

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SUMATRIPTAN TABLETS, USP safely and effectively. See full prescribing information for SUMATRIPTAN TABLETS, USP.

SUMATRIPTAN tablets, USP, for oral use
Initial U.S. Approval: 1992

INDICATIONS AND USAGE

Sumatriptan tablets, USP are 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 25 mg, 50 mg, or 100 mg tablet. (2.1)
- A second dose should only be considered if some response to the first dose was observed. Separate doses by at least 2 hours. (2.1)
- Maximum dose in a 24-hour period: 200 mg. (2.1)
- Maximum single dose should not exceed 50 mg in patients with mild to moderate hepatic impairment. (2.2)

DOSAGE FORMS AND STRENGTHS

Tablets: 25 mg, 50 mg, and 100 mg (3)

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

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Sumatriptan tablets, USP are 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 sumatriptan tablets, USP, reconsider the diagnosis of migraine before sumatriptan tablets, USP are administered to treat any subsequent attacks.
- Sumatriptan tablets, USP are not indicated for the prevention of migraine attacks.
- Safety and effectiveness of sumatriptan tablets have not been established for cluster headache.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended dose of sumatriptan tablets is 25 mg, 50 mg, or 100 mg. Doses of 50 mg and 100 mg may provide a greater effect than the 25 mg dose, but doses of 100 mg may not provide a greater effect than the 50 mg dose. Higher doses may have a greater risk of adverse reactions [see *Clinical Studies* (14)].

If the migraine has not resolved by 2 hours after taking sumatriptan tablets, or returns after a transient improvement, a second dose may be administered at least 2 hours after the first dose. The maximum daily dose is 200 mg in a 24-hour period.

Use after sumatriptan injection

If the migraine returns following an initial treatment with sumatriptan succinate injection, additional single sumatriptan tablets (up to 100 mg/day) may be given with an interval of at least 2 hours between tablet doses. The safety of treating an average of more than 4 headaches in a 30-day period has not been established.

2.2 Dosing in Patients with Hepatic Impairment

If treatment is deemed advisable in the presence of mild to moderate hepatic impairment, the maximum single dose should not exceed 50 mg [see *Use in Specific Populations* (8.6), *Clinical Pharmacology* (12.3)].

3 DOSAGE FORMS AND STRENGTHS

25 mg Tablets: White to off-white, round, biconvex, uncoated tablets, debossed with "R161" on one side and plain on the other side.

50 mg Tablets: White to off-white, round, biconvex, uncoated tablets, debossed with "R162" on one side and plain on the other side.

100 mg Tablets: White to off-white, capsule-shaped, biconvex, uncoated tablets, debossed with "R897" on one side and plain on the other side.

4 CONTRAINDICATIONS

Sumatriptan tablets are 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 or 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 medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine₁ (5-HT₁) agonist [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), *Clinical Pharmacology* (12.3)]
- Hypersensitivity to sumatriptan (angioedema and anaphylaxis seen) [see *Warnings and Precautions* (5.9)]
- Severe hepatic impairment [see *Use in Specific Populations* (8.6), *Clinical Pharmacology* (12.3)]

5 WARNINGS AND PRECAUTIONS

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

The use of sumatriptan tablets 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 sumatriptan tablets. Some of these reactions occurred in patients without known CAD. Sumatriptan tablets may cause coronary artery vasospasm (Prinzmetal's angina), even in patients without a history of CAD.

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

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-HT₁ agonists. Discontinue sumatriptan tablets if these disturbances occur. Sumatriptan tablets are contraindicated in patients with Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.

