APPLICATION NUMBER:
ANDA 079242

LABELING

Labels and Labeling Approved 3/2/2009
SUMATRIPTAN SUCCINATE INJECTION
6 mg (sumatriptan)/0.5 mL*

Sterile, Nonpyrogenic

*Each 0.5 mL of solution contains 6 mg of sumatriptan (as the succinate salt) and 3.5 mg of sodium chloride.

Usual Dosage: See package insert.

Retain in carton until time of use.
Store between 2° and 25°C (36° and 77°F). Protect from light.
Vial stoppers do not contain natural latex rubber.

Rx only
APP Pharmaceuticals, LLC
Schaumburg, IL 60173

NDC 63323-273-01  271301

SUMATRIPTAN SUCCINATE INJECTION
6 mg (sumatriptan)/0.5 mL*
For subcutaneous injection only. Discard unused portion. 1 x 0.5 mL Single Dose Vial Rx only
SUMATRIPTAN SUCCINATE INJECTION
6 mg (sumatriptan)/0.5 mL*
For subcutaneous injection only.
0.5 mL Single Dose Vial
Discard unused portion.

LOT/EXP
Schaumburg, IL 60173
APP Pharmaceuticals, LLC

CrossTech COMMUNICATIONS INC
312 382-0111 FAX 382-0004
SUMATRIPTAN SUCCINATE INJECTION
Rx only

Read this leaflet carefully before you start to take Sumatriptan Succinate Injection. Keep the leaflet for reference because it gives you a summary of important information about Sumatriptan Succinate Injection. Read the leaflet that comes with each refill of your prescription because there may be new information. This leaflet does not have all the information about Sumatriptan Succinate Injection. Ask your healthcare provider for more information or advice.

What is Sumatriptan Succinate Injection?
Sumatriptan Succinate Injection is a 5-HT1 agonist. It is called a “triptan.” You should take it only if you have a prescription. Sumatriptan Succinate Injection is used to relieve your migraine or cluster headache. It is not used to prevent attacks or reduce the number of attacks you have. Use Sumatriptan Succinate Injection only to treat an actual migraine or cluster headache attack.

The decision to use Sumatriptan Succinate Injection is one that you and your healthcare provider should make together, based on your personal needs and health.

Talk with your healthcare provider before taking Sumatriptan Succinate Injection
1. Risk factors for heart disease to tell your healthcare provider:
   Tell your healthcare provider if you have risk factors for heart disease such as:
   • high blood pressure
   • high cholesterol
   • obesity
   • diabetes
   • smoking
   • strong family history of heart disease
   • you are postmenopausal
   • you are a male over 40 years of age
   If you do have risk factors for heart disease, your healthcare provider should check you for heart disease to see if Sumatriptan Succinate Injection is right for you.
Although most of the people who have taken Sumatriptan Succinate Injection have not had any serious side effects, some have had serious heart problems. Deaths have been reported, but these were rare considering the extensive worldwide use of Sumatriptan Succinate Injection. Usually, serious problems happened in people with known heart disease. It was not clear whether Sumatriptan Succinate Injection had anything to do with these deaths.

2. Important questions to ask yourself before you take Sumatriptan Succinate Injection:
If the answer to any of the following questions is YES or if you do not know the answer, then please talk with your healthcare provider before you take Sumatriptan Succinate Injection.

• Are you pregnant? Do you think you might be pregnant? Are you trying to become pregnant? Are you not using adequate contraception? Are you breastfeeding?
• Do you have any chest pain, heart disease, shortness of breath, or irregular heartbeats? Have you had a heart attack?
• Do you have risk factors for heart disease (such as high blood pressure, high cholesterol, obesity, diabetes, smoking, strong family history of heart disease, or you are postmenopausal or a male over 40)?
• Have you had a stroke, transient ischemic attacks (TIAs), or Raynaud syndrome?
• Do you have high blood pressure?
• Have you ever had to stop taking this or any other medicine because of an allergy or other problems?
• Are you taking any other migraine medicines, including other 5-HT, agonists (triptans) or any other medicines containing ergotamine, dihydroergotamine, or methysergide?
• Are you taking any medicine for depression or other disorders such as a monoamine oxidase inhibitor, selective serotonin reuptake inhibitor (SSRI), or serotonin norepinephrine reuptake inhibitor (SNRI)? Common SSRIs are citalopram HBr (CELEXA®), escitalopram oxalate (LEXAPRO®), paroxetine (PAXIL®), fluoxetine (PROZAC®/SARAFEM®), olanzapine/fluoxetine (SYMBAX®), sertraline (ZOLOFT®), and fluvoxamine. Common SNRIs are duloxetine (CYMVALTA®) and venlafaxine (EFFEXOR®).
• Have you had, or do you have, any disease of the liver or kidney?
• Have you had, or do you have, epilepsy or seizures?
• Is this headache different from your usual migraine attacks?
Remember, if you answered YES to any of the above questions, then talk with your healthcare provider about it.

