IMITREX 6 mg had headache relief and were pain free within 2 hours, respectively.

Table 3 shows the 1- and 2-hour efficacy results for IMITREX Injection 6 mg in Studies 2 and 3.

Table 3. Proportion of Subjects With Pain Relief and Relief of Migraine Symptoms After 1 and 2 Hours of Treatment in Studies 2 and 3

	Study 2		Study 3	
1-Hour Data	Placebo (n = 190)	IMITREX 6 mg (n = 384)	Placebo (n = 180)	IMITREX 6 mg (n = 350)
Subjects with pain relief (grade 0/1)	18%	70%[a]	26%	70%[a]
Subjects with no pain	5%	48%[a]	13%	49%[a]
Subjects without nausea	48%	73%[a]	50%	73%[a]
Subjects without photophobia	23%	56%[a]	25%	58%[a]
Subjects with little or no clinical disability[b]	34%	76%[a]	34%	76%[a]
	Study 2		Study 3	
2-Hour Data	Placebo[c]	IMITREX 6 mg[d]	Placebo[c]	IMITREX 6 mg[d]
Subjects with pain relief (grade 0/1)	31%	81%[a]	39%	82%[a]
Subjects with no pain	11%	63%[a]	19%	65%[a]
Subjects without nausea	56%	82%[a]	63%	81%[a]
Subjects without photophobia	31%	72%[a]	35%	71%[a]
Subjects with little or no clinical disability[b]	42%	85%[a]	49%	84%[a]

[a] $P<0.05$ versus placebo.

[b] A successful outcome in terms of clinical disability was defined prospectively as ability to work mildly impaired or ability to work and function normally.

[c] Includes subjects that may have received an additional placebo injection 1 hour after the initial injection.

[d] Includes subjects that may have received an additional 6 mg of IMITREX Injection 1 hour after the initial injection.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

IMITREX Injection also relieved photophobia, phonophobia (sound sensitivity), nausea, and vomiting associated with migraine attacks. Similar efficacy was seen when subjects self-administered IMITREX Injection using the IMITREX STATdose Pen.

The efficacy of IMITREX Injection was unaffected by whether or not the migraine was associated with aura, duration of attack, gender or age of the subject, or concomitant use of common migraine prophylactic drugs (e.g., beta-blockers).

14.2 Cluster Headache

The efficacy of IMITREX Injection in the acute treatment of cluster headache was demonstrated in 2 randomized, double-blind, placebo-controlled, 2-period crossover trials (Studies 4 and 5). Subjects aged 21 to 65 years were enrolled and were instructed to treat a moderate to very severe headache within 10 minutes of onset. Headache relief was defined as a reduction in headache severity to mild or no pain. In both trials, the proportion of individuals gaining relief at 10 or 15 minutes was significantly greater among subjects receiving 6 mg of IMITREX Injection compared with those who received placebo (see Table 4).

Table 4. Proportion of Subjects With Cluster Headache Relief by Time in Studies 4 and 5

	Study 4		Study 5	
	Placebo (n = 39)	IMITREX 6 mg (n = 39)	Placebo (n = 88)	IMITREX 6 mg (n = 92)
Subjects with pain relief (no/mild)				
5 Minutes post-injection	8%	21%	7%	23%[a]
10 Minutes post-injection	10%	49%[a]	25%	49%[a]
15 Minutes post-injection	26%	74%[a]	35%	75%[a]

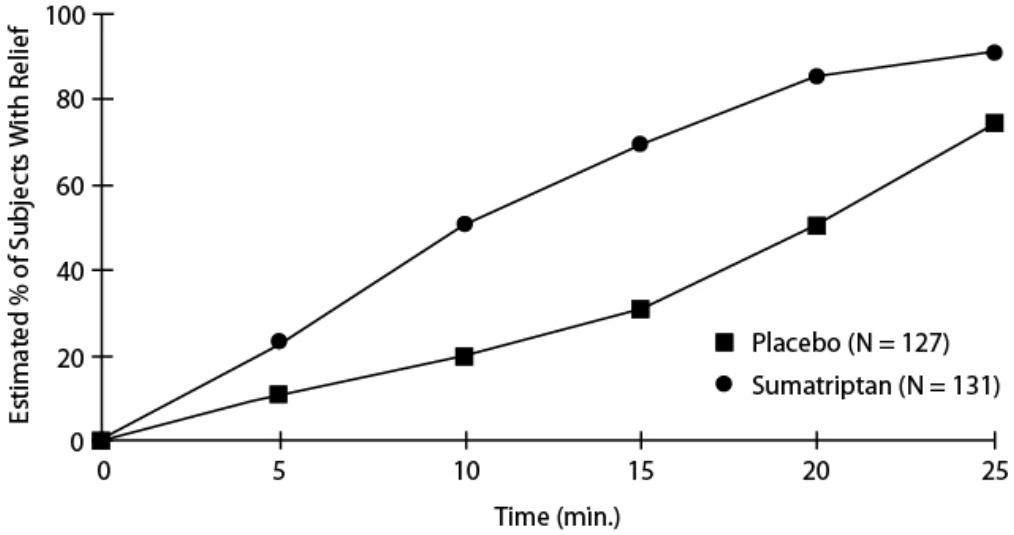
[a] $P<0.05$.

