


Zembrace[®] SYMTOUCH[®]
(sumatriptan injection) 3 mg



Minutes matter

Give your patients
migraine pain relief—fast.



Zembrace[®] SymTouch[®] is for acute treatment of migraine with or without aura in adults. Use only if a clear diagnosis of migraine has been established.

Zembrace[®] SymTouch[®] is not indicated for the prophylactic therapy of migraine, and is contraindicated in patients with a history of hemiplegic or basilar migraine.

**Please see complete Important Safety Information
inside and accompanying full Prescribing Information.**

UPSHER-SMITH

Partners in Health Since 1919



A century of serving patients

Upsher-Smith Laboratories, LLC, has never wavered in our desire to offer people high-quality products that could help improve their health and lives. As we celebrate a century of serving patients, we take pride in providing attentive customer service, having strong industry relationships and being dedicated to uninterrupted supply.

Committed to providing more

Zembrace® SymTouch® continues Upsher-Smith's commitment to ensure you have a variety of medication options that can address the unique needs of migraine patients.



Please see complete Important Safety Information on pages 10 to 11 and accompanying full Prescribing Information.



Zembrace® SymTouch® is indicated for the acute treatment of migraine with or without aura in adults

Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine treated, reconsider the diagnosis before Zembrace® SymTouch® is administered to treat subsequent attacks. Zembrace® SymTouch® is not indicated for the prevention of migraine attacks, and is contraindicated in patients with a history of hemiplegic or basilar migraines.

Do not use Zembrace® SymTouch® in patients with ischemic or vasospastic coronary artery disease, Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders, or a history of stroke or transient ischemic attacks. These are not all of the contraindications for Zembrace® SymTouch®.

Please see complete Important Safety Information on pages 10 to 11 and accompanying full Prescribing Information.

Determining a treatment plan

Some patients may need several acute medication options to address their varying migraine pain and associated symptoms.

37%

of patients were not satisfied with the speed of effect from their current migraine therapy (96.4% were current triptan users).¹

In a survey conducted at three headache centers in the U.S. and Sweden (n=183).

Zembrace® SymTouch® is a ready-to-use, single-use, 3 mg sumatriptan auto-injector

It may be an appropriate option for patients experiencing:²



Morning migraine



Rapid-onset migraine



Breakthrough migraine



Migraine with nausea

When timing is everything

Your migraine patients want relief—fast. Zembrace® SymTouch® can help your patients return to the moments that matter most.

Fast

Can **provide migraine pain relief in as little as 10 minutes**

for your patients who need fast results (17% of patients vs. 5% for placebo).³

Powerful

60% of patients experienced migraine pain relief **2 hours after administration** (vs. 21% for placebo).³

Results from a single-attack, parallel group design study, where six different doses of sumatriptan injection, including 3 mg, were compared (n=30 in each group) with placebo (n=62).

The most common adverse reactions ($\geq 5\%$ and $>$ placebo) of sumatriptan injection were injection site reactions, tingling, dizziness/vertigo, warm/hot sensation, burning sensation, feeling of heaviness, pressure sensation, flushing, feeling of tightness and numbness.

Please see complete Important Safety Information on pages 10 to 11 and accompanying full Prescribing Information.



Simple

Zembrace® SymTouch® is a convenient, ready-to-use auto-injector.

- **Concealed 29 G needle**—the smallest needle in a sumatriptan auto-injector.⁴
- **Discreet, compact design** with a simple two-step injection process.^{3,5}
- **Easy to transport**—no refrigeration needed.*

*Store between 68°F and 77°F. Excursions permitted between 59°F and 86°F.

Two-step injection process

Please see complete Instructions for Use at Zembrace.com.

1 Remove protective cap.



2 Push against clean injection site and hold until you hear the device click.



Wait 5 seconds after second click before removing.

Be sure that the injection site is properly cleaned and that the used needle is properly disposed of immediately after use.

Simple to prescribe

Upsher-Smith is dedicated to reducing the administrative hassles and cost barriers of prescribing medications. It's why we created the Access Pathways® Program.