Important points about Sumatriptan Succinate Injection

1. The use of Sumatriptan Succinate Injection during pregnancy:
Do not take Sumatriptan Succinate Injection if you are pregnant, think you might be pregnant, are trying to become pregnant, or are not using adequate contraception unless you have talked with your healthcare provider about this.

2. How to use Sumatriptan Succinate Injection:
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 migraine start, but it may be given at any time during an attack.
You may give a second injection if your migraine symptoms come back. If your symptoms do not get better after the first injection, do not give a second injection for the same attack without first talking with your healthcare provider. Do not give more than two 6-mg doses in any 24-hour period. Allow at least 1 hour between each dose.
3. What to do if you take an overdose:
   If you have taken more medicine than has been prescribed for you, contact either your healthcare provider, hospital emergency department, or nearest poison control center right away.

4. How to store your medicine:
   Keep your medicine in a safe place where children cannot reach it. It may be harmful to children.

   Store your medicine away from heat and light. Keep your medicine in the carton that comes with it. Do not store at temperatures above 77°F (25°C). The expiration date of your medicine is printed on the carton. If your medicine has expired, throw it away.

   If your healthcare provider decides to stop your treatment, do not keep any leftover medicine unless your healthcare provider tells you to. Throw away your medicine as instructed.

Some possible side effects of Sumatriptan Succinate Injection

- Some patients feel pain or tightness in the chest or throat when using Sumatriptan Succinate Injection. If this happens to you, then discuss it with your healthcare provider before using any more Sumatriptan Succinate Injection. If the chest pain is severe or does not go away, call your healthcare provider right away.

- Call your healthcare provider right away if you have sudden and/or severe abdominal pain after you take Sumatriptan Succinate Injection.

- Some people may have a reaction called serotonin syndrome when they use certain kinds of antidepressants, SSRIs or SNRIs, while taking Sumatriptan Succinate Injection. Symptoms may include confusion, hallucinations, fast heartbeat, feeling faint, fever, sweating, muscle spasm, difficulty walking, and/or diarrhea. Call your healthcare provider right away if you have any of these symptoms after taking Sumatriptan Succinate Injection.

- Shortness of breath; wheezing; heart throbbing; swelling of eyelids, face, or lips; or a skin rash, skin lumps, or hives happens rarely. If it happens to you, then tell your healthcare provider right away. Do not take any more Sumatriptan Succinate Injection unless your healthcare provider tells you to.

- Some people may feel tingling, heat, flushing (redness of face lasting a short time), heaviness, or pressure after taking Sumatriptan Succinate Injection. A few people may feel drowsy, dizzy, tired, or sick. If you have any of these symptoms, tell your healthcare provider at your next visit.

- You may have pain or redness at the site of injection, but this usually lasts less than an hour.

- If you feel unwell in any other way or have any symptoms that you do not understand, you should contact your healthcare provider right away.

Note: The brands listed are trademarks of their respective owners and are not trademarks of APP Pharmaceuticals, LLC. The makers of these brands are not affiliated with and do not endorse APP Pharmaceuticals, LLC or its products.
Sumatriptan Succinate Injection is a selective 5-hydroxytryptamine (5-HT1) receptor subtype agonist. The compound is chemically designated as 3-[2-(dimethylamino)ethyl]-5-methyl-1H-pyrazole-4-carboxylic acid succinate (1:1), and it has the following structure:

\[
\text{C}_7\text{H}_8\text{N}_2\text{O}_5\text{S}+\text{C}_3\text{H}_6\text{Na}_2\text{O}_3
\]
M.W. 413.5

Sumatriptan succinate is a white to off-white powder that is readily soluble in water and in saline. Sumatriptan succinate injection is a clear, colorless to pale yellow, sterile, nonpyrogenic solution for subcutaneous injection. Each 0.5 mL of sumatriptan succinate 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 the solution is approximately 4.2 to 5.3. The osmolality of the injection is 291 mOsmol.