- triptan) or of an ergotamine-containing medication. (4)
- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor. (4)
- Hypersensitivity to sumatriptan (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 sumatriptan 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 sumatriptan if occurs. (5.4)
- Gastrointestinal ischemic reactions and peripheral vasospastic reactions: Discontinue sumatriptan if occurs. (5.5)
- Medication overuse headache: Detoxification may be necessary. (5.6)
- Serotonin syndrome: Discontinue sumatriptan if occurs. (5.7)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.10)

ADVERSE REACTIONS

Most common adverse reactions (≥ 2% and > placebo) were paresthesia, warm/cold sensation, chest pain/tightness/pressure and/or heaviness, neck/throat/jaw pain/tightness/pressure, other sensations of pain/pressure/tightness/heaviness, vertigo, and malaise/fatigue. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-406-7984 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)

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

Revised: 09/2020

- Monoamine Oxidase-A Inhibitors
- Other 5-HT₁ Agonists
- Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome

8 USE IN SPECIFIC POPULATIONS

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

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 commonly occur after treatment with sumatriptan tablets and are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk. The use of sumatriptan tablets 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-HT₁ agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the 5-HT₁ 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 sumatriptan tablets 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. Sumatriptan tablets are contraindicated in patients with a history of stroke or TIA.

5.5 Other Vasospasm Reactions

Sumatriptan tablets 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-HT₁ agonist, rule out a vasospastic reaction before receiving additional sumatriptan tablets.

Reports of transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT₁ agonists. Since visual disorders may be part of a migraine attack, a causal relationship between these events and the use of 5-HT₁ agonists has 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 sumatriptan tablets, 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 sumatriptan tablets 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 in rare occasions in patients treated with 5-HT₁ agonists, including patients without a history of hypertension. Monitor blood pressure in patients treated with sumatriptan. Sumatriptan tablets are 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. Sumatriptan tablets are contraindicated in patients with a history of hypersensitivity reaction to sumatriptan.

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. Sumatriptan tablets 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 prescribing information:

- 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)]
- Serotonin syndrome [see *Warnings and Precautions* (5.7)]
- Increase in blood pressure [see *Warnings and Precautions* (5.8)]
- Hypersensitivity reactions [see *Contraindications* (4), *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.

Table 1 lists adverse reactions that occurred in placebo-controlled clinical

trials in patients who took at least 1 dose of study drug. Only treatment-emergent adverse reactions that occurred at a frequency of 2% or more in any group treated with sumatriptan tablets 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 Patients Treated with Sumatriptan Tablets and at a Greater Frequency than Placebo

Adverse Reaction	Percent of Patients Reporting			
	Sumatriptan Tablets 25 mg (n = 417)	Sumatriptan Tablets 50 mg (n = 771)	Sumatriptan Tablets 100 mg (n = 437)	Placebo (n = 309)
Atypical sensations	5	6	6	4
Paresthesia (all types)	3	5	3	2
Sensation warm/cold	3	2	3	2
Pain and other pressure sensations	6	6	8	4
Chest - pain/tightness/pressure and/or heaviness	1	2	2	1
Neck/throat/jaw - pain/tightness/pressure	<1	2	3	<1
Pain - location specified	2	1	1	1
Other - pressure/tightness/heaviness	1	1	3	2
Neurological				
Vertigo	<1	<1	2	<1
Other				
Malaise/fatigue	2	2	3	<1

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

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of sumatriptan tablets, sumatriptan nasal spray, and sumatriptan 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 sumatriptan or a combination of these factors.

Cardiovascular
Hypotension, palpitations.

Neurological
Dystonia, tremor.

7 DRUG INTERACTIONS

7.1 Ergot-Containing Drugs

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 sumatriptan tablets within 24 hours of each other is contraindicated.

7.2 Monoamine Oxidase-A Inhibitors

MAO-A inhibitors increase systemic exposure by 7-fold. Therefore, the use of sumatriptan tablets in patients receiving MAO-A inhibitors is contraindicated [see *Clinical Pharmacology* (12.3)].

7.3 Other 5-HT₁ Agonists

Because their vasospastic effects may be additive, coadministration of sumatriptan tablets and other 5-HT₁ 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, SNRIs, TCAs, and MAO inhibitors [see *Warnings and Precautions* (5.7)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Data from a prospective pregnancy exposure registry and epidemiological studies of pregnant women have not detected an increased frequency of birth defects or a consistent pattern of birth defects among women exposed to sumatriptan compared with the general population (see *Data*). In developmental toxicity studies in rats and rabbits, oral administration of sumatriptan to pregnant animals was associated with embryolethality, fetal abnormalities, and pup mortality. When administered by the intravenous route to pregnant rabbits, sumatriptan was embryolethal (see *Data*).