ACCESS PATHWAYS®
PROGRAM

Access Pathways® provides savings and support services for patients.



Accessible

Patients can immediately fill their prescription at the pharmacy of their choice, even if the commercial payer has rejected the prior authorization or the product is not covered.



Affordable

Patients can present their Access Pathways® Platinum Pass® savings card for Zembrace® SymTouch® to their pharmacist for instant savings. Patients pay \$0 per prescription,* per month, renewable annually.



Platinum Pass® savings card

Eligible commercially insured patients pay as little as \$0 on their prescription with the Platinum Pass® savings card.*

It's easy to enroll or activate

Visit Zembrace.com/patient-savings, or call 1-855-699-6062

*Restrictions apply. Maximum of eight single-use injections per month. Medicare, Medicaid, and other state and federal health care program patients are not eligible.



Not an actual Platinum Pass - For illustrative purposes only.

IMPORTANT SAFETY INFORMATION

Zembrace® SymTouch® is contraindicated in patients with:

- Ischemic Coronary Artery Disease (CAD) (angina pectoris, history of myocardial infarction, or documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina.
- Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.
- 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.
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Recent (i.e., within 24 hours) use of ergotamine-containing medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine₁ (5-HT₁) agonist
- Concurrent administration of an MAO-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor
- Known hypersensitivity to sumatriptan (angioedema and anaphylaxis seen)
- Severe hepatic impairment.

There have been rare reports of serious cardiac adverse reactions, including acute myocardial infarction, occurring within a few hours following administration of sumatriptan injection. Some of these reactions occurred in patients without known CAD. 5-HT₁ agonists, including Zembrace SymTouch, may cause coronary artery vasospasm (Prinzmetal's angina), even in patients without a history of CAD.

Perform a cardiovascular evaluation in triptan-naive patients who have multiple cardiovascular risk factors prior to receiving Zembrace SymTouch. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider administering the first dose of Zembrace SymTouch in a medically supervised setting and performing an electrocardiogram (ECG) immediately following Zembrace SymTouch. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of Zembrace SymTouch.

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 Zembrace SymTouch if these disturbances occur.

Sensations of tightness, pain, pressure, and heaviness in the precordium, throat, neck, and jaw commonly occur after treatment with sumatriptan injection and are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk.

Cerebrovascular events including cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT₁ agonists, and some have resulted in fatalities. Discontinue Zembrace SymTouch if a cerebrovascular event occurs.

Zembrace SymTouch may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction, splenic infarction, and Raynaud's syndrome.

Overuse of acute migraine drugs may lead to exacerbation of headache (medication overuse headache). Detoxification of patients, including withdrawal of the overused drugs, and treatment of withdrawal symptoms may be necessary.

Serotonin syndrome may occur with Zembrace SymTouch, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors. 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). Discontinue Zembrace SymTouch if serotonin syndrome is suspected.

Significant elevation in blood pressure, including hypertensive crisis with acute impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT₁ agonists, including patients without a history of hypertension. Monitor blood pressure in patients treated with Zembrace SymTouch.

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. Zembrace SymTouch should be used with caution in patients with a history of epilepsy or conditions associated with a lowered seizure threshold.

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

This safety information is not comprehensive. Please refer to the Zembrace SymTouch full Prescribing Information, Patient Information, and Instructions for Use. You can also visit www.upsher-smith.com or call 1-888-650-3789.

You are encouraged to report suspected adverse reactions to Upsher-Smith Laboratories, LLC at 1-855-899-9180 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

INDICATION AND USAGE

Zembrace SymTouch is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:

- Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Zembrace SymTouch, reconsider the diagnosis before Zembrace SymTouch is administered to treat any subsequent attacks.
- Zembrace SymTouch is not indicated for the prevention of migraine attacks.



