

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IMITREX safely and effectively. See full prescribing information for IMITREX.

**IMITREX (sumatriptan succinate) Tablets, for oral use**  
**Initial U.S. Approval: 1992**

### INDICATIONS AND USAGE

IMITREX is a serotonin (5-HT<sub>1B/1D</sub>) 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-HT<sub>1</sub> agonist (e.g., another triptan) or of an ergotamine-containing medication. (4)

- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor. (4)
- Hypersensitivity to IMITREX (angioedema and anaphylaxis seen). (4)
- Severe hepatic impairment. (4)

### WARNINGS AND PRECAUTIONS

- Myocardial ischemia/infarction and Prinzmetal's angina: Perform cardiac evaluation in patients with multiple cardiovascular risk factors. (5.1)
- Arrhythmias: Discontinue IMITREX if occurs. (5.2)
- Chest/throat/neck/jaw pain, tightness, pressure, or heaviness: Generally not associated with myocardial ischemia; evaluate for coronary artery disease in patients at high risk. (5.3)
- Cerebral hemorrhage, subarachnoid hemorrhage, and stroke: Discontinue IMITREX if occurs. (5.4)
- Gastrointestinal ischemic reactions and peripheral vasospastic reactions: Discontinue IMITREX if occurs. (5.5)
- Medication overuse headache: Detoxification may be necessary. (5.6)
- Serotonin syndrome: Discontinue IMITREX if occurs. (5.7)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.10)

### 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 GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://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: XX/2013

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## 1 FULL PRESCRIBING INFORMATION

### 2 1 INDICATIONS AND USAGE

3 IMITREX<sup>®</sup> Tablets are indicated for the acute treatment of migraine with or without aura  
4 in adults.

#### 5 Limitations of Use:

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

### 11 2 DOSAGE AND ADMINISTRATION

#### 12 2.1 Dosing Information

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

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

20 Use after IMITREX Injection: If the migraine returns following an initial treatment with  
21 IMITREX (sumatriptan succinate) Injection, additional single IMITREX Tablets (up to  
22 100 mg/day) may be given with an interval of at least 2 hours between tablet doses.

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

#### 25 2.2 Dosing in Patients With Hepatic Impairment

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

### 29 3 DOSAGE FORMS AND STRENGTHS

30 *25 mg Tablets:* White, triangular-shaped, film-coated, and debossed with “I” on one side  
31 and “25” on the other.

32 *50 mg Tablets:* White, triangular-shaped, film-coated, and debossed with “IMITREX 50”  
33 on one side and a chevron shape (^) on the other.

34            100 mg Tablets: Pink, triangular-shaped, film-coated, and debossed with “IMITREX  
35 100” on one side and a chevron shape (^) on the other.

#### 36    **4        CONTRAINDICATIONS**

37            IMITREX Tablets are contraindicated in patients with:

- 38    • Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or  
39    documented silent ischemia) or coronary artery vasospasm, including Prinzmetal’s angina  
40    [see Warnings and Precautions (5.1)]
- 41    • Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory  
42    conduction pathway disorders [see Warnings and Precautions (5.2)]
- 43    • History of stroke or transient ischemic attack (TIA) or history of hemiplegic or basilar  
44    migraine because these patients are at a higher risk of stroke [see Warnings and Precautions  
45    (5.4)]
- 46    • Peripheral vascular disease [see Warnings and Precautions (5.5)]
- 47    • Ischemic bowel disease [see Warnings and Precautions (5.5)]
- 48    • Uncontrolled hypertension [see Warnings and Precautions (5.8)]
- 49    • Recent use (i.e., within 24 hours) of ergotamine-containing medication, ergot-type  
50    medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine<sub>1</sub>  
51    (5-HT<sub>1</sub>) agonist [see Drug Interactions (7.1, 7.3)]
- 52    • Concurrent administration of a monoamine oxidase (MAO)-A inhibitor or recent (within 2  
53    weeks) use of an MAO-A inhibitor [see Drug Interactions (7.2) and Clinical Pharmacology  
54    (12.3)]
- 55    • Hypersensitivity to IMITREX (angioedema and anaphylaxis seen) [see Warnings and  
56    Precautions (5.9)]
- 57    • Severe hepatic impairment [see Use in Specific Populations (8.6) and Clinical Pharmacology  
58    (12.3)]

#### 59    **5        WARNINGS AND PRECAUTIONS**

##### 60    **5.1      Myocardial Ischemia, Myocardial Infarction, and Prinzmetal’s Angina**

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

67            Perform a cardiovascular evaluation in triptan-naïve patients who have multiple  
68    cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong  
69    family history of CAD) prior to receiving IMITREX Tablets. If there is evidence of CAD or

70 coronary artery vasospasm, IMITREX Tablets are contraindicated. For patients with multiple  
71 cardiovascular risk factors who have a negative cardiovascular evaluation, consider  
72 administering the first dose of IMITREX Tablets in a medically supervised setting and  
73 performing an electrocardiogram (ECG) immediately following administration of IMITREX  
74 Tablets. For such patients, consider periodic cardiovascular evaluation in intermittent long-term  
75 users of IMITREX Tablets.

## 76 **5.2 Arrhythmias**

77 Life-threatening disturbances of cardiac rhythm, including ventricular tachycardia and  
78 ventricular fibrillation leading to death, have been reported within a few hours following the  
79 administration of 5-HT<sub>1</sub> agonists. Discontinue IMITREX Tablets if these disturbances occur.  
80 IMITREX Tablets are contraindicated in patients with Wolff-Parkinson-White syndrome or  
81 arrhythmias associated with other cardiac accessory conduction pathway disorders.

## 82 **5.3 Chest, Throat, Neck, and/or Jaw Pain/Tightness/Pressure**

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

## 88 **5.4 Cerebrovascular Events**

89 Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients  
90 treated with 5-HT<sub>1</sub> agonists, and some have resulted in fatalities. In a number of cases, it appears  
91 possible that the cerebrovascular events were primary, the 5-HT<sub>1</sub> agonist having been  
92 administered in the incorrect belief that the symptoms experienced were a consequence of  
93 migraine when they were not. Also, patients with migraine may be at increased risk of certain  
94 cerebrovascular events (e.g., stroke, hemorrhage, TIA). Discontinue IMITREX Tablets if a  
95 cerebrovascular event occurs.

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

## 99 **5.5 Other Vasospasm Reactions**

100 IMITREX Tablets may cause non-coronary vasospastic reactions, such as peripheral  
101 vascular ischemia, gastrointestinal vascular ischemia and infarction (presenting with abdominal  
102 pain and bloody diarrhea), splenic infarction, and Raynaud's syndrome. In patients who  
103 experience symptoms or signs suggestive of non-coronary vasospasm reaction following the use  
104 of any 5-HT<sub>1</sub> agonist, rule out a vasospastic reaction before receiving additional IMITREX  
105 Tablets.

106 Reports of transient and permanent blindness and significant partial vision loss have been  
107 reported with the use of 5-HT<sub>1</sub> agonists. Since visual disorders may be part of a migraine attack,  
108 a causal relationship between these events and the use of 5-HT<sub>1</sub> agonists have not been clearly  
109 established.

#### 110 **5.6 Medication Overuse Headache**

111 Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, or combination of  
112 these drugs for 10 or more days per month) may lead to exacerbation of headache (medication  
113 overuse headache). Medication overuse headache may present as migraine-like daily headaches  
114 or as a marked increase in frequency of migraine attacks. Detoxification of patients, including  
115 withdrawal of the overused drugs, and treatment of withdrawal symptoms (which often includes  
116 a transient worsening of headache) may be necessary.

#### 117 **5.7 Serotonin Syndrome**

118 Serotonin syndrome may occur with IMITREX Tablets, particularly during co-  
119 administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine  
120 reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors [*see Drug*  
121 *Interactions (7.4)*]. Serotonin syndrome symptoms may include mental status changes (e.g.,  
122 agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure,  
123 hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or  
124 gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually  
125 occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication.  
126 Discontinue IMITREX Tablets if serotonin syndrome is suspected.