In the U.S. general population, the estimated background risk of major birth defects and of miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The reported rate of major birth defects among deliveries to women with migraine ranged from 2.2% to 2.9% and the reported rate of miscarriage was 17%, which were similar to rates reported in women without migraine.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: Several studies have suggested that women with migraine may be at increased risk of preclampsia during pregnancy.

Data

Human Data: The Sumatriptan/Naratriptan/Treximet (sumatriptan and naproxen sodium) Pregnancy Registry, a population-based international prospective study, collected data for sumatriptan from January 1996 to September 2012. The Registry documented outcomes of 626 infants and fetuses exposed to sumatriptan during pregnancy (528 with earliest exposure during the first trimester, 78 during the second trimester, 16 during the third trimester, and 4 unknown). The occurrence of major birth defects (excluding fetal deaths and induced abortions without reported defects and all spontaneous pregnancy losses) during first-trimester exposure to sumatriptan was 4.2% (20/478 [95% CI: 2.6% to 6.5%]) and during any trimester of exposure was 4.2% (24/576 [95% CI: 2.7% to 6.2%]). The sample size in this study had 80% power to detect at least a 1.73 to 1.91-fold increase in the rate of major malformations. The number of exposed pregnancy outcomes accumulated during the registry was insufficient to support definitive conclusions about overall malformation risk or for making comparisons of the frequencies of specific birth defects. Of the 20 infants with reported birth defects after exposure to sumatriptan in the first trimester, 4 infants had ventricular septal defects, including one infant who was exposed to both sumatriptan and naratriptan, and 3 infants had pyloric stenosis. No other birth defect was reported for more than 2 infants in this group.

In a study using data from the Swedish Medical Birth Register, live births to women who reported using triptans or ergots during pregnancy were compared with those of women who did not. Of the 2,257 births with first-trimester exposure to sumatriptan, 107 infants were born with malformations (relative risk 0.99 [95% CI: 0.91 to 1.21]). A study using linked data from the Medical Birth Registry of Norway to the Norwegian Prescription Database compared pregnancy outcomes in women who redeemed prescriptions for triptans during pregnancy, as well as a migraine disease comparison group who redeemed prescriptions for sumatriptan before pregnancy only, compared with a population control group. Of the 415 women who redeemed prescriptions for sumatriptan during the first trimester, 15 had infants with major congenital malformations (OR 1.16 [95% CI: 0.69 to 1.94]) while for the 364 women who redeemed prescriptions for sumatriptan before, but not during, pregnancy, 20 had infants with major congenital malformations (OR 1.83 [95% CI: 1.17 to 2.88]), each compared with the population comparison group. Additional smaller observational studies evaluating use of sumatriptan during pregnancy have not suggested an increased risk of teratogenicity.

Animal Data: Oral administration of sumatriptan to pregnant rats during the period of organogenesis resulted in an increased incidence of fetal blood vessel (cervicothoracic and umbilical) abnormalities. The highest no-effect dose for embryofetal developmental toxicity in rats was 60 mg/kg/day, or approximately 3 times the maximum recommended human dose (MRHD) of 200 mg/day on a mg/m² basis. Oral administration of sumatriptan to pregnant rabbits during the period of organogenesis resulted in increased incidences of embryolethality and fetal cervicothoracic vascular and skeletal abnormalities. Intravenous administration of sumatriptan to pregnant rabbits during the period of organogenesis resulted in an increased incidence of embryolethality. The highest oral and intravenous no-effect doses for developmental toxicity in rabbits were 15 (approximately 2 times the MRHD on a mg/m² basis) and 0.75 mg/kg/day, respectively.