(n = Number of headaches treated.)

An estimate of the cumulative probability of a subject with a cluster headache obtaining relief after being treated with either IMITREX Injection or placebo is presented in Figure 1.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Figure 1. Time to Relief of Cluster Headache from Time of Injection[a]



[a] The figure uses Kaplan-Meier (product limit) Survivorship Plot. Subjects taking rescue medication were censored at 15 minutes.

The plot was constructed with data from subjects who either experienced relief or did not require (request) rescue medication within a period of 2 hours following treatment. As a consequence, the data in the plot are derived from only a subset of the 258 headaches treated (rescue medication was required in 52 of the 127 placebo-treated headaches and 18 of the 131 headaches treated with IMITREX Injection).

Other data suggest that treatment with IMITREX Injection is not associated with an increase in early recurrence of headache and has little effect on the incidence of later-occurring headaches (i.e., those occurring after 2, but before 18 or 24 hours).

16 HOW SUPPLIED/STORAGE AND HANDLING

IMITREX Injection contains sumatriptan (base) as the succinate salt and is supplied as a clear, colorless to pale yellow, sterile, nonpyrogenic solution as follows:

Prefilled Syringe and/or Autoinjector Pen: Each pack contains a Patient Information and Patients Instructions for Use leaflet.

- IMITREX STATdose System®, 4 mg, containing 1 IMITREX STATdose Pen, 2 prefilled single-dose syringe cartridges, and 1 carrying case (NDC 0173-0739-00).
- IMITREX STATdose System, 6 mg, containing 1 IMITREX STATdose Pen, 2 prefilled single-dose syringe cartridges, and 1 carrying case (NDC 0173-0479-00).
- Two 4-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose System (NDC 0173-0739-02).
- Two 6-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose System (NDC 0173-0478-00).

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Single-Dose Vial:

- IMITREX Injection single-dose vial (6 mg/0.5 mL) in cartons containing 5 vials (NDC 0173-0449-02).

Store between 2° and 30°C (36° and 86°F). Protect from light.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use).

17.1 Risk of Myocardial Ischemia and/or Infarction, Prinzmetal's Angina, Other Vasospasm-Related Events, Arrhythmias, and Cerebrovascular Events

Inform patients that IMITREX Injection may cause serious cardiovascular side effects such as myocardial infarction or stroke. Although serious cardiovascular events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, irregular heartbeat, significant rise in blood pressure, weakness, and slurring of speech and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up *[see Warnings and Precautions (5.1, 5.2, 5.4, 5.5, 5.8)]*.

17.2 Anaphylactic/Anaphylactoid Reactions

Inform patients that anaphylactic/anaphylactoid reactions have occurred in patients receiving IMITREX Injection. 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 *[see Warnings and Precautions (5.9)]*.

17.3 Medication Overuse Headache

Inform patients that use of acute migraine drugs for 10 or more days per month may lead to an exacerbation of headache and encourage patients to record headache frequency and drug use (e.g., by keeping a headache diary) *[see Warnings and Precautions (5.6)]*.

17.4 Pregnancy

Inform patients that IMITREX Injection should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus *[see Use in Specific Populations (8.1)]*.

17.5 Nursing Mothers

Advise patients to notify their healthcare provider if they are breastfeeding or plan to breastfeed *[see Use in Specific Populations (8.3)]*.