#### 127 **5.8 Increase in Blood Pressure**

128 Significant elevation in blood pressure, including hypertensive crisis with acute  
129 impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT<sub>1</sub>  
130 agonists, including patients without a history of hypertension. Monitor blood pressure in patients  
131 treated with IMITREX. IMITREX Tablets are contraindicated in patients with uncontrolled  
132 hypertension.

#### 133 **5.9 Anaphylactic/Anaphylactoid Reactions**

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

#### 138 **5.10 Seizures**

139 Seizures have been reported following administration of IMITREX. Some have occurred  
140 in patients with either a history of seizures or concurrent conditions predisposing to seizures.  
141 There are also reports in patients where no such predisposing factors are apparent. IMITREX

142 Tablets should be used with caution in patients with a history of epilepsy or conditions  
143 associated with a lowered seizure threshold.

## 144 **6 ADVERSE REACTIONS**

145 The following adverse reactions are discussed in more detail in other sections of the  
146 prescribing information:

- 147 • Myocardial ischemia, myocardial infarction, and Prinzmetal's angina [*see Warnings and*  
148 *Precautions (5.1)*]
- 149 • Arrhythmias [*see Warnings and Precautions (5.2)*]
- 150 • Chest, throat, neck, and/or jaw pain/tightness/pressure [*see Warnings and Precautions (5.3)*]
- 151 • Cerebrovascular events [*see Warnings and Precautions (5.4)*]
- 152 • Other vasospasm reactions [*see Warnings and Precautions (5.5)*]
- 153 • Medication overuse headache [*see Warnings and Precautions (5.6)*]
- 154 • Serotonin syndrome [*see Warnings and Precautions (5.7)*]
- 155 • Increase in blood pressure [*see Warnings and Precautions (5.8)*]
- 156 • Hypersensitivity reactions [*see Contraindications (4) and Warnings and Precautions (5.9)*]
- 157 • Seizures [*see Warnings and Precautions (5.10)*]

### 158 **6.1 Clinical Trials Experience**

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

162 Table 1 lists adverse reactions that occurred in placebo-controlled clinical trials in  
163 patients who took at least 1 dose of study drug. Only treatment-emergent adverse reactions that  
164 occurred at a frequency of 2% or more in any group treated with IMITREX Tablets and that  
165 occurred at a frequency greater than the placebo group are included in Table 1.

166

167 **Table 1. Adverse Reactions Reported by at Least 2% of Patients Treated With IMITREX Tablets**  
168 **and at a Greater Frequency Than Placebo**

Adverse Reaction	Percent of Patients Reporting			
	IMITREX Tablets 25 mg (n = 417)	IMITREX Tablets 50 mg (n = 771)	IMITREX 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

169  
170       The incidence of adverse reactions in controlled clinical trials was not affected by gender  
171 or age of the patients. There were insufficient data to assess the impact of race on the incidence  
172 of adverse reactions.

173 **6.2 Postmarketing Experience**

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

180       Cardiovascular: Hypotension, palpitations.

181       Neurological: Dystonia, tremor.

182 **7 DRUG INTERACTIONS**

183 **7.1 Ergot-Containing Drugs**

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

188 **7.2 Monoamine Oxidase-A Inhibitors**

189 MAO-A inhibitors increase systemic exposure by 7-fold. Therefore, the use of IMITREX  
190 Tablets in patients receiving MAO-A inhibitors is contraindicated [*see Clinical Pharmacology*  
191 (*12.3*)].

192 **7.3 Other 5-HT<sub>1</sub> Agonists**

193 Because their vasospastic effects may be additive, co-administration of IMITREX  
194 Tablets and other 5-HT<sub>1</sub> agonists (e.g., triptans) within 24 hours of each other is contraindicated.

195 **7.4 Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine  
196 Reuptake Inhibitors and Serotonin Syndrome**

197 Cases of serotonin syndrome have been reported during co-administration of triptans and  
198 SSRIs, SNRIs, TCAs, and MAO inhibitors [*see Warnings and Precautions (5.7)*].

199 **8 USE IN SPECIFIC POPULATIONS**

200 **8.1 Pregnancy**

201 Pregnancy Category C: There are no adequate and well-controlled trials in pregnant  
202 women. In developmental toxicity studies in rats and rabbits, oral administration of sumatriptan  
203 to pregnant animals was associated with embryoletality, fetal abnormalities, and pup mortality.  
204 When administered by the intravenous route to pregnant rabbits, sumatriptan was embryoletal.  
205 IMITREX Tablets should be used during pregnancy only if the potential benefit justifies the  
206 potential risk to the fetus.

207 Oral administration of sumatriptan to pregnant rats during the period of organogenesis  
208 resulted in an increased incidence of fetal blood vessel (cervicothoracic and umbilical)  
209 abnormalities. The highest no-effect dose for embryofetal developmental toxicity in rats was  
210 60 mg/kg/day, or approximately 3 times the maximum recommended human dose (MRHD) of  
211 200 mg/day on a mg/m<sup>2</sup> basis. Oral administration of sumatriptan to pregnant rabbits during the  
212 period of organogenesis resulted in increased incidences of embryoletality and fetal  
213 cervicothoracic vascular and skeletal abnormalities. Intravenous administration of sumatriptan to  
214 pregnant rabbits during the period of organogenesis resulted in an increased incidence of  
215 embryoletality. The highest oral and intravenous no-effect doses for developmental toxicity in  
216 rabbits were 15 (approximately 2 times the MRHD on a mg/m<sup>2</sup> basis) and 0.75 mg/kg/day,  
217 respectively.

218 Oral administration of sumatriptan to rats prior to and throughout gestation resulted in  
219 embryofetal toxicity (decreased body weight, decreased ossification, increased incidence of  
220 skeletal abnormalities). The highest no-effect dose was 50 mg/kg/day, or approximately 2 times  
221 the MRHD on a mg/m<sup>2</sup> basis. In offspring of pregnant rats treated orally with sumatriptan during  
222 organogenesis, there was a decrease in pup survival. The highest no-effect dose for this effect  
223 was 60 mg/kg/day, or approximately 3 times the MRHD on a mg/m<sup>2</sup> basis. Oral treatment of  
224 pregnant rats with sumatriptan during the latter part of gestation and throughout lactation  
225 resulted in a decrease in pup survival. The highest no-effect dose for this finding was  
226 100 mg/kg/day, or approximately 5 times the MRHD on a mg/m<sup>2</sup> basis.

### 227 **8.3 Nursing Mothers**

228 Sumatriptan is excreted in human milk following subcutaneous administration. Infant  
229 exposure to sumatriptan can be minimized by avoiding breastfeeding for 12 hours after treatment  
230 with IMITREX Tablets.

### 231 **8.4 Pediatric Use**

232 Safety and effectiveness in pediatric patients have not been established. IMITREX  
233 Tablets are not recommended for use in patients younger than 18 years of age.

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

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

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

### 253 **8.5 Geriatric Use**

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

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

### 263 **8.6 Hepatic Impairment**

264 The maximum single dose in patients with mild to moderate hepatic impairment should  
265 not exceed 50 mg. IMITREX Tablets are contraindicated in patients with severe hepatic  
266 impairment [see Clinical Pharmacology (12.3)].

## 267 **10 OVERDOSAGE**

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

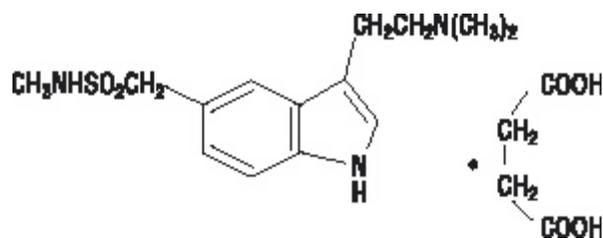
271 Overdose in animals has been fatal and has been heralded by convulsions, tremor,  
272 paralysis, inactivity, ptosis, erythema of the extremities, abnormal respiration, cyanosis, ataxia,  
273 mydriasis, salivation, and lacrimation.