Oral administration of sumatriptan to rats prior to and throughout gestation resulted in embryofetal toxicity (decreased body weight, decreased ossification, increased incidence of skeletal abnormalities). The highest no-effect dose for this effect was 60 mg/kg/day, or approximately 3 times the MRHD on a mg/m² basis. Oral treatment of pregnant rats with sumatriptan during the latter part of gestation and throughout lactation resulted in a decrease in pup survival. The highest no-effect dose for this finding was 100 mg/kg/day, or approximately 5 times the MRHD on a mg/m² basis.

8.2 Lactation

Risk Summary

Sumatriptan is excreted in human milk following subcutaneous administration (see *Data*). There is no information regarding sumatriptan concentrations in milk from lactating women following administration of sumatriptan tablets. There are no data on the effects of sumatriptan on the breastfed infant or the effects of sumatriptan on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sumatriptan tablets and any potential adverse effects on the breastfed infant from sumatriptan or from the underlying maternal condition.

Clinical Considerations

Infant exposure to sumatriptan can be minimized by avoiding breastfeeding for 12 hours after treatment with sumatriptan tablets.

Data

Following subcutaneous administration of a 6 mg dose of sumatriptan injection in 5 lactating volunteers, sumatriptan was present in milk.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

PATIENT INFORMATION

SUMATRIPTAN (sue-mah-TRIP-tan) TABLETS, USP

Rx only

What is the most important information I should know about sumatriptan tablets, USP? Sumatriptan tablets, USP can cause serious side effects, including: Heart attack and other heart problems. Heart problems may lead to death. Stop taking sumatriptan tablets, USP 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

Sumatriptan tablets, USP are 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 are sumatriptan tablets, USP?

Sumatriptan tablets, USP are a prescription

- Take sumatriptan tablets, USP whole with water or other liquids.
- If you do not get any relief after your first tablet, do not take a second tablet without first talking with your healthcare provider.
- If your headache comes back or you only get some relief from your headache, you can take a second tablet 2 hours after the first tablet.
- Do not take more than 200 mg of sumatriptan tablets, USP in a 24-hour period.
- If you take too much sumatriptan tablets, USP, 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 sumatriptan tablets, USP so you can talk with your healthcare provider about how sumatriptan tablets, USP is working for you.

What should I avoid while taking sumatriptan tablets, USP?

Sumatriptan tablets, USP 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 sumatriptan tablets, USP?

Sumatriptan tablets, USP may cause serious side effects. See "What is the most important information I should know about sumatriptan tablets, USP?"

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
- fever
- nausea or vomiting
- constipation or diarrhea
- bloody diarrhea
- 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 sumatriptan tablets, USP may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with sumatriptan tablets, USP.

- serotonin syndrome. Serotonin syndrome is a rare but serious problem that can happen in people using sumatriptan tablets, USP, especially if sumatriptan tablets, USP are 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

- hives (itchy bumps); swelling of your tongue, mouth, or throat.
- seizures. Seizures have happened in people taking sumatriptan tablets, USP who have never had seizures before. Talk with your healthcare provider about your chance of having seizures while you take sumatriptan tablets, USP.

The most common side effects of sumatriptan tablets, USP include:

- tingling or numbness in your fingers or toes
- warm or cold feeling
- feeling weak, drowsy, or tired
- pain, discomfort, or stiffness in your neck, throat, jaw, or chest
- dizziness

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 sumatriptan tablets, USP. 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 sumatriptan tablets, USP?

Store sumatriptan tablets, USP between 68° F to 77° F (20° C to 25° C).

Keep sumatriptan tablets, USP and all medicines out of the reach of children.

General information about the safe and effective use of sumatriptan tablets, USP.

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use sumatriptan tablets, USP for a condition for which it was not prescribed. Do not give sumatriptan tablets, USP 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 sumatriptan tablets, USP. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about sumatriptan tablets, USP that is written for healthcare professionals. For more information, call 1-888-726-2299.

What are the ingredients in sumatriptan tablets, USP? Active ingredient: sumatriptan succinate, USP. Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, lactose anhydrous, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and talc. This Patient Information has been approved by the U.S. Food and Drug Administration. The brands listed are trademarks of their respective owners.