Zembrace[®]**SYMTOUCH**[®]
(sumatriptan injection) 3 mg

Because minutes matter

Learn how Zembrace[®] SymTouch[®] is simple to prescribe and convenient for patients to use, at [Zembrace.com/hcp](https://www.zembrace.com/hcp)

References

1. Bigal M et al. Satisfaction with current migraine therapy: experience from 3 centers in US and Sweden. *Headache*. 2007;47(4):475-479.
2. Rothrock JF, Friedman DI. Information for health care professionals: triptan therapy for acute migraine. American Headache Society website. https://americanheadachesociety.org/wp-content/uploads/2018/05/John_Rothrock_and_Deborah_Friedman_-_Triptans.pdf. Published July 2016. Accessed September 6, 2018.
3. Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: July 2019.
4. Data on file. Maple Grove, MN: Upsher-Smith Laboratories, LLC: 2019.
5. Brand-Schieber E, Munjal S, Kumar R, et al. Human factors validation study of 3 mg sumatriptan autoinjector, for migraine patients. *Med Devices (Auckl)*. 2016;9:131-137.

UPSHER-SMITH

Partners in Health Since 1919

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

The most common side effects of ZEMBRACE SymTouch include:

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

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

These are not all the possible side effects of ZEMBRACE SymTouch. 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 ZEMBRACE SymTouch?

- Store between 68° to 77°F (20° to 25°C)
- Store your medicine away from light.
- Keep your medicine in the packaging or carrying case provided with it.

Keep ZEMBRACE SymTouch and all medicines out of the reach of children.

General information about the safe and effective use of ZEMBRACE SymTouch.

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use ZEMBRACE SymTouch for a condition for which it was not prescribed. Do not give ZEMBRACE SymTouch 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 ZEMBRACE SymTouch. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ZEMBRACE SymTouch that is written for healthcare professionals.

For more information, go to www.upsher-smith.com or call 1-888-650-3789.

What are the ingredients in ZEMBRACE SymTouch Injection?

Active ingredient: sumatriptan succinate
Inactive ingredients: sodium chloride, water for injection

Manufactured for
UPSHER-SMITH LABORATORIES, LLC
Maple Grove, MN 55369

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

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The pH range of solution is approximately 4.2 to 5.3 and the osmolality of injection is approximately 291 mOsmol (275 to 315 mOsmol).

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 subjects in clinical trials carried out during sumatriptan's development as a treatment for migraine were not accompanied by any clinically significant changes in heart rate.

12.3 Pharmacokinetics

After a single 3 mg dose, ZEMBRACE SymTouch was bioequivalent to IMITREX subcutaneous injection.

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

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

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

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

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

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

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

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

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

Drug Interaction Studies:

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

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In carcinogenicity studies in mouse and rat, sumatriptan was administered orally for 78 weeks 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). The highest dose tested in mice and rats was approximately 130 and 260 times, respectively, the single MRHD of 6 mg administered subcutaneously on a mg/m² basis. There was no evidence in either species of an increase in tumors related to sumatriptan administration.

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 (0, 5, 50, or 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. 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; however, the relative plasma exposure at the lowest dose tested was approximately 3 times the human exposure after a 6-mg subcutaneous dose.

14 CLINICAL STUDIES

Clinical Studies with Sumatriptan Injection

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

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

Table 2: Proportion of Patients with Migraine Relief and Incidence of Adverse Reactions by Time and by Sumatriptan Dose in Study 1

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

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

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

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

Table 3: Proportion of Patients with Pain Relief and Relief of Migraine Symptoms After 1 and 2 Hours of Treatment in Studies 2 and 3

1-Hour Data	Study 2		Study 3	
	Placebo (n = 190)	Sumatriptan 6 mg (n = 384)	Placebo (n = 180)	Sumatriptan 6 mg (n = 350)
Subjects with pain relief (grade 0/1)	18%	70% ^a	26%	70% ^a
Subjects with no pain	5%	48% ^a	13%	49% ^a
Subjects without nausea	48%	73% ^a	50%	73% ^a
Subjects without photophobia	23%	56% ^a	25%	58% ^a
Subjects with little or no clinical disability ^b	34%	76% ^a	34%	76% ^a

2-Hour Data	Study 2		Study 3	
	Placebo ^c	Sumatriptan 6 mg ^d	Placebo ^c	Sumatriptan 6 mg ^d
Subjects with pain relief (grade 0/1)	31%	81% ^a	39%	82% ^a
Subjects with no pain	11%	63% ^a	19%	65% ^a
Subjects without nausea	56%	82% ^a	63%	81% ^a
Subjects without photophobia	31%	72% ^a	35%	71% ^a
Subjects with little or no clinical disability ^b	42%	85% ^a	49%	84% ^a

^a P<0.05 versus placebo.