CLINICAL PHARMACOLOGY:
Mechanism of Action
Sumatriptan has been demonstrated to be a selective agonist for a vascular 5-HT1 receptor subtype; recent in vitro studies (probably a member of the 5-HT1D family) with no significant affinity (as measured using standard radioligand binding assays) or pharmacological activity at 5-HT1A, 5-HT1B receptor subtypes or at alpha1-, alpha2- or beta-adrenergic; dopaminergic; serotonergic; muscarinic; or benzodiazepine receptors.

The vascular 5-HT1 receptor subtype to which sumatriptan binds selectively, and through which it presumably exerts its antimigraine effect, has been shown to be present on cranial arteries in both dog and primate, on the human basilar artery, and in the vasculature of the isolated dura mater of humans. In these tissues, sumatriptan activates this receptor to cause vasoconstriction, an action in humans correlating with the relief of migraine and cluster headache. In the anesthetized dog, sumatriptan selectively reduces the carotid arterial blood flow with little or no effect on arterial blood pressure or total peripheral resistance. In the cat, sumatriptan selectively constricts the carotid arterial anastomoses while having little effect on blood flow or resistance in cerebral or extra-cerebral tissues.

Oral Dosages
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; however, the relative exposure at the lowest dose tested was approximately 5 times the human exposure after a 6-mg subcutaneous dose. After a single 6-mg subcutaneous manual injection into the deltidial area of the arm in 9 males (mean age, 33 years; mean weight, 77 kg) who were systemic clearance: 1,184 ± 149 mL/min (mean ± SD), distribution half-life: 10 ± 2 minutes, terminal half-life: 115 ± 19 minutes, and volume of distribution central compartment: 50 ± 8 liters. Of this dose, 22% ± 4% was excreted in the urine as unchanged sumatriptan and 38% ± 7% as the indole acetic acid metabolite.

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

The bioavailability of sumatriptan via subcutaneous site injection to 18 healthy male subjects was 97% ± 16% of that obtained following intravenous injection. Protein binding, determined by equilibrium dialysis over the concentration range of 0.01-10.0 ng/mL, is low, approximately 14% to 21%. The effect of sumatriptan on the protein binding of other drugs has not been evaluated.

Table 2. Efficacy Data From US Phase III Trials

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Sumatriptan (6 mg)</td>
</tr>
<tr>
<td>Patients with pain relief (Grade 0/1)</td>
<td>12%</td>
</tr>
<tr>
<td>Patients without nausea</td>
<td>88%</td>
</tr>
<tr>
<td>Patients without vomiting</td>
<td>88%</td>
</tr>
<tr>
<td>Patients with headache</td>
<td>75%</td>
</tr>
<tr>
<td>Patients with nausea</td>
<td>88%</td>
</tr>
<tr>
<td>Patients with vomiting</td>
<td>88%</td>
</tr>
<tr>
<td>Patients with headache or vomiting</td>
<td>75%</td>
</tr>
</tbody>
</table>

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

However, the liver plays an important role in the presystemic clearance of orally administered sumatriptan. According to the pharmacokinetics of sumatriptan following oral administration, the bioavailability of sumatriptan orally administered may be markedly increased in patients with hepatic impairment. In one small study, 6 healthy patients with hepatic impairment (N = 8) matched for sex, age, and weight with healthy subjects, the hepatically impaired patients had an approximately 70% increase in AUC and Cmax and a T1/2 of 40 minutes earlier compared to the healthy subjects.

Age
The pharmacokinetics of sumatriptan in the elderly (mean age, 72 years, 2 males and 4 females) and in patients with migraine (mean age, 38 years, 25 males and 155 females) were similar to that in healthy male subjects (mean age, 30 years) (see PRECAUTIONS: Genotypic Use). Race
The systemic clearance and Cmax of sumatriptan were similar in black (n = 34) and Caucasian (n = 38) healthy male subjects.

Drug Interactions
Monoamine Oxidase Inhibitors
In vitro studies with human microsomes suggest that sumatriptan is metabolized by monoamine oxidase (MAO), predominantly the A isozyme. In one study of 14 healthy females, pretreatment with MAO-A inhibitor decreased the clearance of sumatriptan. Under the conditions of this experiment, the result was a 2-fold increase in the area under the sumatriptan plasma concentration vs time curve (AUOC), corresponding to a 40% increase in elimination half-life. No significant effect was seen with MAO-B inhibitor.