Manufactured by:
Ohm Laboratories Inc.
New Brunswick, NJ 08901

Distributed by:
Sun Pharmaceutical Industries, Inc.
Cranbury, NJ 08512

September 2020 FDA-11

Sumatriptan tablets are not recommended for use in patients younger than 18 years of age.

Two controlled clinical trials evaluated sumatriptan 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 sumatriptan 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 sumatriptan (25 to 100 mg) in pediatric patients aged 12 to 17 years enrolled a total of 701 adolescent migraineurs. These trials did not establish the efficacy of oral sumatriptan 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 patients appeared to be both dose- and age-dependent, with younger patients 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 sumatriptan. 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 sumatriptan; clinical signs occurred within 1 day of drug administration. Clinical data to determine the frequency of serious adverse reactions in pediatric patients who might receive subcutaneous, oral, or intranasal sumatriptan are not presently available.

8.5 Geriatric Use

Clinical trials of sumatriptan tablets did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. 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 sumatriptan tablets [See *Warnings and Precautions* (5.1)].

8.6 Hepatic Impairment

The maximum single dose in patients with mild to moderate hepatic impairment should not exceed 50 mg. Sumatriptan tablets are contraindicated in patients with severe hepatic impairment [See *Clinical Pharmacology* (12.3)].

10 OVERDOSAGE

Patients in clinical trials (N = 670) received single oral doses of 140 to 300 mg without significant adverse reactions. Volunteers (N = 174) received single oral doses of 140 to 400 mg without serious adverse reactions.

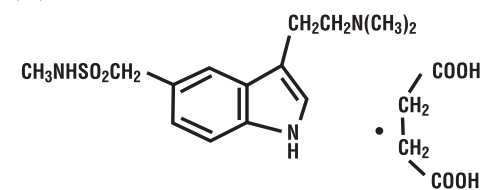
Overdose in animals has been fatal and has been heralded by convulsions, tremor, paralysis, inactivity, ptosis, erythema of the extremities, abnormal respiration, cyanosis, ataxia, mydriasis, salivation, and lacrimation.

The elimination half-life of sumatriptan is approximately 2.5 hours [See *Clinical Pharmacology* (12.3)], and therefore monitoring of patients after overdose with sumatriptan tablets should continue for at least 12 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

Sumatriptan tablets, USP contain 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 molecular formula is C₁₄H₂₁N₃O₅S•C₄H₆O₄, representing a molecular weight of 413.5. Sumatriptan succinate, USP is a white or almost white powder that is freely soluble in water, sparingly soluble in methanol and practically insoluble in methylene chloride.

Each sumatriptan tablet, USP for oral administration contains 35, 70, or 140 mg of sumatriptan succinate, USP equivalent to 25, 50, or 100 mg of sumatriptan, respectively. Each tablet also contains the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, lactose anhydrous, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and talc.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Sumatriptan binds with high affinity to human cloned 5-HT_{1B/1D} receptors. Sumatriptan presumably exerts its therapeutic effects in the treatment of migraine headache through agonist effects at the 5-HT_{1B/1D} receptors on intracranial blood vessels 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 patients 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

The mean maximum concentration following oral dosing with 25 mg is 18 ng/mL (range: 7 to 47 ng/mL) and 51 ng/mL (range: 28 to 100 ng/mL) following oral dosing with 100 mg of sumatriptan. This compares with a C_{max} of 5 and 16 ng/mL following dosing with a 5 and 20 mg intranasal dose, respectively. The mean C_{max} following a 6 mg subcutaneous injection is 71 ng/mL (range: 49 to 110 ng/mL). The bioavailability is approximately 15%, primarily due to presystemic metabolism and partly due to incomplete absorption. The C_{max} is similar during a migraine attack and during a migraine-free period, but the T_{max} is slightly later during the attack, approximately 2.5 hours compared with 2 hours. When given as a single dose, sumatriptan displays dose proportionality in its extent of absorption (area under the curve [AUC]) over the dose range of 25 to 200 mg, but the C_{max} after 100 mg is approximately 25% less than expected (based on the 25 mg dose).