17.6 Ability To Perform Complex Tasks

Since migraines or treatment with IMITREX Injection may cause somnolence and dizziness, instruct patients to evaluate their ability to perform complex tasks during migraine attacks and after administration of IMITREX Injection.

17.7 Serotonin Syndrome

Patients should be cautioned about the risk of serotonin syndrome with the use of IMITREX Injection or other triptans, particularly during combined use with SSRIs, SNRIs, TCAs, and MAO inhibitors *[see Warnings and Precautions (5.7) and Drug Interactions (7.4)]*.

17.8 How to Use IMITREX Injection

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Provide patients instruction on the proper use of IMITREX Injection if they are able to self-administer IMITREX Injection in medically unsupervised situation.

Inform patients that the needle in the IMITREX STATdose Pen penetrates approximately 1/4 of an inch (5 to 6 mm). Inform patients that the injection is intended to be given subcutaneously and intramuscular or intravascular delivery should be avoided. Instruct patients to use injection sites with an adequate skin and subcutaneous thickness to accommodate the length of the needle.

IMITREX, IMITREX STATdose Pen, and IMITREX STATdose System are registered trademarks of GlaxoSmithKline.

GlaxoSmithKline
Research Triangle Park, NC 27709

©2012, GlaxoSmithKline. All rights reserved.

Patient Information
IMITREX® (IM-i-trex)
(sumatriptan succinate)
Injection

Read this Patient Information before you start taking IMITREX and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about IMITREX?

IMITREX can cause serious side effects, including:

Heart attack and other heart problems. Heart problems may lead to death.

Stop taking IMITREX and get emergency medical help right away if you have any of the following symptoms of a heart attack:

- discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

IMITREX is not for people with risk factors for heart disease unless a heart exam is done and shows no problem. You have a higher risk for heart disease if you:

- have high blood pressure
- have high cholesterol levels
- smoke
- are overweight
- have diabetes
- have a family history of heart disease

What is IMITREX?

IMITREX is a prescription medicine used to treat acute migraine headaches with or without aura and acute cluster headaches in adults who have been diagnosed with migraine or cluster headaches.

IMITREX is not used to treat other types of headaches such as hemiplegic (that make you unable to move on one side of your body) or basilar (rare form of migraine with aura) migraines.

IMITREX is not used to prevent or decrease the number of migraine or cluster headaches you have.

It is not known if IMITREX is safe and effective in children under 18 years of age.

Who should not take IMITREX?

Do not take IMITREX if you have:

- heart problems or a history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- hemiplegic migraines or basilar migraines. If you are not sure if you have these types of migraines, ask your healthcare provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with your blood circulation
- taken any of the following medicines in the last 24 hours:
  - almotriptan (AXERT®)
  - eletriptan (RELPAX®)
  - frovatriptan (FROVA®)
  - naratriptan (AMERGE®)
  - rizatriptan (MAXALT®, MAXALT-MLT®)
  - sumatriptan and naproxen (TREXIMET®)

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- ergotamines (CAFERGOT®, ERGOMAR®, MIGERGOT®)
- dihydroergotamine (D.H.E. 45®, MIGRANAL®)

Ask your healthcare provider if you are not sure if your medicine is listed above.

- an allergy to sumatriptan or any of the ingredients in IMITREX. See the end of this leaflet for a complete list of ingredients in IMITREX.

What should I tell my healthcare provider before taking IMITREX?

Before you take IMITREX, tell your healthcare provider about all of your medical conditions, including if you:

- have high blood pressure
- have high cholesterol
- have diabetes
- smoke
- are overweight
- have heart problems or family history of heart problems or stroke
- have liver problems
- have had epilepsy or seizures
- are not using effective birth control
- become pregnant while taking IMITREX
- are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk and may harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take IMITREX.

Tell your healthcare provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

Using IMITREX with certain other medicines can affect each other, causing serious side effects.

Especially tell your healthcare provider if you take anti-depressant medicines called:

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin norepinephrine reuptake inhibitors (SNRIs)
- tricyclic antidepressants (TCAs)
- monoamine oxidase inhibitors (MAOIs)

Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take IMITREX?