Pharmacodynamics
Typical Physiologic Responses
Blood Pressure: (see WARNINGS: Increase in Blood Pressure).
Peripheral (small Arteries): In healthy volunteers (N = 18), a study 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 a few patients in clinical studies cannot be ruled out during sumatriptan's development as a treatment for migraine were not accompanied by any clinically significant changes in heart rate.

Respiratory Rate: Experience gained during the clinical development of sumatriptan as a treatment for migraine failed to detect an effect of the drug on respiratory rate.

CLINICAL TRIALS:
Migraine
In US controlled clinical trials enrolling more than 1,000 patients who were experiencing moderate or severe pain and 1 or more of the symptoms enumerated in Table 2, onset of relief began as early as 10 minutes following a 6-mg sumatriptan succinate injection. Smaller doses of sumatriptan may also be effective; the proportion of patients obtaining adequate relief is decreased and the latency to that relief is greater.

In one well-controlled study where placebo (n = 62) was compared to 6 different doses of sumatriptan succinate injection (n = 30 each group) in a single-attack, parallel-group design, no-dose response relationship was found to be as shown in Table 1.

Table 1. Dose Response Relationship for Efficacy

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Minutes</th>
<th>% Incidence</th>
<th>% Incidence</th>
<th>% Incidence</th>
<th>% Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>30</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>50</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>70</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>30</td>
<td>10</td>
<td>80</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>40</td>
<td>10</td>
<td>90</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>50</td>
<td>10</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Relief is defined as the reduction of moderate or severe pain to no or mild pain after dosing without use of rescue medication.
Table 2. Efficacy Data From US Phase III Trials (cont.)

| Study | Placebo | Sumatriptan 6 mg | Sumatriptan 12 mg | Sumatriptan 12 mg Higher Doses
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with pain relief</td>
<td>41%</td>
<td>49%</td>
<td>61%</td>
<td>52%</td>
</tr>
<tr>
<td>Patients with severe pain relief</td>
<td>16%</td>
<td>24%</td>
<td>36%</td>
<td>40%</td>
</tr>
<tr>
<td>Patients without pain or with mild pain</td>
<td>43%</td>
<td>50%</td>
<td>62%</td>
<td>55%</td>
</tr>
<tr>
<td>Patients without severe pain</td>
<td>68%</td>
<td>74%</td>
<td>83%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*p<0.05 versus placebo.

† Includes patients that may have received an additional 6 mg of sumatriptan on a rescue basis, 1 hour after the initial injection.

| Study | Placebo | Sumatriptan 6 mg | Sumatriptan 12 mg | Sumatriptan 12 mg Higher Doses
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with pain relief</td>
<td>41%</td>
<td>49%</td>
<td>61%</td>
<td>52%</td>
</tr>
<tr>
<td>Patients with severe pain relief</td>
<td>16%</td>
<td>24%</td>
<td>36%</td>
<td>40%</td>
</tr>
<tr>
<td>Patients without pain or with mild pain</td>
<td>43%</td>
<td>50%</td>
<td>62%</td>
<td>55%</td>
</tr>
<tr>
<td>Patients without severe pain</td>
<td>68%</td>
<td>74%</td>
<td>83%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*p<0.05 versus placebo.

† Includes patients that may have received an additional 6 mg of sumatriptan on a rescue basis, 1 hour after the initial injection.

Success in outcomes in terms of clinical disability was defined prospectively as ability to work mildly impaired or ability to work and function normally.

Table 3. Efficacy Data From the Pivotal Cluster Headache Studies

| Study | Placebo | Sumatriptan 6 mg | Sumatriptan 12 mg | Sumatriptan 12 mg Higher Doses
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with pain relief</td>
<td>41%</td>
<td>49%</td>
<td>61%</td>
<td>52%</td>
</tr>
<tr>
<td>Patients with severe pain relief</td>
<td>16%</td>
<td>24%</td>
<td>36%</td>
<td>40%</td>
</tr>
<tr>
<td>Patients without pain or with mild pain</td>
<td>43%</td>
<td>50%</td>
<td>62%</td>
<td>55%</td>
</tr>
<tr>
<td>Patients without severe pain</td>
<td>68%</td>
<td>74%</td>
<td>83%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*p<0.05 versus placebo.

† Includes patients that may have received an additional 6 mg of sumatriptan on a rescue basis, 1 hour after the initial injection.