Effect of Food: A food effect trial involving administration of sumatriptan tablets 100 mg to healthy volunteers under fasting conditions and with a high-fat meal indicated that the C_{max} and AUC were increased by 15% and 12%, respectively, when administered in the fed state.

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. The apparent volume of distribution is 2.7 L/kg.

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

The elimination half-life of sumatriptan is approximately 2.5 hours. Radiolabeled ¹⁴C-sumatriptan administered orally is largely renally excreted (about 60%) with about 40% found in the feces. Most of the radiolabeled compound excreted in the urine is the major metabolite, IAA, which is inactive, or the IAA glucuronide. Only 3% of the dose can be recovered as unchanged sumatriptan.

Specific 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).

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

Patients with Hepatic Impairment: The liver plays an important role in the presystemic clearance of orally administered sumatriptan. Accordingly, the bioavailability of sumatriptan following oral administration may be markedly increased in patients with liver disease. In one small trial of patients with moderate liver impairment (n = 8) matched for sex, age, and weight with healthy subjects (n = 8), the hepatically-impaired patients had an approximately 70% increase in AUC and C_{max}, and a T_{max} 40 minutes earlier compared with the healthy subjects.

The pharmacokinetics of sumatriptan in patients with severe hepatic impairment has not been studied. The use of sumatriptan tablets in this population is contraindicated [See *Contraindications* (4), *Use in Specific Populations* (8.6)].

Male and Female Patients: In a trial comparing females to males, no pharmacokinetic differences were observed between genders for AUC, C_{max}, T_{max}, and half-life.

Racial Groups: The systemic clearance and C_{max} of subcutaneous sumatriptan were similar in black (n = 34) and Caucasian (n = 38) healthy male subjects. Oral sumatriptan has not been evaluated for race differences.

Drug Interaction Studies

Monoamine Oxidase-A Inhibitors: Treatment with MAO-A inhibitors generally leads to an increase of sumatriptan plasma levels [See *Contraindications* (4), *Drug Interactions* (7.2)].

Due to gut and hepatic metabolic first-pass effects, the increase of systemic exposure after coadministration of an MAO-A inhibitor with oral sumatriptan is greater than after coadministration of the MAO inhibitors with subcutaneous sumatriptan.

In a trial of 14 healthy females, pretreatment with an MAO-A inhibitor decreased the clearance of subcutaneous 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.

A small trial evaluating the effect of pretreatment with an MAO-A inhibitor on the bioavailability from a 25 mg oral sumatriptan tablet resulted in an approximately 7-fold increase in systemic exposure.

Alcohol: Alcohol consumed 30 minutes prior to sumatriptan ingestion had no effect on the pharmacokinetics of sumatriptan.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In carcinogenicity studies in mouse and rat, sumatriptan was administered orally for 78 and 104 weeks, respectively, at doses up to 160 mg/kg/day (the high dose in rat was reduced from 360 mg/kg/day during Week 21). There was no evidence in either species of an increase in tumors related to sumatriptan administration. Plasma exposures (AUC) at the highest doses tested were 20 and 8 times that in humans at the maximum recommended human dose (MRHD) of 200 mg/day.

Mutagenesis

Sumatriptan was negative in *in vitro* (bacterial reverse mutation [Ames], gene cell mutation in Chinese hamster V79/HGPRT, chromosomal aberration in human lymphocytes) and *in vivo* (rat micronucleus) assays.

Impairment of Fertility

When sumatriptan (5, 50, 500 mg/kg/day) was administered orally to male and female rats prior to and throughout the mating period, there was a treatment-related decrease in fertility secondary to a decrease in mating in animals treated with doses greater than 5 mg/kg/day (less than the MRHD on a mg/m² basis). It is not clear whether this finding was due to an effect on males or females or both.

When sumatriptan was administered by subcutaneous injection to male and female rats prior to and throughout the mating period, there was no evidence of impaired fertility at doses up to 60 mg/kg/day.

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 dose 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. Plasma exposure at the lowest dose tested was approximately 2 times that in humans at the MRHD.