274 The elimination half-life of sumatriptan is approximately 2.5 hours [see Clinical  
275 Pharmacology (12.3)], and therefore monitoring of patients after overdose with IMITREX  
276 Tablets should continue for at least 12 hours or while symptoms or signs persist.

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

## 279 **11 DESCRIPTION**

280 IMITREX Tablets contain sumatriptan succinate, a selective 5-HT<sub>1B/1D</sub> receptor agonist.  
281 Sumatriptan succinate is chemically designated as 3-[2-(dimethylamino)ethyl]-N-methyl-indole-  
282 5-methanesulfonamide succinate (1:1), and it has the following structure:  
283



285  
286 The empirical formula is  $C_{14}H_{21}N_3O_2S \cdot C_4H_6O_4$ , representing a molecular weight of  
287 413.5. Sumatriptan succinate is a white to off-white powder that is readily soluble in water and in  
288 saline.

289 Each IMITREX Tablet for oral administration contains 35, 70, or 140 mg of sumatriptan  
290 succinate equivalent to 25, 50, or 100 mg of sumatriptan, respectively. Each tablet also contains  
291 the inactive ingredients croscarmellose sodium, dibasic calcium phosphate, magnesium stearate,  
292 microcrystalline cellulose, and sodium bicarbonate. Each 100-mg tablet also contains  
293 hypromellose, iron oxide, titanium dioxide, and triacetin.

## 294 **12 CLINICAL PHARMACOLOGY**

### 295 **12.1 Mechanism of Action**

296 Sumatriptan binds with high affinity to human cloned 5-HT<sub>1B/1D</sub> receptors. Sumatriptan  
297 presumably exerts its therapeutic effects in the treatment of migraine headache through agonist  
298 effects at the 5-HT<sub>1B/1D</sub> receptors on intracranial blood vessels and sensory nerves of the  
299 trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory  
300 neuropeptide release.

### 301 **12.2 Pharmacodynamics**

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

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

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

### 311 **12.3 Pharmacokinetics**

312 Absorption and Bioavailability: The mean maximum concentration following oral  
313 dosing with 25 mg is 18 ng/mL (range: 7 to 47 ng/mL) and 51 ng/mL (range: 28 to 100 ng/mL)  
314 following oral dosing with 100 mg of sumatriptan. This compares with a C<sub>max</sub> of 5 and 16 ng/mL  
315 following dosing with a 5- and 20-mg intranasal dose, respectively. The mean C<sub>max</sub> following a  
316 6-mg subcutaneous injection is 71 ng/mL (range: 49 to 110 ng/mL). The bioavailability is  
317 approximately 15%, primarily due to presystemic metabolism and partly due to incomplete  
318 absorption. The C<sub>max</sub> is similar during a migraine attack and during a migraine-free period, but  
319 the T<sub>max</sub> is slightly later during the attack, approximately 2.5 hours compared with 2.0 hours.  
320 When given as a single dose, sumatriptan displays dose proportionality in its extent of absorption

321 (area under the curve [AUC]) over the dose range of 25 to 200 mg, but the  $C_{\max}$  after 100 mg is  
322 approximately 25% less than expected (based on the 25-mg dose).

323 A food effect trial involving administration of IMITREX Tablets 100 mg to healthy  
324 volunteers under fasting conditions and with a high-fat meal indicated that the  $C_{\max}$  and AUC  
325 were increased by 15% and 12%, respectively, when administered in the fed state.

326 **Distribution:** Protein binding, determined by equilibrium dialysis over the concentration  
327 range of 10 to 1,000 ng/mL is low, approximately 14% to 21%. The effect of sumatriptan on the  
328 protein binding of other drugs has not been evaluated. The apparent volume of distribution is  
329 2.7 L/kg.

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

334 **Elimination:** The elimination half-life of sumatriptan is approximately 2.5 hours.  
335 Radiolabeled  $^{14}\text{C}$ -sumatriptan administered orally is largely renally excreted (about 60%) with  
336 about 40% found in the feces. Most of the radiolabeled compound excreted in the urine is the  
337 major metabolite, indole acetic acid (IAA), which is inactive, or the IAA glucuronide. Only 3%  
338 of the dose can be recovered as unchanged sumatriptan.

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

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

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

350 The pharmacokinetics of sumatriptan in patients with severe hepatic impairment has not  
351 been studied. The use of IMITREX Tablets in this population is contraindicated [*see*  
352 *Contraindications (4) and Use in Specific Populations (8.6)*].

353 *Gender:* In a trial comparing females to males, no pharmacokinetic differences were  
354 observed between genders for AUC,  $C_{\max}$ ,  $T_{\max}$ , and half-life.

355 *Race:* The systemic clearance and  $C_{\max}$  of subcutaneous sumatriptan were similar in  
356 black (n = 34) and Caucasian (n = 38) healthy male subjects. Oral sumatriptan has not been  
357 evaluated for race differences.

358            **Drug Interaction Studies: Monoamine Oxidase-A Inhibitors:** Treatment with MAO-  
359 A inhibitors generally leads to an increase of sumatriptan plasma levels [*see Contraindications*  
360 (*4*) and *Drug Interactions (7.2)*].

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

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

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

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

### 373 **13 NONCLINICAL TOXICOLOGY**

#### 374 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

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

384            **Impairment of Fertility:** When sumatriptan (5, 50, 500 mg/kg/day) was administered  
385 orally to male and female rats prior to and throughout the mating period, there was a treatment-  
386 related decrease in fertility secondary to a decrease in mating in animals treated with doses  
387 greater than 5 mg/kg/day (less than the MRHD on a mg/m<sup>2</sup> basis). It is not clear whether this  
388 finding was due to an effect on males or females or both.

#### 389 **13.2 Animal Toxicology and/or Pharmacology**

390            **Corneal Opacities:** Dogs receiving oral sumatriptan developed corneal opacities and  
391 defects in the corneal epithelium. Corneal opacities were seen at the lowest dose tested,  
392 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium  
393 were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and

394 no-effect doses were not established. Plasma exposure at the lowest dose tested was  
395 approximately 2 times that in humans at the MRHD.

396 **14 CLINICAL STUDIES**

397 The efficacy of IMITREX Tablets in the acute treatment of migraine headaches was  
398 demonstrated in 3, randomized, double-blind, placebo-controlled trials. Patients enrolled in these  
399 3 trials were predominately female (87%) and Caucasian (97%), with a mean age of 40 years  
400 (range of 18 to 65 years). Patients were instructed to treat a moderate to severe headache.  
401 Headache response, defined as a reduction in headache severity from moderate or severe pain to  
402 mild or no pain, was assessed up to 4 hours after dosing. Associated symptoms such as nausea,  
403 photophobia, and phonophobia were also assessed. Maintenance of response was assessed for up  
404 to 24 hours postdose. A second dose of IMITREX Tablets or other medication was allowed 4 to  
405 24 hours after the initial treatment for recurrent headache. Acetaminophen was offered to  
406 patients in Trials 2 and 3 beginning at 2 hours after initial treatment if the migraine pain had not  
407 improved or worsened. Additional medications were allowed 4 to 24 hours after the initial  
408 treatment for recurrent headache or as rescue in all 3 trials. The frequency and time to use of  
409 these additional treatments were also determined. In all trials, doses of 25, 50, and 100 mg were  
410 compared with placebo in the treatment of migraine attacks. In 1 trial, doses of 25, 50, and  
411 100 mg were also compared with each other.