Success in outcomes in terms of clinical disability was defined prospectively as ability to work mildly impaired or ability to work and function normally.
threathing or fatal. In general, hypersensitivity reactions to drugs are more likely to occur in individuals with a history of allergy to multiple allergens (see CONTRAINDICATIONS).

PRECAUTIONS:
General
Chest, jaw, or neck tightness is relatively common with ergot alkaloids. This symptom is not always significantly worse than placebo and is more commonly reported in patients with a history of sensitivity to multiple allergens (see CLINICAL PHARMACOLOGICALLY : Melanin Binding).

Drug Interactions
Ergot-Containing Drugs
Ergot-containing drugs have been reported to cause prolonged vasospasm, including vasospasm in the coronary arteries. There is a theoretical risk that these effects may be additive, use of ergotamine-containing or ergot-type medications (e.g., dihydroergotamine or methysergide) and sumatriptan within 24 hours of each other should be avoided (see CLINICAL PHARMACOLOGICALLY : Drug-Drug Interactions and WARNINGS: Concomitant Drug Use and Other Adverse Cardiac Events).

Carcinogenesis, Mutagenesis, Impairment of Fertility
In carcinogenicity studies, rats and mice were given sumatriptan by daily oral gavage (7450 mg/kg) or drinking water (mice, 78 mg/kg). Average exposures achieved in mice receiving the highest dose were approximately 110 times the exposure 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/m² basis. There were no evidence of an increase in tumors in either species related to sumatriptan administration. Sumatriptan was not mutagenic in the presence or absence of metabolic activation in the mouse bone marrow micronucleus test, the mouse lymphoma assay or the rat liver mutagenesis assay. Sumatriptan was not clastogenic in the Chinese hamster ovary assay. A fertility study in rats showed that the compound had no effect on fertility or conception. In the presence of a 10-fold greater risk of congenital abnormalities, the use of ergot alkaloids is not recommended during pregnancy. There was no evidence of an increase in tumor formation in male and female rats given doses up to 260 times the maximum human exposure after the maximum recommended single dose of 6 mg on a mg/m² basis. However, following oral administration, a treatment-related increase in the incidence of pituitary gland adenomas, secondary to a decrease in mating, was seen for rats treated with 50 and 500 mg/kg/day of sumatriptan. These findings were accompanied by an increase in 9/10 times the maximum recommended single human dose of 6 mg on a mg/m² basis. It is not known whether sumatriptan is associated with the treatment of males or females or both.

Pregnancy
Category C. Sumatriptan has been shown to be embryolethal in rabbits when given daily at a dose approximately 310 times the maximum recommended single human subcutaneous dose of 6 mg on a mg/m² basis. The intravenous administration of subcutaneous to pregnant rabbits through organ interposition and subcutaneous administration of subcutaneous dose of 6 mg on a mg/m² basis, did not cause any adverse effects. In a study of pregnant rabbits given subcutaneous sumatriptan daily prior to and throughout pregnancy, there was no evidence of increased embryo/fetal lethality. Teratogenicity
Term fetuses from Dutch Stride rabbits treated during organogenesis with oral sumatriptan exhibited an increased incidence of cardiovascular and skeletal abnormalities. The functional significance of these abnormalities is not known. Two control groups of each receiving 6 mg/kg/day, were not treated with single-attack single-attack administration. The studies did not establish the efficacy of oral sumatriptan compared to placebo in the treatment of acute migraine. Adverse events observed in these clinical trials were similar in nature to those reported in clinical trials in adults. The frequency of all adverse events in these patients appeared to be both dose- and age-dependent, with younger patients reporting events more commonly than older patients.

Geriatric Use
The use of sumatriptan in elderly patients is not recommended because elderly patients are more likely to have decreased hepatic function, as they are at higher risk for CAD, and blood pressure increases may be more pronounced in the elderly (see WARNINGS: Risk of Myocardial Ischemia and/or Infarction and Other Adverse Cardiac Events).

ADVERSE REACTIONS:
Serious cardiac events, including some that have been fatal, have occurred following the use of oral sumatriptan, sumatriptan nasal spray, and sumatriptan succinate injection. These events are extremely rare and most have been reported in patients with risk factors predictive of CAD. Events reported have included coronary artery disease, myocardial infarction, ventricular tachycardia, and ventricular fibrillation (see CONTRAINDICATIONS, WARNINGS: Risk of Myocardial Ischemia and/or Infarction and Other Adverse Cardiac Events, and PRECAUTIONS: General).