14 CLINICAL STUDIES

The efficacy of sumatriptan tablets in the acute treatment of migraine headaches was demonstrated in 3, randomized, double-blind, placebo-controlled trials. Patients enrolled in these 3 trials were predominately female (87%) and Caucasian (97%), with a mean age of 40 years (range: 18 to 65 years). Patients were instructed to treat a moderate to severe headache. Headache response, defined as a reduction in headache severity from moderate or severe pain to mild or no pain, was assessed up to 4 hours after dosing. Associated symptoms such as nausea, photophobia, and phonophobia were also assessed. Maintenance of response was assessed for up to 24 hours postdose. A second dose of sumatriptan tablets or other medication was allowed 4 to 24 hours after the initial treatment for recurrent headache. Acetaminophen was offered to patients in Trials 2 and 3 beginning at 2 hours after initial treatment if the migraine pain had not improved or had worsened. Additional medications were allowed 4 to 24 hours after the initial treatment for recurrent headache or as rescue in all 3 trials. The frequency and time to use of these additional treatments were also determined. In all trials, doses of 25, 50, and 100 mg were compared with placebo in the treatment of migraine attacks. In Trial 1, doses of 25, 50, and 100 mg were also compared with each other.

In all 3 trials, the percentage of patients achieving headache response 2 and 4 hours after treatment was significantly greater among patients receiving sumatriptan tablets at all doses compared with those who received placebo. In 1 of the 3 trials, there was a statistically significant greater percentage of patients with headache response at 2 and 4 hours in the 50 mg or 100 mg group when compared with the 25 mg dose groups. There were no statistically significant differences between the 50 mg and 100 mg dose groups in any trial. The results from the 3 controlled clinical trials are summarized in Table 2.

Table 2. Percentage of Patients with Headache Response (Mild or No Headache) 2 and 4 Hours following Treatment

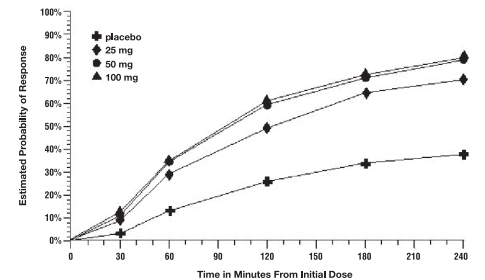
Trial	Sumatriptan Tablets 25 mg		Sumatriptan Tablets 50 mg		Sumatriptan Tablets 100 mg		Placebo	
	2 h	4 h	2 h	4 h	2 h	4 h	2 h	4 h
Trial 1	52% ^a	67% ^a	61% ^{a,b}	78% ^{a,b}	62% ^{a,b}	79% ^{a,b}	27%	38%
	(n = 298)		(n = 296)		(n = 296)		(n = 94)	
Trial 2	52% ^a	70% ^a	50% ^a	68% ^a	56% ^a	71% ^a	26%	38%
	(n = 66)		(n = 62)		(n = 66)		(n = 65)	
Trial 3	52% ^a	65% ^a	54% ^a	72% ^a	57% ^a	78% ^a	17%	19%
	(n = 48)		(n = 46)		(n = 46)		(n = 47)	

^a P < 0.05 in comparison with placebo.

^b P < 0.05 in comparison with 25 mg.

The estimated probability of achieving an initial headache response over the 4 hours following treatment in pooled Trials 1, 2, and 3 is depicted in Figure 1.

Figure 1. Estimated Probability of Achieving Initial Headache Response within 4 Hours of Treatment in Pooled Trials 1, 2, and 3^a

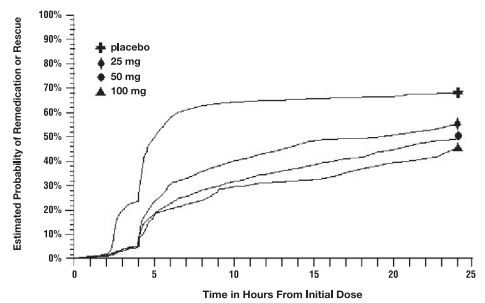


^a The figure shows the probability over time of obtaining headache response (no or mild pain) following treatment with oral sumatriptan. The averages displayed are based on pooled data from the 3 clinical controlled trials providing evidence of efficacy. Kaplan-Meier plot with patients not achieving response and/or taking rescue within 240 minutes censored to 240 minutes.