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

419  
420 **Table 2. Percentage of Patients With Headache Response (Mild or No Headache) 2 and 4**  
421 **Hours Following Treatment**

	IMITREX Tablets 25 mg		IMITREX Tablets 50 mg		IMITREX Tablets 100 mg		Placebo	
	2 hr	4 hr	2 hr	4 hr	2 hr	4 hr	2 hr	4 hr
Trial 1	52% <sup>a</sup>	67% <sup>a</sup>	61% <sup>a,b</sup>	78% <sup>a,b</sup>	62% <sup>a,b</sup>	79% <sup>a,b</sup>	27%	38%
	(n = 298)		(n = 296)		(n = 296)		(n = 94)	
Trial 2	52% <sup>a</sup>	70% <sup>a</sup>	50% <sup>a</sup>	68% <sup>a</sup>	56% <sup>a</sup>	71% <sup>a</sup>	26%	38%
	(n = 66)		(n = 62)		(n = 66)		(n = 65)	
Trial 3	52% <sup>a</sup>	65% <sup>a</sup>	54% <sup>a</sup>	72% <sup>a</sup>	57% <sup>a</sup>	78% <sup>a</sup>	17%	19%

	(n = 48)	(n = 46)	(n = 46)	(n = 47)
--	----------	----------	----------	----------

422 <sup>a</sup>  $P < 0.05$  in comparison with placebo.

423 <sup>b</sup>  $P < 0.05$  in comparison with 25 mg.

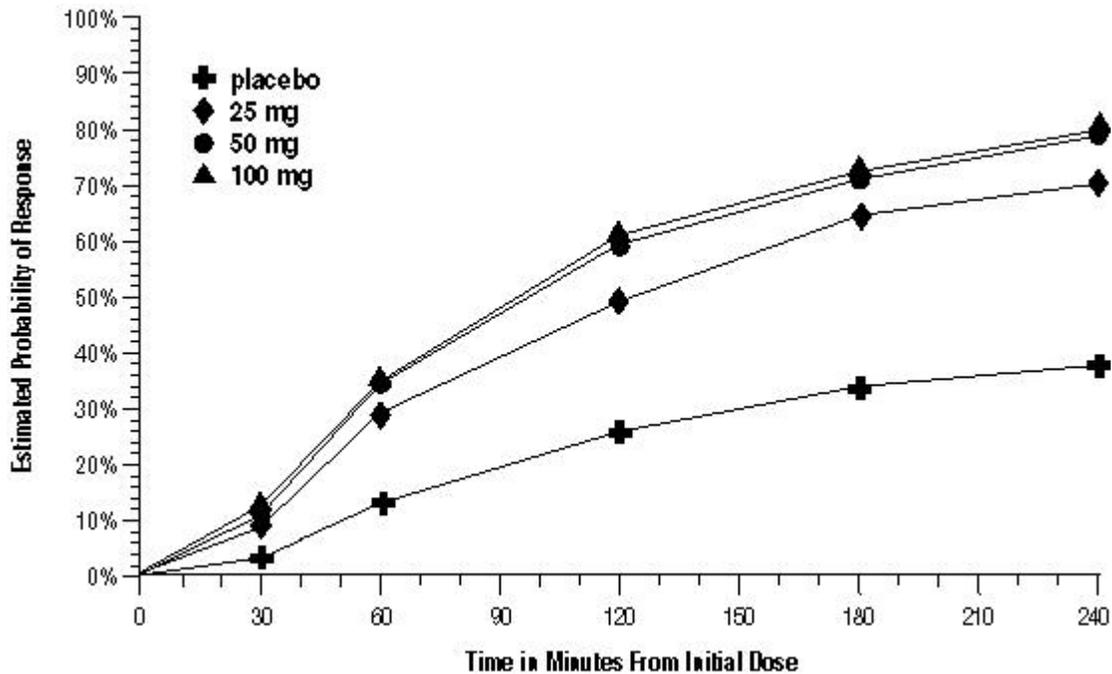
424

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

427

428 **Figure 1. Estimated Probability of Achieving Initial Headache Response Within 4 Hours of**  
429 **Treatment in Pooled Trials 1, 2, and 3<sup>a</sup>**

430



431

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

437

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

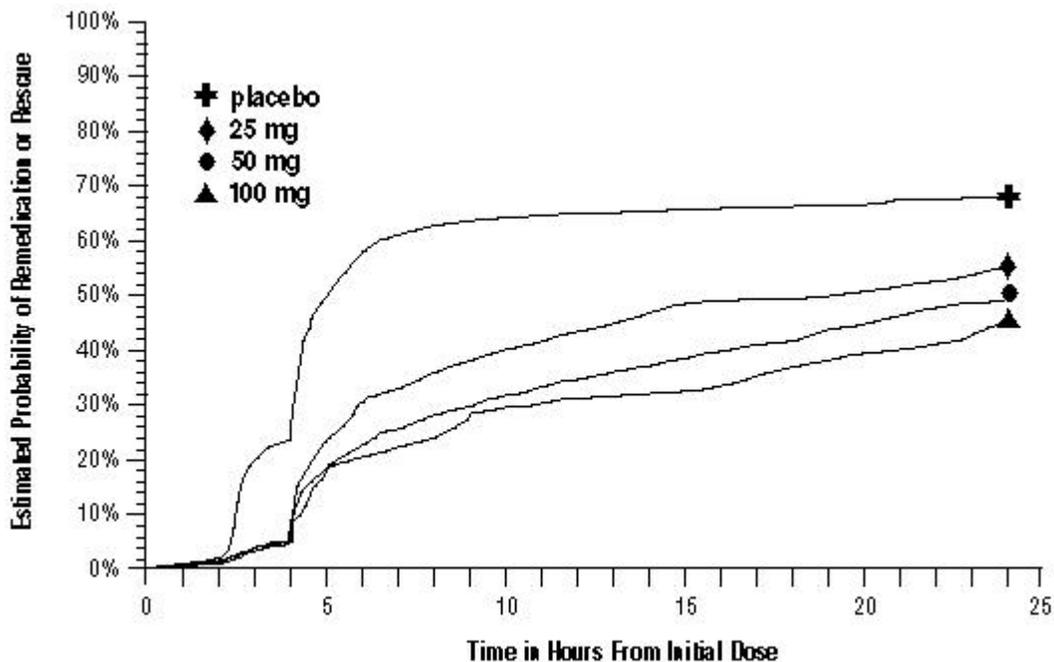
441 As early as 2 hours in Trials 2 and 3, or as early as 4 hours in Trial 1, through 24 hours  
442 following the initial dose of study treatment, patients were allowed to use additional treatment

443 for pain relief in the form of a second dose of study treatment or other medication. The estimated  
444 probability of patients taking a second dose or other medication for migraine over the 24 hours  
445 following the initial dose of study treatment is summarized in Figure 2.

446

447 **Figure 2. The Estimated Probability of Patients Taking a Second Dose of IMITREX**  
448 **Tablets or Other Medication to Treat Migraine Over the 24 Hours Following the**  
449 **Initial Dose of Study Treatment in Pooled Trials 1, 2, and 3<sup>a</sup>**

450



451

452 <sup>a</sup> Kaplan-Meier plot based on data obtained in the 3 clinical controlled trials providing evidence  
453 of efficacy with patients not using additional treatments censored to 24 hours. Plot also  
454 includes patients who had no response to the initial dose. No remedication was allowed within  
455 2 hours postdose.

456

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

464 **16 HOW SUPPLIED/STORAGE AND HANDLING**

465 IMITREX Tablets, 25 mg, 50 mg, and 100 mg of sumatriptan (base) as the succinate.

466 IMITREX Tablets, 25 mg, are white, triangular-shaped, film-coated tablets debossed with  
467 “I” on one side and “25” on the other in blister packs of 9 tablets (NDC 0173-0735-00).

468 IMITREX Tablets, 50 mg, are white, triangular-shaped, film-coated tablets debossed with  
469 “IMITREX 50” on one side and a chevron shape (^) on the other in blister packs of 9 tablets  
470 (NDC 0173-0736-01).

471 IMITREX Tablets, 100 mg, are pink, triangular-shaped, film-coated tablets debossed  
472 with “IMITREX 100” on one side and a chevron shape (^) on the other in blister packs of  
473 9 tablets (NDC 0173-0737-01).