Significant hypertensive episodes, including hypertensive crises, have been reported on rare occasions in patients with or without a history of hypertension (see PRECAUTIONS: Increase in Blood Pressure).

Among patients in clinical trials of subcutaneous sumatriptan succinate injection (N = 6,218), up to 3.3% of patients withdrew for reasons related to adverse events. Incidence in Controlled Clinical Trials of Migraine

Table 4 lists adverse events that occurred in two large-scale, randomized, double-blind, placebo-controlled clinical trials: Events Reported by at Least 2% of Patients Treated With Subcutaneous Sumatriptan Injection 6 mg (N = 547).
The incidence of adverse events in controlled clinical trials was not affected by gender or age of the patients. The events were sufficiently different to assess the impact of race on the incidence of adverse events.

**Incidence of Adverse Events**

The incidence of adverse events was generally similar for patients treated with the drug and those not treated with the drug. Overall, the frequency of adverse events reported in this study was generally similar to that of placebo. Exceptions include reports of paresthesia (5% sumatriptan succinate, 0% placebo), nausea and vomiting (4% sumatriptan succinate, 0% placebo). The most frequent adverse effects reported were muscular events, anxiety, headache, and somnolence (15% sumatriptan succinate, 1% placebo).

**Other Events Observed in Association With the Administration of Sumatriptan Succinate Injection**

In the paragraphs that follow, the frequencies of less commonly reported adverse clinical findings are presented. Because the reports include events observed in open and uncontrolled studies, the role of sumatriptan succinate injection in their causation cannot be determined. Furthermore, the possibility that a drug is associated with an event in an open clinical trial is limited by the value of the quantitative frequency estimates provided.

Event frequencies are calculated as the number of patients in whom an event is observed divided by the total number of patients (N = 6,218) exposed to sumatriptan succinate injection. All reported events are included except those already listed in the previ- ous table, those too general to be informative, and those not reasonably associated with the use of the drug. Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events (≥25% of patients); infrequent adverse events (1/100 to 25% of patients); and rare adverse events are those occurring in fewer than 1/100 patients.

**Cardiovascular**

Infrequent hypertension, hypotension, bradycardia, and tachycardia were observed. Patients with various transient ECG changes ( nonspecific ST or T wave changes, QT prolongation, ventricular extrasystoles, sinus arrhythmia, nonsustained ventricular premature beats, isolated junctional ectopic beats, atrial ectopic beats, degree of left bundle-branch block, and syncope. Rare were paresthesia, arrhythmia, abnormal pulse, vasodilatation, and Raynaud syndrome.

**Endocrine and Metabolic**

Infrequent was thirst. Rare were polydipsia and dehydration.

**Eye**

Rare was visual illusion. Infrequent was iridid-

**Gastrointestinal**

Infrequent were abdominal discomfort and dysphagia. Infrequent were gastroesophageal reflux and diarrhea.

**Musculoskeletal**

Muscle cramps were frequent. Infrequent were vari- ous joint disturbances (pain, stiffness, swelling, ache).

**Neurological**

Frequent were fatigue and dizziness. Rare were mental confusion, amnesia, agitation, depression, and sedation.

**Urogenital**

Frequent were dysuria, frequency, dysmenorrhea, and renal calculus.

**Miscellaneous**

Infrequent were miscellaneous laboratory abnormalities, including minor disturbances in liver function tests, “serotonin against effect,” and hypersensitivity to sumatriptan. Rare was fever.

**Other Events Observed in the Clinical Development of Sumatriptan Succinate Injection**

The following adverse events occurred in clinical trials with sumatriptan succinate tablets and sumatriptan succinate injection. Because the reports include events observed in open and uncontrolled studies, the role of sumatriptan succinate injection 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.

**Breasts**

Breast swelling, cysts, disorder of breasts, lumps, milk, nipple discharge, primary malignant breast neoplasm, and tenderness.

**Cardiovascular**

Acute myocardial infarction, cerebral ischemia, cerebrovascular lesion, heart block, pericardial effusion, pericarditis, and myocardial infarction.

**Ear, Nose, and Throat**

Allergic rhinitis, disorder of ear, sinusitis, and naso- pharyngeal syndrome (base) as the succinate salt and is supplied as a clear, colorless, parenteral drug product. Sumatriptan succinate injection is 6 mg injected subcutaneously. The injection is intended to be given subcutaneously.