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- Certain people should take their first dose of IMITREX in their healthcare provider's office or in another medical setting. Ask your healthcare provider if you should take your first dose in a medical setting.
- Use IMITREX exactly as your healthcare provider tells you to use it.
- Your healthcare provider may change your dose. Do not change your dose without first talking with your healthcare provider.
- For adults, the usual dose is a single injection given just below the skin.
- You should give an injection as soon as the symptoms of your headache start, but it may be given at any time during a migraine attack.
- If you did not get any relief after the first injection, do not give a second injection without first talking with your healthcare provider.
- You can take a second injection 1 hour after the first injection, but not sooner, if your headache came back after your first injection.
- Do not take more than 12 mg in a 24-hour period.
- If you use too much IMITREX, call your healthcare provider or go to the nearest hospital emergency room right away.
- You should write down when you have headaches and when you take IMITREX so you can talk with your healthcare provider about how IMITREX is working for you.

What should I avoid while taking IMITREX?

IMITREX can cause dizziness, weakness, or drowsiness. If you have these symptoms, do not drive a car, use machinery, or do anything where you need to be alert.

What are the possible side effects of IMITREX?

IMITREX may cause serious side effects. See "What is the most important information I should know about IMITREX?"

These serious side effects include:

- changes in color or sensation in your fingers and toes (Raynaud's syndrome)
- stomach and intestinal problems (gastrointestinal and colonic ischemic events). Symptoms of gastrointestinal and colonic ischemic events include:
  - sudden or severe stomach pain
  - stomach pain after meals
  - weight loss
  - nausea or vomiting
  - constipation or diarrhea
  - bloody diarrhea
  - fever
- problems with blood circulation to your legs and feet (peripheral vascular ischemia). Symptoms of peripheral vascular ischemia include:

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- cramping and pain in your legs or hips
- feeling of heaviness or tightness in your leg muscles
- burning or aching pain in your feet or toes while resting
- numbness, tingling, or weakness in your legs
- cold feeling or color changes in 1 or both legs or feet

- medication overuse headaches. Some people who use too many IMITREX injections may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with IMITREX.
- serotonin syndrome. Serotonin syndrome is a rare but serious problem that can happen in people using IMITREX, especially if IMITREX is used with anti-depressant medicines called SSRIs or SNRIs.

  Call your healthcare provider right away if you have any of the following symptoms of serotonin syndrome:
  - mental changes such as seeing things that are not there (hallucinations), agitation, or coma
  - fast heartbeat
  - changes in blood pressure
  - high body temperature
  - tight muscles
  - trouble walking
- seizures. Seizures have happened in people taking IMITREX who have never had seizures before. Talk with your healthcare provider about your chance of having seizures while you take IMITREX.

The most common side effects of IMITREX include:

- pain or redness at your injection site
- tingling or numbness in your fingers or toes
- dizziness
- warm, hot, burning feeling to your face (flushing)
- discomfort or stiffness in your neck
- feeling weak, drowsy, or tired

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of IMITREX. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

How should I store IMITREX Injection?

- Store IMITREX between 36°F to 86°F (2°C to 30°C).
- Store your medicine away from light.
- Keep your medicine in the packaging or carrying case provided with it.

Keep IMITREX and all medicines out of the reach of children.

General information about the safe and effective use of IMITREX

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use IMITREX for a condition for which it was not prescribed. Do not give IMITREX to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about IMITREX. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about IMITREX that is written for healthcare professionals.

For more information, go to www.gsk.com or call 1-888-825-5249.

What are the ingredients in IMITREX Injection?

Active ingredient: sumatriptan succinate

Inactive ingredients: sodium chloride, water for injection

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

IMITREX, AMERGE, TREXIMET are registered trademarks of GlaxoSmithKline. The other brands listed are trademarks of their respective owners and are not trademarks of GlaxoSmithKline. The makers of these brands are not affiliated with and do not endorse GlaxoSmithKline or its products.

GlaxoSmithKline
Research Triangle Park, NC 27709

©2012, GlaxoSmithKline. All rights reserved.

September 2012

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Patient Information
IMITREX® (IM-i-trex)
(sumatriptan succinate)
Injection

Read this Patient Information before you start taking IMITREX and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about IMITREX?

IMITREX can cause serious side effects, including:

Heart attack and other heart problems. Heart problems may lead to death.

Stop taking IMITREX and get emergency medical help right away if you have any of the following symptoms of a heart attack:

- discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

IMITREX is not for people with risk factors for heart disease unless a heart exam is done and shows no problem. You have a higher risk for heart disease if you:

- have high blood pressure
- have high cholesterol levels
- smoke
- are overweight
- have diabetes
- have a family history of heart disease

What is IMITREX?