474 Store between 2°C and 30°C (36°F and 86°F).

475 **17 PATIENT COUNSELING INFORMATION**

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

477 Risk of Myocardial Ischemia and/or Infarction, Prinzmetal’s Angina, Other  
478 Vasospasm-Related Events, Arrhythmias, and Cerebrovascular Events: Inform patients  
479 that IMITREX Tablets may cause serious cardiovascular side effects such as myocardial  
480 infarction or stroke. Although serious cardiovascular events can occur without warning  
481 symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath,  
482 irregular heartbeat, significant rise in blood pressure, weakness, and slurring of speech, and  
483 should ask for medical advice if any indicative sign or symptoms are observed. Apprise patients  
484 of the importance of this follow-up [see *Warnings and Precautions (5.1, 5.2, 5.4, 5.5, 5.8)*].

485 Anaphylactic/Anaphylactoid Reactions: Inform patients that  
486 anaphylactic/anaphylactoid reactions have occurred in patients receiving IMITREX Tablets.  
487 Such reactions can be life threatening or fatal. In general, anaphylactic reactions to drugs are  
488 more likely to occur in individuals with a history of sensitivity to multiple allergens [see  
489 *Contraindications (4) and Warnings and Precautions (5.9)*].

490 Concomitant Use With Other Triptans or Ergot Medications: Inform patients that  
491 use of IMITREX Tablets within 24 hours of another triptan or an ergot-type medication  
492 (including dihydroergotamine or methysergide) is contraindicated [see *Contraindications (4),*  
493 *Drug Interactions (7.1, 7.3)*].

494 Serotonin Syndrome: Caution patients about the risk of serotonin syndrome with the  
495 use of IMITREX Tablets or other triptans, particularly during combined use with SSRIs, SNRIs,  
496 TCAs, and MAO inhibitors [see *Warnings and Precautions (5.7), Drug Interactions (7.4)*].

497 Medication Overuse Headache: Inform patients that use of acute migraine drugs for  
498 10 or more days per month may lead to an exacerbation of headache and encourage patients to

499 record headache frequency and drug use (e.g., by keeping a headache diary) [*see Warnings and*  
500 *Precautions (5.6)*].

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

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

506 **Ability to Perform Complex Tasks:** Treatment with IMITREX Tablets may cause  
507 somnolence and dizziness; instruct patients to evaluate their ability to perform complex tasks  
508 after administration of IMITREX Tablets.

509

510 IMITREX is a registered trademark of the GlaxoSmithKline group of companies.

511

512



513

514 GlaxoSmithKline

515 Research Triangle Park, NC 27709

516

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518

519 IMT:XPI

520

521

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

524

525

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

529

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

531 **IMITREX can cause serious side effects, including:**

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

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

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

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

- 545 • have high blood pressure
- 546 • have high cholesterol levels
- 547 • smoke
- 548 • are overweight
- 549 • have diabetes
- 550 • have a family history of heart disease

551  
552 **What is IMITREX?**

553 IMITREX is a prescription medicine used to treat acute migraine headaches with or  
554 without aura in adults.

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

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

560 It is not known if IMITREX is safe and effective to treat cluster headaches.

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

562  
563 **Who should not take IMITREX?**

564 **Do not take IMITREX if you have:**

- 565 • heart problems or a history of heart problems
- 566 • narrowing of blood vessels to your legs, arms, stomach, or kidneys (peripheral  
567 vascular disease)

- 568 • uncontrolled high blood pressure
- 569 • severe liver problems
- 570 • hemiplegic migraines or basilar migraines. If you are not sure if you have these
- 571 types of migraines, ask your healthcare provider.
- 572 • had a stroke, transient ischemic attacks (TIAs), or problems with your blood
- 573 circulation
- 574 • taken any of the following medicines in the last 24 hours:
- 575 • almotriptan (AXERT<sup>®</sup>)
- 576 • eletriptan (RELPAX<sup>®</sup>)
- 577 • frovatriptan (FROVA<sup>®</sup>)
- 578 • naratriptan (AMERGE<sup>®</sup>)
- 579 • rizatriptan (MAXALT<sup>®</sup>, MAXALT-MLT<sup>®</sup>)
- 580 • sumatriptan and naproxen (TREXIMET<sup>®</sup>)
- 581 • ergotamines (CAFERGOT<sup>®</sup>, ERGOMAR<sup>®</sup>, MIGERGOT<sup>®</sup>)
- 582 • dihydroergotamine (D.H.E. 45<sup>®</sup>, MIGRANAL<sup>®</sup>)
- 583 Ask your healthcare provider if you are not sure if your medicine is listed above.
- 584 • an allergy to sumatriptan or any of the ingredients in IMITREX. See the end of
- 585 this leaflet for a complete list of ingredients in IMITREX.
- 586

587 **What should I tell my healthcare provider before taking IMITREX?**

- 588 Before you take IMITREX, tell your healthcare provider about all of your medical
- 589 conditions, including if you:
- 590 • have high blood pressure
  - 591 • have high cholesterol
  - 592 • have diabetes
  - 593 • smoke
  - 594 • are overweight
  - 595 • have heart problems or family history of heart problems or stroke
  - 596 • have kidney problems
  - 597 • have liver problems
  - 598 • have had epilepsy or seizures
  - 599 • are not using effective birth control
  - 600 • become pregnant while taking IMITREX.
  - 601 • are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk
  - 602 and may harm your baby. Talk with your healthcare provider about the best way
  - 603 to feed your baby if you take IMITREX.

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

606 IMITREX and certain other medicines can affect each other, causing serious side  
607 effects.

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

- 610 • selective serotonin reuptake inhibitors (SSRIs)
- 611 • serotonin norepinephrine reuptake inhibitors (SNRIs)
- 612 • tricyclic antidepressants (TCAs)
- 613 • monoamine oxidase inhibitors (MAOIs)

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

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

618

#### 619 **How should I take IMITREX?**

- 620 • Certain people should take their first dose of IMITREX in their healthcare  
621 provider's office or in another medical setting. Ask your healthcare provider if  
622 you should take your first dose in a medical setting.
- 623 • Take IMITREX exactly as your healthcare provider tells you to take it.
- 624 • Your healthcare provider may change your dose. Do not change your dose  
625 without first talking to your healthcare provider.
- 626 • Take IMITREX Tablets whole with water or other liquids.
- 627 • If you do not get any relief after your first tablet, do not take a second tablet  
628 without first talking with your healthcare provider.
- 629 • If your headache comes back or you only get some relief from your headache,  
630 you can take a second tablet 2 hours after the first tablet.
- 631 • Do not take more than 200 mg of IMITREX Tablets in a 24-hour period.
- 632 • If you take too much IMITREX, call your healthcare provider or go to the nearest  
633 hospital emergency room right away.
- 634 • You should write down when you have headaches and when you take IMITREX  
635 so you can talk with your healthcare provider about how IMITREX is working for  
636 you.

637

#### 638 **What should I avoid while taking IMITREX?**

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

642

643 **What are the possible side effects of IMITREX?**

644 **IMITREX may cause serious side effects.** See “What is the most important  
645 information I should know about IMITREX?”

646 These serious side effects include:

- 647 • changes in color or sensation in your fingers and toes (Raynaud’s syndrome)
- 648 • stomach and intestinal problems (gastrointestinal and colonic ischemic events).  
649 Symptoms of gastrointestinal and colonic ischemic events include:
  - 650 • sudden or severe stomach pain
  - 651 • stomach pain after meals
  - 652 • weight loss
  - 653 • nausea or vomiting
  - 654 • constipation or diarrhea
  - 655 • bloody diarrhea
  - 656 • fever
- 657 • problems with blood circulation to your legs and feet (peripheral vascular  
658 ischemia). Symptoms of peripheral vascular ischemia include:
  - 659 • cramping and pain in your legs or hips
  - 660 • feeling of heaviness or tightness in your leg muscles
  - 661 • burning or aching pain in your feet or toes while resting
  - 662 • numbness, tingling, or weakness in your legs
  - 663 • cold feeling or color changes in 1 or both legs or feet
- 664 • hives (itchy bumps); swelling of your tongue, mouth, or throat
- 665 • medication overuse headaches. Some people who use too many IMITREX tablets  
666 may have worse headaches (medication overuse headache). If your headaches  
667 get worse, your healthcare provider may decide to stop your treatment with  
668 IMITREX.
- 669 • serotonin syndrome. Serotonin syndrome is a rare but serious problem that can  
670 happen in people using IMITREX, especially if IMITREX is used with  
671 anti-depressant medicines called SSRIs or SNRIs.  
672 Call your healthcare provider right away if you have any of the following  
673 symptoms of serotonin syndrome:
  - 674 • mental changes such as seeing things that are not there (hallucinations),  
675 agitation, or coma

- 676 • fast heartbeat
- 677 • changes in blood pressure
- 678 • high body temperature
- 679 • tight muscles
- 680 • trouble walking
- 681 • seizures. Seizures have happened in people taking IMITREX who have never had
- 682 seizures before. Talk with your healthcare provider about your chance of having
- 683 seizures while you take IMITREX.