For patients with migraine-associated nausea, photophobia, and/or phonophobia at baseline, there was a lower incidence of these symptoms at 2 hours (Trial 1) and at 4 hours (Trials 1, 2, and 3) following administration of sumatriptan tablets compared with placebo.

As early as 2 hours in Trials 2 and 3, or as early as 4 hours in Trial 1, through 24 hours following the initial dose of study treatment, patients were allowed to use additional treatment for pain relief in the form of a second dose of study treatment or other medication. The estimated probability of patients taking a second dose or other medication for migraine over the 24 hours following the initial dose of study treatment is summarized in Figure 2.

Figure 2. The Estimated Probability of Patients Taking a Second Dose of Sumatriptan Tablets or Other Medication to Treat Migraine over the 24 Hours following the Initial Dose of Study Treatment in Pooled Trials 1, 2, and 3^a



^a Kaplan-Meier plot based on data obtained in the 3 clinical controlled trials providing evidence of efficacy with patients not using additional treatments censored to 24 hours. Plot also includes patients who had no response to the initial dose. No remedication was allowed within 2 hours postdose.

There is evidence that doses above 50 mg do not provide a greater effect than 50 mg. There was no evidence to suggest that treatment with sumatriptan tablets was associated with an increase in the severity of recurrent headaches. The efficacy of sumatriptan tablets was unaffected by presence of aura; duration of headache prior to treatment; gender, age, or weight of the subject; relationship to menses; or concomitant use of common migraine prophylactic drugs (e.g., beta-blockers, calcium channel blockers, tricyclic antidepressants). There were insufficient data to assess the impact of race on efficacy.

16 HOW SUPPLIED/STORAGE AND HANDLING

Sumatriptan tablets, USP, 25 mg, 50 mg, and 100 mg of sumatriptan (base) as the succinate.

Sumatriptan tablets, USP, 25 mg, are white to off-white, round, biconvex, uncoated tablets, debossed with "R161" on one side and plain on the other side.

NDC 63304-097-45 Bottles of 5
NDC 63304-097-13 Bottles of 120
NDC 63304-097-19 Blisters of 9

Sumatriptan tablets, USP, 50 mg, are white to off-white, round, biconvex, uncoated tablets, debossed with "R162" on one side and plain on the other side.

NDC 63304-098-45 Bottles of 5
NDC 63304-098-13 Bottles of 120
NDC 63304-098-19 Blisters of 9

Sumatriptan tablets, USP, 100 mg, are white to off-white, capsule-shaped, biconvex, uncoated tablets, debossed with "R997" on one side and plain on the other side.

NDC 63304-099-09 Bottles of 9
NDC 63304-099-13 Bottles of 120
NDC 63304-099-19 Blisters of 9

Store at 20° - 25° C (68° - 77° F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

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

Inform patients that sumatriptan tablets, USP 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 if any indicative sign or symptoms are observed. Advise patients of the importance of this follow-up [See *Warnings and Precautions* (5.1, 5.2, 5.4, 5.5, 5.8)].

Anaphylactic/Anaphylactoid Reactions

Inform patients that anaphylactic/anaphylactoid reactions have occurred in patients receiving sumatriptan tablets, USP. 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 *Contraindications* (4), *Warnings and Precautions* (5.9)].

Concomitant Use with Other Triptans or Ergot Medications

Inform patients that use of sumatriptan tablets, USP within 24 hours of another triptan or an ergot-type medication (including dihydroergotamine or methysergide) is contraindicated [See *Contraindications* (4), *Drug Interactions* (7.1, 7.3)].

Serotonin Syndrome

Caution patients about the risk of serotonin syndrome with the use of sumatriptan tablets, USP or other triptans, particularly during combined use with SSRIs, SNRIs, TCAs, and MAO inhibitors [See *Warnings and Precautions* (5.7), *Drug Interactions* (7.4)].