IMITREX is a prescription medicine used to treat acute migraine headaches with or without aura and acute cluster headaches in adults who have been diagnosed with migraine or cluster headaches.

IMITREX is not used to treat other types of headaches such as hemiplegic (that make you unable to move on one side of your body) or basilar (rare form of migraine with aura) migraines.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

IMITREX is not used to prevent or decrease the number of migraine or cluster headaches you have.

It is not known if IMITREX is safe and effective in children under 18 years of age.

Who should not take IMITREX?

Do not take IMITREX if you have:

- heart problems or a history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- hemiplegic migraines or basilar migraines. If you are not sure if you have these types of migraines, ask your healthcare provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with your blood circulation
- taken any of the following medicines in the last 24 hours:
  - almotriptan (AXERT®)
  - eletriptan (RELPAX®)
  - frovatriptan (FROVA®)
  - naratriptan (AMERGE®)
  - rizatriptan (MAXALT®, MAXALT-MLT®)
  - sumatriptan and naproxen (TREXIMET®)
  - ergotamines (CAFERGOT®, ERGOMAR®, MIGERGOT®)
  - dihydroergotamine (D.H.E. 45®, MIGRANAL®)

  Ask your healthcare provider if you are not sure if your medicine is listed above.
- an allergy to sumatriptan or any of the ingredients in IMITREX. See the end of this leaflet for a complete list of ingredients in IMITREX.

What should I tell my healthcare provider before taking IMITREX?

Before you take IMITREX, tell your healthcare provider about all of your medical conditions, including if you:

- have high blood pressure
- have high cholesterol
- have diabetes
- smoke
- are overweight
- have heart problems or family history of heart problems or stroke
- have liver problems
- have had epilepsy or seizures
- are not using effective birth control

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- become pregnant while taking IMITREX
- are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk and may harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take IMITREX.

Tell your healthcare provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

Using IMITREX with certain other medicines can affect each other, causing serious side effects.

Especially tell your healthcare provider if you take anti-depressant medicines called:

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin norepinephrine reuptake inhibitors (SNRIs)
- tricyclic antidepressants (TCAs)
- monoamine oxidase inhibitors (MAOIs)

Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take IMITREX?

- Certain people should take their first dose of IMITREX in their healthcare provider's office or in another medical setting. Ask your healthcare provider if you should take your first dose in a medical setting.
- Use IMITREX exactly as your healthcare provider tells you to use it.
- Your healthcare provider may change your dose. Do not change your dose without first talking with your healthcare provider.
- For adults, the usual dose is a single injection given just below the skin.
- You should give an injection as soon as the symptoms of your headache start, but it may be given at any time during a migraine attack.
- If you did not get any relief after the first injection, do not give a second injection without first talking with your healthcare provider.
- You can take a second injection 1 hour after the first injection, but not sooner, if your headache came back after your first injection.
- Do not take more than 12 mg in a 24-hour period.
- If you use too much IMITREX, call your healthcare provider or go to the nearest hospital emergency room right away.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- You should write down when you have headaches and when you take IMITREX so you can talk with your healthcare provider about how IMITREX is working for you.

What should I avoid while taking IMITREX?

IMITREX can cause dizziness, weakness, or drowsiness. If you have these symptoms, do not drive a car, use machinery, or do anything where you need to be alert.

What are the possible side effects of IMITREX?

IMITREX may cause serious side effects. See "What is the most important information I should know about IMITREX?"

These serious side effects include:

- changes in color or sensation in your fingers and toes (Raynaud's syndrome)
- stomach and intestinal problems (gastrointestinal and colonic ischemic events). Symptoms of gastrointestinal and colonic ischemic events include:
  - sudden or severe stomach pain
  - stomach pain after meals
  - weight loss
  - nausea or vomiting
  - constipation or diarrhea
  - bloody diarrhea
  - fever
- problems with blood circulation to your legs and feet (peripheral vascular ischemia). Symptoms of peripheral vascular ischemia include:
  - cramping and pain in your legs or hips
  - feeling of heaviness or tightness in your leg muscles
  - burning or aching pain in your feet or toes while resting
  - numbness, tingling, or weakness in your legs
  - cold feeling or color changes in 1 or both legs or feet
- medication overuse headaches. Some people who use too many IMITREX injections may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with IMITREX.
- serotonin syndrome. Serotonin syndrome is a rare but serious problem that can happen in people using IMITREX, especially if IMITREX is used with anti-depressant medicines called SSRIs or SNRIs.