684 The most common side effects of IMITREX Tablets include:

- 685 • tingling or numbness in your fingers or toes
- 686 • warm or cold feeling
- 687 • feeling weak, drowsy, or tired
- 688 • pain, discomfort, or stiffness in your neck, throat, jaw, or chest
- 689 • dizziness

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

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

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

696

#### 697 **How should I store IMITREX Tablets?**

698 Store IMITREX between 36°F to 86°F (2°C to 30°C).

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

700

#### 701 **General information about the safe and effective use of IMITREX.**

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

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

710 For more information, go to [www.gsk.com](http://www.gsk.com) or call 1-888-825-5249.

711

712 **What are the ingredients in IMITREX Tablets?**

713 Active ingredient: sumatriptan succinate

714 Inactive ingredients: croscarmellose sodium, dibasic calcium phosphate,  
715 magnesium stearate, microcrystalline cellulose, and sodium bicarbonate

716 100-mg tablets also contain hypromellose, iron oxide, titanium dioxide, and  
717 triacetin.

718

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

721

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735 Month Year

736 IMT:xPIL

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IMITREX safely and effectively. See full prescribing information for IMITREX.

**IMITREX (sumatriptan) Nasal Spray**  
**Initial U.S. Approval: 1992**

### INDICATIONS AND USAGE

IMITREX is a serotonin (5-HT<sub>1B/1D</sub>) receptor agonist (triptan) indicated for acute treatment of migraine with or without aura in adults. (1)

#### Limitations of Use:

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

### DOSAGE AND ADMINISTRATION

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

### DOSAGE FORMS AND STRENGTHS

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

### CONTRAINDICATIONS

- History of coronary artery disease or coronary artery vasospasm (4)
- Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders (4)
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine (4)
- Peripheral vascular disease (4)
- Ischemic bowel disease (4)
- Uncontrolled hypertension (4)
- Recent (within 24 hours) use of another 5-HT<sub>1</sub> agonist (e.g., another triptan) or of an ergotamine-containing medication. (4)

- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor. (4)
- Hypersensitivity to IMITREX (angioedema and anaphylaxis seen). (4)
- Severe hepatic impairment (4)

### WARNINGS AND PRECAUTIONS

- Myocardial ischemia/infarction and Prinzmetal's angina: Perform cardiac evaluation in patients with multiple cardiovascular risk factors. (5.1)
- Arrhythmias: Discontinue IMITREX if occurs. (5.2)
- Chest/throat/neck/jaw pain, tightness, pressure, or heaviness: Generally not associated with myocardial ischemia; evaluate for coronary artery disease in patients at high risk. (5.3)
- Cerebral hemorrhage, subarachnoid hemorrhage, and stroke: Discontinue IMITREX if occurs. (5.4)
- Gastrointestinal ischemic reactions and peripheral vasospastic reactions: Discontinue IMITREX if occurs. (5.5)
- Medication overuse headache: Detoxification may be necessary. (5.6)
- Serotonin syndrome: Discontinue IMITREX if occurs. (5.7)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.11)

### ADVERSE REACTIONS

Most common adverse reactions (≥1% and >placebo) were burning sensation, disorder/discomfort of nasal cavity/sinuses, throat discomfort, nausea and/or vomiting, bad/unusual taste, and dizziness/vertigo. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://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: XX/2013

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## 1 FULL PRESCRIBING INFORMATION

### 2 1 INDICATIONS AND USAGE

3 IMITREX<sup>®</sup> Nasal Spray is indicated for the acute treatment of migraine with or without  
4 aura in adults.

#### 5 Limitations of Use:

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

### 12 2 DOSAGE AND ADMINISTRATION

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

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

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

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

### 23 3 DOSAGE FORMS AND STRENGTHS

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

### 25 4 CONTRAINDICATIONS

26 IMITREX Nasal Spray is contraindicated in patients with:

- 27 • Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or  
28 documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina  
29 [*see Warnings and Precautions (5.1)*]
- 30 • Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory  
31 conduction pathway disorders [*see Warnings and Precautions (5.2)*]

- 32 • History of stroke, transient ischemic attack (TIA), or history of hemiplegic or basilar  
33 migraine because these patients are at a higher risk of stroke [*see Warnings and Precautions*  
34 (5.4)]
- 35 • Peripheral vascular disease [*see Warnings and Precautions (5.5)*]
- 36 • Ischemic bowel disease [*see Warnings and Precautions (5.5)*]
- 37 • Uncontrolled hypertension [*see Warnings and Precautions (5.8)*]
- 38 • Recent use (i.e., within 24 hours) of ergotamine-containing medication, ergot-type  
39 medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine<sub>1</sub>  
40 (5-HT<sub>1</sub>) agonist [*see Drug Interactions (7.1, 7.3)*]
- 41 • Concurrent administration of a monoamine oxidase (MAO)-A inhibitor or recent (within 2  
42 weeks) use of an MAO-A inhibitor [*see Drug Interactions (7.2) and Clinical Pharmacology*  
43 (12.3)]
- 44 • Hypersensitivity to IMITREX (angioedema and anaphylaxis seen) [*see Warnings and*  
45 *Precautions (5.10)*]
- 46 • Severe hepatic impairment [*see Clinical Pharmacology (12.3)*]

## 47 **5 WARNINGS AND PRECAUTIONS**

### 48 **5.1 Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina**

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

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

### 64 **5.2 Arrhythmias**

65 Life-threatening disturbances of cardiac rhythm, including ventricular tachycardia and  
66 ventricular fibrillation leading to death, have been reported within a few hours following the  
67 administration of 5-HT<sub>1</sub> agonists. Discontinue IMITREX Nasal Spray if these disturbances

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

### 70 **5.3 Chest, Throat, Neck, and/or Jaw Pain/Tightness/Pressure**

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

### 76 **5.4 Cerebrovascular Events**

77 Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients  
78 treated with 5-HT<sub>1</sub> agonists, and some have resulted in fatalities. In a number of cases, it appears  
79 possible that the cerebrovascular events were primary, the 5-HT<sub>1</sub> agonist having been  
80 administered in the incorrect belief that the symptoms experienced were a consequence of  
81 migraine when they were not. Also, patients with migraine may be at increased risk of certain  
82 cerebrovascular events (e.g., stroke, hemorrhage, TIA). Discontinue IMITREX Nasal Spray if a  
83 cerebrovascular event occurs.

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

### 87 **5.5 Other Vasospasm Reactions**

88 IMITREX Nasal Spray may cause non-coronary vasospastic reactions, such as peripheral  
89 vascular ischemia, gastrointestinal vascular ischemia and infarction (presenting with abdominal  
90 pain and bloody diarrhea), splenic infarction, and Raynaud's syndrome. In patients who  
91 experience symptoms or signs suggestive of non-coronary vasospasm reaction following the use  
92 of any 5-HT<sub>1</sub> agonist, rule out a vasospastic reaction before using additional IMITREX Nasal  
93 Spray.

94 Reports of transient and permanent blindness and significant partial vision loss have been  
95 reported with the use of 5-HT<sub>1</sub> agonists. Since visual disorders may be part of a migraine attack,  
96 a causal relationship between these events and the use of 5-HT<sub>1</sub> agonists have not been clearly  
97 established.