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

^c Includes patients that may have received an additional placebo injection 1 hour after the initial injection.

^d Includes patients that may have received an additional 6 mg of sumatriptan injection 1 hour after the initial injection.

Sumatriptan injection also relieved photophobia, phonophobia (sound sensitivity), nausea, and vomiting associated with migraine attacks.

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

Clinical Study with ZEMBRACE SymTouch

In a double-blind, randomized, placebo-controlled clinical trial of ZEMBRACE SymTouch, 230 patients with migraine with or without aura received either ZEMBRACE SymTouch (N=111) or placebo (N=119) for a single migraine attack. The patients had a mean age of 41 years (range 18 to 65 years); approximately 76% were White and 85% were female.

The study excluded patients with medication overuse headache, treatment with onabotulinumtoxin A within 180 days, and patients with a history of cluster headache.

The primary efficacy endpoint was the proportion of patients who were pain-free (defined as a reduction from pre-dose moderate [Grade 2] or severe [Grade 3] pain to none [Grade 0]) 2 hours after the first dose. Of the ZEMBRACE SymTouch-treated patients, 46% were pain free at 2 hours after treatment compared to 27% of the placebo-treated patients.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- ZEMBRACE SymTouch 3 mg/0.5 mL Injection contains sumatriptan as the succinate salt and is supplied as a clear, colorless to pale yellow, sterile, nonpyrogenic solution in a prefilled, ready-to-use, single dose, disposable auto-injector unit (NDC # 0245-0809-89).
- Each carton contains 4 units (NDC # 0245-0809-38) and a Patient Information and Instructions for Use leaflet.

16.2 Storage and Handling

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F). Protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

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

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

Hypersensitivity Reactions

Inform patients that anaphylactic reactions have occurred in patients receiving sumatriptan injection. Such reactions can be life-threatening or fatal. In general, anaphylactic reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens [see *Contraindications (4) and Warnings and Precautions (5.9)*].

Concomitant Use with Other Triptans or Ergot Medications

Inform patients that use of ZEMBRACE SymTouch injection 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 ZEMBRACE SymTouch injection or other triptans, particularly during combined use with SSRIs, SNRIs, TCAs, and MAO inhibitors [see *Warnings and Precautions (5.7), Drug Interactions (7.4)*].

Medication Overuse Headache

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

Pregnancy

Advise patients to notify their healthcare provider if they become pregnant during treatment or plan to become pregnant [see *Use in Specific Populations (8.1)*].

Lactation

Advise patients to notify their healthcare provider if they are breastfeeding or plan to breastfeed [see *Use in Specific Populations (8.2)*].

Ability to Perform Complex Tasks

Treatment with ZEMBRACE SymTouch injection may cause somnolence and dizziness; instruct patients to evaluate their ability to perform complex tasks during migraine attacks and after administration of ZEMBRACE SymTouch injection.

How to Use ZEMBRACE SymTouch

Provide patients instruction on the proper use of ZEMBRACE SymTouch injection if they are able to self-administer ZEMBRACE SymTouch injection in medically unsupervised conditions.

Inform patients that the needle in the ZEMBRACE SymTouch penetrates approximately ¼ of an inch (6 mm). Inform patients that the injection is intended to be given subcutaneous and intramuscular or intravascular delivery should be avoided. Instruct patients to use injection sites with an adequate skin and subcutaneous thickness to accommodate the length of the needle.

Manufactured for
UPSHER-SMITH LABORATORIES, LLC
Maple Grove, MN 55369

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