  Call your healthcare provider right away if you have any of the following symptoms of serotonin syndrome:

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

- mental changes such as seeing things that are not there (hallucinations), agitation, or coma
- fast heartbeat
- changes in blood pressure
- high body temperature
- tight muscles
- trouble walking

- seizures. Seizures have happened in people taking IMITREX who have never had seizures before. Talk with your healthcare provider about your chance of having seizures while you take IMITREX.

The most common side effects of IMITREX include:

- pain or redness at your injection site
- tingling or numbness in your fingers or toes
- dizziness
- warm, hot, burning feeling to your face (flushing)
- discomfort or stiffness in your neck
- feeling weak, drowsy, or tired

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of IMITREX. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store IMITREX Injection?

- Store IMITREX between 36°F to 86°F (2°C to 30°C).
- Store your medicine away from light.
- Keep your medicine in the packaging or carrying case provided with it.

Keep IMITREX and all medicines out of the reach of children.

General information about the safe and effective use of IMITREX

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use IMITREX for a condition for which it was not prescribed. Do not give IMITREX to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about IMITREX. If you would like more information, talk with your healthcare provider.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

You can ask your healthcare provider or pharmacist for information about IMITREX that is written for healthcare professionals.

For more information, go to www.gsk.com or call 1-888-825-5249.

What are the ingredients in IMITREX Injection?

Active ingredient: sumatriptan succinate

Inactive ingredients: sodium chloride, water for injection

Month Year
IMJ:xPPI

Patient Instructions for Use
IMITREX STATdose System®

Read this Patient Instructions for Use before you start to use the IMITREX STATdose System. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment. You and your healthcare provider should talk about IMITREX Injection when you start taking it and at regular checkups.

Keep the IMITREX STATdose System out of the reach of children.

Before you use the IMITREX STATdose System

When you first open the IMITREX STATdose System box, the Cartridge Pack and the IMITREX STATdose Pen® are already in the Carrying Case for your convenience.

The grey and blue **Carrying Case** is used for storing the unloaded Pen and the Cartridge Pack when they are not being used.

The **Cartridge Pack** holds 2 individually sealed **Syringe Cartridges**. Each Syringe Cartridge holds 1 dose of IMITREX® (sumatriptan succinate) Injection. The Cartridge Pack for the 4-mg strength of this

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

medicine is yellow, and the Cartridge Pack for the 6-mg strength is blue (as shown). Refill Cartridge Packs are available.

The grey and blue **Pen** is used to automatically inject 1 dose of medicine from a Syringe Cartridge. Do not touch the **Blue Button** until you have pressed the Pen against your skin to give a dose. If you press it at any other time, you might lose a dose. The **Safety Catch** keeps the Pen from accidentally firing until you are ready. The Pen will only work when you slide the grey part of the barrel down to the blue part. Always check to make sure that the white Priming Rod is not sticking out from the end of the Pen (as shown in Figure B) before you load a new Syringe Cartridge. If it is sticking out, you will lose that dose.

How to load the IMITREX STATdose Pen

Do not load the Pen until you are ready to give yourself an injection.
Do not touch the Blue Button on top of the Pen (see Figure A)
while you are loading the Pen.

Figure A

1. Open the lid of the Carrying Case. The tamper-evident seals over the 2 Syringe Cartridges are labeled “A” and “B” **(see Figure A inset)**.

   Always use the Syringe Cartridge marked “A” before the one marked “B” to help you keep track of your doses. **Do not use if either seal is broken or missing when you first open the Carrying Case.**

2. Tear off one of the tamper-evident seals **(see Figure A)**. Throw away the seal. Open the lid over the Syringe Cartridge.

Figure B

3. Hold the Pen by the ridges at the top. Take the Pen out of the Carrying Case **(see Figure B)**.

   Check to make sure the white Priming Rod is not sticking out from the lower end of the Pen **(see Figure B inset)**. If it is sticking out, put the Pen back into the Carrying Case and press down firmly until you feel it click. Take the Pen out of the Carrying Case.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Figure C

Figure D

4. Put the Pen in the Cartridge Pack. Turn it to the right (clockwise) until it will not turn any more (about half a turn) **(see Figure C)**.