### 98 **5.6 Medication Overuse Headache**

99 Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, or combination of  
100 these drugs for 10 or more days per month) may lead to exacerbation of headache (medication  
101 overuse headache). Medication overuse headache may present as migraine-like daily headaches  
102 or as a marked increase in frequency of migraine attacks. Detoxification of patients, including  
103 withdrawal of the overused drugs, and treatment of withdrawal symptoms (which often includes  
104 a transient worsening of headache) may be necessary.

105 **5.7 Serotonin Syndrome**

106 Serotonin syndrome may occur with IMITREX Nasal Spray, particularly during co-  
107 administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine  
108 reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors [*see Drug*  
109 *Interactions (7.4)*]. Serotonin syndrome symptoms may include mental status changes (e.g.,  
110 agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure,  
111 hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or  
112 gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually  
113 occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication.  
114 Discontinue IMITREX Nasal Spray if serotonin syndrome is suspected.

115 **5.8 Increase in Blood Pressure**

116 Significant elevation in blood pressure, including hypertensive crisis with acute  
117 impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT<sub>1</sub>  
118 agonists, including patients without a history of hypertension. Monitor blood pressure in patients  
119 treated with IMITREX. IMITREX Nasal Spray is contraindicated in patients with uncontrolled  
120 hypertension.

121 **5.9 Local Irritation**

122 Local irritative symptoms such as burning, numbness, paresthesia, discharge, and pain or  
123 soreness were reported in approximately 5% of patients in controlled clinical trials and were  
124 noted to be severe in about 1%. The symptoms were transient and generally resolved in less than  
125 2 hours. Limited examinations of the nose and throat did not reveal any clinically noticeable  
126 injury in these patients. The consequences of extended and repeated use of IMITREX Nasal  
127 Spray on the nasal and/or respiratory mucosa have not been systematically evaluated in patients.

128 **5.10 Anaphylactic/Anaphylactoid Reactions**

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

134 **5.11 Seizures**

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

140 **6 ADVERSE REACTIONS**

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

142 prescribing information:

- 143 • Myocardial ischemia, myocardial infarction, and Prinzmetal's angina [*see Warnings and*
- 144 *Precautions (5.1)*]
- 145 • Arrhythmias [*see Warnings and Precautions (5.2)*]
- 146 • Chest, throat, neck, and/or jaw pain/tightness/pressure [*see Warnings and Precautions (5.3)*]
- 147 • Cerebrovascular events [*see Warnings and Precautions (5.4)*]
- 148 • Other vasospasm reactions [*see Warnings and Precautions (5.5)*]
- 149 • Medication overuse headache [*see Warnings and Precautions (5.6)*]
- 150 • Serotonin syndrome [*see Warnings and Precautions (5.7)*]
- 151 • Increase in blood pressure [*see Warnings and Precautions (5.8)*]
- 152 • Local irritation [*see Warnings and Precautions (5.9)*]
- 153 • Hypersensitivity reactions [*see Contraindications (4) and Warnings and Precautions (5.10)*]
- 154 • Seizures [*see Warnings and Precautions (5.11)*]

#### 155 **6.1 Clinical Trials Experience**

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

159 Table 1 lists adverse reactions that occurred in worldwide placebo-controlled clinical  
160 trials in 3,419 patients with migraine. Only treatment-emergent adverse reactions that occurred at  
161 a frequency of 1% or more in the group treated with IMITREX Nasal Spray 20 mg and that  
162 occurred at a frequency greater than the placebo group are included in Table 1.

163

164 **Table 1. Adverse Reactions Reported by at Least 1% of Patients and at a Greater**  
165 **Frequency Than Placebo in Controlled Migraine Clinical Trials**

Adverse Reaction	Percent of Patients Reporting			
	IMITREX Nasal Spray 5 mg (n = 496)	IMITREX Nasal Spray 10 mg (n = 1,007)	IMITREX Nasal Spray 20 mg (n = 1,212)	Placebo (n = 704)
Atypical sensations				
Burning sensation	0.4	0.6	1.4	0.1
Ear, nose, and throat Disorder/discomfort of nasal cavity/sinuses	2.8	2.5	3.8	2.4
Throat discomfort	0.8	1.8	2.4	0.9
Gastrointestinal Nausea and/or vomiting	12.2	11.0	13.5	11.3
Neurological Bad/unusual taste	13.5	19.3	24.5	1.7
Dizziness/vertigo	1.0	1.7	1.4	0.9

166  
167 The incidence of adverse reactions in controlled clinical trials was not affected by gender,  
168 weight, or age of the patients; use of prophylactic medications; or presence of aura. There were  
169 insufficient data to assess the impact of race on the incidence of adverse reactions.

170 **6.2 Postmarketing Experience**

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

177 Cardiovascular: Hypotension, palpitations.

178 Neurological: Dystonia, tremor.

179 **7 DRUG INTERACTIONS**

180 **7.1 Ergot-Containing Drugs**

181 Ergot-containing drugs have been reported to cause prolonged vasospastic reactions.  
182 Because these effects may be additive, use of ergotamine-containing or ergot-type medications

183 (like dihydroergotamine or methysergide) and IMITREX Nasal Spray within 24 hours of each  
184 other is contraindicated.

## 185 **7.2 Monoamine Oxidase-A Inhibitors**

186 MAO-A inhibitors increase systemic exposure by up to 7-fold. Therefore, the use of  
187 IMITREX Nasal Spray in patients receiving MAO-A inhibitors is contraindicated [*see Clinical*  
188 *Pharmacology (12.3)*].

## 189 **7.3 Other 5-HT<sub>1</sub> Agonists**

190 Because their vasospastic effects may be additive, co-administration of IMITREX Nasal  
191 Spray and other 5-HT<sub>1</sub> agonists (e.g., triptans) within 24 hours of each other is contraindicated.

## 192 **7.4 Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine 193 Reuptake Inhibitors and Serotonin Syndrome**

194 Cases of serotonin syndrome have been reported during co-administration of triptans and  
195 SSRIs, SNRIs, TCAs, and MAO inhibitors [*see Warnings and Precautions (5.7)*].

## 196 **8 USE IN SPECIFIC POPULATIONS**

### 197 **8.1 Pregnancy**

198 Pregnancy Category C: There are no adequate and well-controlled trials in pregnant  
199 women. In developmental toxicity studies in rats and rabbits, oral administration of sumatriptan  
200 to pregnant animals was associated with embryoletality, fetal abnormalities, and pup mortality.  
201 When administered by the intravenous route to pregnant rabbits, sumatriptan was embryoletal.  
202 Developmental toxicity studies of sumatriptan by the intranasal route have not been conducted.  
203 IMITREX Nasal Spray should be used during pregnancy only if the potential benefit justifies the  
204 potential risk to the fetus.

205 Oral administration of sumatriptan to pregnant rats during the period of organogenesis  
206 resulted in an increased incidence of fetal blood vessel (cervicothoracic and umbilical)  
207 abnormalities. The highest no-effect dose for embryofetal developmental toxicity in rats was  
208 60 mg/kg/day. Oral administration of sumatriptan to pregnant rabbits during the period of  
209 organogenesis resulted in increased incidences of embryoletality and fetal cervicothoracic  
210 vascular and skeletal abnormalities. Intravenous administration of sumatriptan to pregnant  
211 rabbits during the period of organogenesis resulted in an increased incidence of embryoletality.  
212 The highest oral and intravenous no-effect doses for developmental toxicity in rabbits were 15  
213 and 0.75 mg/kg/day, respectively.

214 Oral administration of sumatriptan to rats prior to and throughout gestation resulted in  
215 embryofetal toxicity (decreased body weight, decreased ossification, increased incidence of  
216 skeletal abnormalities). The highest no-effect dose was 50 mg/kg/day. In offspring of pregnant  
217 rats treated orally with sumatriptan during organogenesis, there was a decrease in pup survival.  
218 The highest no-effect dose for this effect was 60 mg/kg/day. Oral treatment of pregnant rats with

219 sumatriptan during the latter part of gestation and throughout lactation resulted in a decrease in  
220 pup survival. The highest no-effect dose for this finding was 100 mg/kg/day.