**Hepatic**

Hepatic abnormalities were rare, but included elevated liver enzymes, cholestasis, and jaundice.

**Psychiatry**

Paranoid disorder. Breach of trust in patients with and without a history of depression.

**Skin**

Exacerbation of sunburn, hypersensitivity reactions (allergic, urticaria, erythema, rash, shortness of breath, urticaria, in severe, anaphylaxis/ anaphylactoid reactions have been reported [see WARNINGS; Hypersensitivity]), photosensitivity. Following subcutaneous administration of sumatrip- tan, pruritus, redness, itching, induration, swelling, con- fusion, subcutaneous bloating, and, on rare occasions, ischemia. A rare event was ischemia. Patients with Raynaud’s disease should be informed that the drug may cause ischemia.

**Urogenital**

Acute renal failure.

**Drug Abuse and Dependence**

The abuse potential of sumatriptan succinate injection cannot be fully delineated in advance of extensive marketing experience. One clinical study enrolling 12 patients with a history of substance abuse failed to indicate that sumatriptan succinate injection was likely to be abused, diverted, or used for nontherapeutic purposes. Patients responding to therapy with sumatriptan succinate injection may experience symptoms of drug withdrawal upon abrupt discontinuation of dosage.

**OVERDOSAGE**

Patients (N = 269) have received single injections of 8 to 12 mg without significant adverse effects. Volunteers (N = 47) have received single subcuta- neous doses of up to 16 mg without serious adverse events. Toxicity and overdoses in clinical practice have been reported. Coronary vasospasm was observed after intravenous administration of sumatriptan succinate injection. See CONTRAINDICATIONS. Overdose at a dose of 2 g/kg to possibly cause convulsions, tremor, hyperthermia, and tachycardia. Rare were peptic ulcer, retching, flatulence/eructation, and acute pancreatitis.

**DISPOSITION**

Following subcutaneous administration of sumatri- 

**ADVERSE REACTIONS**

The following adverse reactions were observed in a separate needle-protective device from the sumatriptan succinate injection. The following adverse reactions were observed in a separate needle-protective device from the sumatriptan succinate injection.

**INCIDENCE IN CONTROLLED TRIALS OF CLUSTER HEADACHE**

The incidence of adverse events in controlled clinical trials was not affected by gender or age of the patients. The events were sufficiently different to assess the impact of race on the incidence of adverse events.
Read the leaflet that comes with each refill of your prescription because there may be new information. This leaflet does not have all the information about Sumatriptan Succinate Injection. Ask your healthcare provider for more information or advice.

What is Sumatriptan Succinate Injection?
Sumatriptan Succinate Injection is a 5-HT1 agonist. It is called a “triptan.” You should take it only if you have a prescription.

Sumatriptan Succinate Injection is used to relieve your migraine or cluster headache. It is not used to prevent attacks or reduce the number of attacks you have. Use Sumatriptan Succinate Injection only to treat an actual migraine or cluster headache attack.

The decision to use Sumatriptan Succinate Injection is one that you and your healthcare provider should make together, based on your personal needs and health.

Talk with your healthcare provider before taking Sumatriptan Succinate Injection
1. Risk factors for heart disease to tell your healthcare provider:
Tell your healthcare provider if you have risk factors for heart disease such as:
- high blood pressure
- high cholesterol
- obesity
- diabetes
- smoking
- strong family history of heart disease
- you are postmenopausal
- you are a male over 40 years of age

If you do have risk factors for heart disease, your healthcare provider should check you for heart disease to see if Sumatriptan Succinate Injection is right for you.

Although most of the people who have taken Sumatriptan Succinate Injection have not had any serious side effects, some have had serious heart problems. Deaths have been reported, but these were rare considering the extensive worldwide use of Sumatriptan Succinate Injection. Usually, serious problems happened in people with known heart disease. It was not clear whether Sumatriptan Succinate Injection had anything to do with these deaths.

2. Important questions to ask yourself before you take Sumatriptan Succinate Injection:
If the answer to any of the following questions is YES or if you do not know the answer, then please talk with your healthcare provider before you take Sumatriptan Succinate Injection.