5. Hold the loaded Pen by the ridges and pull it **straight out (see Figure D)**. You may need to pull hard on the Pen, but this is normal. **Do not** press the Blue Button yet.

The Pen is now ready to use. **Do not** put the loaded Pen back into the Carrying Case because that will damage the needle.

How to use the IMITREX STATdose Pen to take your medicine

Before injecting your medicine, choose an area with a fatty tissue layer (see Figure E **or** Figure F). Ask your healthcare provider if you have a question about where to inject your medicine.

To prepare the area of skin where IMITREX is to be injected, wipe the injection site with an alcohol swab. Do not touch this area again before giving the injection.

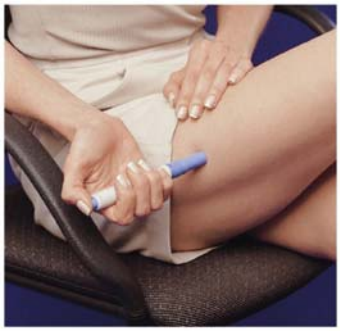


Figure E

or

Figure F

Figure G

6. Without pushing the Blue Button, press the loaded Pen firmly against the skin so that the grey barrel slides down toward the blue section that holds the

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Syringe Cartridge **(see Figure D)**. (This releases the Safety Catch that keeps the Pen from firing by mistake until you are ready.)

7. Push the Blue Button. Hold the Pen still for **at least 5 seconds**. If the Pen is taken away from the skin too soon, not all the medicine will come out.

8. **After 5 seconds,** carefully take the Pen away from your skin. The needle will be showing **(see Figure G)**. **Do not touch the needle.**

How to unload the IMITREX STATdose Pen after taking your medicine

Right after you take a dose with the Pen, you need to return the used Syringe Cartridge to the Cartridge Pack.

Figure H

Figure I

Figure J

9. Push the Pen down into the empty side of the Cartridge Pack as far as it will go **(see Figure H)**.

10. Turn the Pen to the left (counterclockwise) about half a turn until it is released from the Syringe Cartridge **(see Figure I)**.

11. Pull the empty Pen out of the Cartridge Pack **(see Figure J)**.

    Because the Pen has now been used, the white Priming Rod will stick out from the lower end of the Pen **(see Figure J)**.

12. Close the Cartridge Pack lid over the used Syringe Cartridge. When the used Syringe Cartridges are inserted correctly, the Cartridge Pack is a disposable, protective case to help you avoid needle sticks and use the syringes correctly.

13. Put the Pen back into the Carrying Case and press it down firmly until you feel it click. Close the Carrying Case lid. This gets the Pen ready for the next use.

    If the lid will not close, push the Pen down until you feel it click. Then close the lid.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

How to take out a used Cartridge Pack

After both Syringe Cartridges have been used, take the Cartridge Pack out of the Carrying Case. **Never reuse or recycle a Syringe Cartridge.**

Figure K

Figure L

14. Open the Carrying Case lid.
15. Hold the Carrying Case with one hand and press the 2 buttons on either side of the Carrying Case **(see Figure K)**.
16. Gently pull out the Cartridge Pack with the other hand **(see Figure L)**.
17. Throw away the Cartridge Pack or dispose of it as instructed by your healthcare provider. There may be special state and local laws for disposing of used needles and syringes. Always keep out of the reach of children.

How to insert a new Cartridge Pack

Figure M

Figure N

Figure O

17. Take the new Cartridge Pack out of its box. **Do not take off the tamper-evident seals (see Figure M)**.
18. Put the Cartridge Pack in the Carrying Case. Slide it down smoothly **(see Figure N)**.
19. The Cartridge Pack will click into place when the 2 buttons show through the holes in the Carrying Case **(see Figure O)**. Close the lid.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

AMERGE, IMITREX, IMITREX STATdose System, IMITREX STATdose Pen, and TREXIMET are registered trademarks of GlaxoSmithKline. The other brands listed are trademarks of their respective owners and are not trademarks of GlaxoSmithKline. The makers of these brands are not affiliated with and do not endorse GlaxoSmithKline or its products.

GlaxoSmithKline
Research Triangle Park, NC 27709

©2012, GlaxoSmithKline. All rights reserved.

Month Year
IMJ:xPIL