- Are you pregnant? Do you think you might be pregnant? Are you trying to become pregnant? Are you not using adequate contraception? Are you breast-feeding?
- Do you have any chest pain, heart disease, shortness of breath, or irregular heartbeats? Have you had a heart attack?
- Do you have risk factors for heart disease (such as high blood pressure, high cholesterol, obesity, diabetes, smoking, strong family history of heart disease, or you are postmenopausal or a male over 40)?
- Have you had a stroke, transient ischemic attacks (TIAs), or Raynaud syndrome?
- Do you have high blood pressure?
- Have you ever had to stop taking this or any other medicine because of an allergy or other problems?
- Are you taking any other migraine medications, including other 5-HT1, agonists (triptans) or any other medicines containing ergotamine, dihydroergotamine, or methysergide?
- Are you taking any medicine for depression or other disorders such as a monoamine oxidase inhibitor, selective serotonin reuptake inhibitor (SSRI), or serotonin norepinephrine reuptake inhibitor (SNRI)? Common SSRIs are citalopram HBr (CELEPA®), escitalopram oxalate (LEXAPRO®), paroxetine (PAXIL®), fluoxetine (PROZAC®/SARAFEM®), clonazepam/fluoxetine (SYMBYAX®), sertraline (ZOLFO®), and fluvoxamine. Common SNRIs are duloxetine (CYMBALT®) and venlafaxine (EFFERD®).
- Have you, or do you have, any disease of the liver or kidney?
- Have you, or do you have, epilepsy or seizures?
- Is this headache different from your usual migraine attacks?

Remember, if you answered YES to any of the above questions, then talk with your healthcare provider about it.

Important points about Sumatriptan Succinate Injection
1. The use of Sumatriptan Succinate Injection during pregnancy:
Do not take Sumatriptan Succinate Injection if you are pregnant. If you think you might be pregnant, are trying to become pregnant, or are not using adequate contraception unless you have talked with your healthcare provider about this.

2. How to use Sumatriptan Succinate Injection:
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 migraine symptoms start, but it may be given at any time during an attack.

You may give a second injection if your migraine symptoms come back, if your symptoms do not get better after the first injection, do not give a second injection for the same attack without first talking with your healthcare provider. Do not give more than two 6-mg doses in any 24-hour period. Allow at least 1 hour between each dose.

3. What to do if you take an overdose:
If you have taken more medicine than has been prescribed for you, contact your healthcare provider, hospital emergency department, or nearest poison control center right away.

4. How to store your medicine:
Keep your medicine in a safe place where children cannot reach it. It may be harmful to children. Store your medicine away from heat and light. Keep your medicine in the carton that comes with it. Do not store at temperatures above 77 °F (25 °C). The expiration date of your medicine is printed on the carton label. If your medicine has expired, throw it away.

If your healthcare provider decides to stop your treatment, do not keep any leftover medicine unless your healthcare provider tells you to. Throw away your medicine as instructed.

Some possible side effects of Sumatriptan Succinate Injection
- Some patients feel numbness in the chest or throat when using Sumatriptan Succinate Injection. If this happens to you, then discuss it with your healthcare provider before using any more Sumatriptan Succinate Injection. If the chest pain is severe or it lasts more than 30 minutes away, call your healthcare provider right away.
- Call your healthcare provider right away if you have had sudden and/or severe abdominal pain after you take Sumatriptan Succinate Injection.
- Some people may have a reaction called serotonin syndrome when they use Sumatriptan Succinate Injection. Symptoms may include confusion, hallucinations, fast heart rate, feeling faint, fever, sweating, muscle spasm, difficulty walking, and/or diarrhea. Call your healthcare provider right away if you have any of these symptoms after taking Sumatriptan Succinate Injection.

Some possible side effects of Sumatriptan Succinate Injection.
- Shortness of breath; wheezing; heart throbbing; swelling of eyelids, face, or lips; or a skin rash, skin lumps, or hives happens rarely. If it happens to you, then tell your healthcare provider right away. Do not take any more Sumatriptan Succinate Injection unless your healthcare provider tells you to.
- Some people may feel tingling, heat, flushing (redness of face lasting a short time), heaviness, or pressure after taking Sumatriptan Succinate Injection. A few people may feel drowsy, dizzy, tired, or sick. If you have any of these symptoms, tell your healthcare provider at your next visit.
- You may have pain or redness at the site of injection, but this usually lasts less than an hour.
- If you feel unwell in any other way or have any symptoms that you do not understand, you should contact your healthcare provider right away.

Note: The brands listed are trademarks of their respective owners and are not trademarks of APP Pharmaceuticals, LLC. The makers of these brands are not affiliated with and do not endorse APP Pharmaceuticals, LLC or its products.