### 221 **8.3 Nursing Mothers**

222 Sumatriptan is excreted in human milk following subcutaneous administration. Infant  
223 exposure to sumatriptan can be minimized by avoiding breastfeeding for 12 hours after treatment  
224 with IMITREX Nasal Spray.

### 225 **8.4 Pediatric Use**

226 Safety and effectiveness in pediatric patients have not been established. IMITREX Nasal  
227 Spray is not recommended for use in patients younger than 18 years of age.

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

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

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

### 247 **8.5 Geriatric Use**

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

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

## 257 10 OVERDOSAGE

258 In clinical trials, the highest single doses of IMITREX Nasal Spray administered without  
259 significant reactions were 40 mg to 12 volunteers and 40 mg to 85 subjects with migraine, which  
260 is twice the highest single recommended dose. In addition, 12 volunteers were administered a  
261 total daily dose of 60 mg (20 mg 3 times daily) for 3.5 days without significant adverse  
262 reactions.

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

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

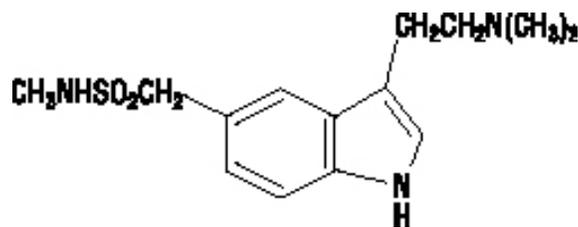
269 It is unknown what effect hemodialysis or peritoneal dialysis has on the serum  
270 concentrations of sumatriptan.

## 271 11 DESCRIPTION

272 IMITREX Nasal Spray contains sumatriptan, a selective 5-HT<sub>1B/1D</sub> receptor agonist.

273 Sumatriptan is chemically designated as 3-[2-(dimethylamino)ethyl]-N-methyl-indole-5-  
274 methanesulfonamide, and it has the following structure:

275



276

277

278 The empirical formula is C<sub>14</sub>H<sub>21</sub>N<sub>3</sub>O<sub>2</sub>S, representing a molecular weight of 295.4.

279 Sumatriptan is a white to off-white powder that is readily soluble in water and in saline.

280 Each IMITREX Nasal Spray contains 5 or 20 mg of sumatriptan in a 100-μL unit dose  
281 aqueous buffered solution containing monobasic potassium phosphate NF, anhydrous dibasic  
282 sodium phosphate USP, sulfuric acid NF, sodium hydroxide NF, and purified water USP. The  
283 pH of the solution is approximately 5.5. The osmolality of the solution is 372 or 742 mOsmol for  
284 the 5- and 20-mg IMITREX Nasal Spray, respectively.

285 **12 CLINICAL PHARMACOLOGY**

286 **12.1 Mechanism of Action**

287 Sumatriptan binds with high affinity to human cloned 5-HT<sub>1B/1D</sub> receptors. Sumatriptan  
288 presumably exerts its therapeutic effects in the treatment of migraine headache through agonist  
289 effects at the 5-HT<sub>1B/1D</sub> receptors on intracranial blood vessels and sensory nerves of the  
290 trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory  
291 neuropeptide release.

292 **12.2 Pharmacodynamics**

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

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

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

302 **12.3 Pharmacokinetics**

303 Absorption and Bioavailability: In a trial of 20 female volunteers, the mean maximum  
304 concentration following a 5- and 20-mg intranasal dose was 5 and 16 ng/mL, respectively. The  
305 mean C<sub>max</sub> following a 6-mg subcutaneous injection is 71 ng/mL (range: 49 to 110 ng/mL). The  
306 mean C<sub>max</sub> is 18 ng/mL (range: 7 to 47 ng/mL) following oral dosing with 25 mg and 51 ng/mL  
307 (range: 28 to 100 ng/mL) following oral dosing with 100 mg of sumatriptan. In a trial of 24 male  
308 volunteers, the bioavailability relative to subcutaneous injection was low, approximately 17%,  
309 primarily due to presystemic metabolism and partly due to incomplete absorption.

310 Clinical and pharmacokinetic data indicate that administration of two 5-mg doses, 1 dose  
311 in each nostril, is equivalent to administration of a single 10-mg dose in 1 nostril.

312 Distribution: Protein binding, determined by equilibrium dialysis over the concentration  
313 range of 10 to 1,000 ng/mL, is low, approximately 14% to 21%. The effect of sumatriptan on the  
314 protein binding of other drugs has not been evaluated. The apparent volume of distribution is  
315 2.7 L/kg.

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

320 Elimination: The elimination half-life of sumatriptan administered as a nasal spray is  
321 approximately 2 hours, similar to the half-life seen after subcutaneous injection. Only 3% of the

322 dose is excreted in the urine as unchanged sumatriptan; 42% of the dose is excreted as the major  
323 metabolite, the indole acetic acid analogue of sumatriptan. The total plasma clearance is  
324 approximately 1,200 mL/min.

325 **Special Populations: Age:** The pharmacokinetics of sumatriptan in the elderly (mean  
326 age: 72 years, 2 males and 4 females) and in subjects with migraine (mean age: 38 years, 25  
327 males and 155 females) were similar to that in healthy male subjects (mean age: 30 years).  
328 Intranasal sumatriptan has not been evaluated for age differences.

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

331 **Hepatic Impairment:** The effect of mild to moderate hepatic disease on the  
332 pharmacokinetics of the intranasal formulation of sumatriptan has not been evaluated.  
333 Sumatriptan bioavailability following intranasal administration is 17%, similar to that after oral  
334 administration (15%). Following oral administration, an approximately 70% increase in  $C_{max}$  and  
335 AUC was observed in one small trial of patients with moderate liver impairment ( $n = 8$ ) matched  
336 for sex, age and weight with healthy subjects ( $n = 8$ ). Similar changes can be expected following  
337 intranasal administration.

338 The pharmacokinetics of sumatriptan in patients with severe hepatic impairment has not  
339 been studied. The use of IMITREX Nasal Spray in patients with severe hepatic impairment is  
340 contraindicated [see *Contraindications (4)*].

341 **Race:** The systemic clearance and  $C_{max}$  of subcutaneous sumatriptan were similar in  
342 black ( $n = 34$ ) and Caucasian ( $n = 38$ ) healthy male subjects. Intranasal sumatriptan has not been  
343 evaluated for race differences.

344 **Drug Interaction Studies: Monoamine Oxidase-A Inhibitors:** Treatment with MAO-A  
345 inhibitors generally leads to an increase of sumatriptan plasma levels [see *Contraindications (4)*  
346 *and Drug Interactions (7.2)*]. MAO inhibitors interaction studies have not been performed with  
347 intranasal sumatriptan.

348 Due to gut and hepatic metabolic first-pass effects, the increase of systemic exposure after  
349 co-administration of an MAO-A inhibitor with oral sumatriptan is greater than after co-  
350 administration of the MAO inhibitors with subcutaneous sumatriptan. The effects of an MAO  
351 inhibitor on systemic exposure after intranasal sumatriptan would be expected to be greater than  
352 the effect after subcutaneous sumatriptan but smaller than the effect after oral sumatriptan  
353 because only swallowed drug would be subject to first-pass effects.

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

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

361 *Xylometazoline*: An in vivo drug interaction trial indicated that 3 drops of  
362 xylometazoline (0.1% w/v), a decongestant, administered 15 minutes prior to a 20-mg nasal dose  
363 of sumatriptan did not alter the pharmacokinetics of sumatriptan.

## 364 **13 NONCLINICAL TOXICOLOGY**

### 365 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

366 Carcinogenesis: In carcinogenicity studies in mouse and rat in which sumatriptan was  
367 administered orally for 78 and 104 weeks, respectively, there was no evidence in either species of  
368 an increase in tumors related to sumatriptan administration.

369 Carcinogenicity studies of sumatriptan using the nasal route have not been conducted.

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

373 Impairment of Fertility: When sumatriptan was administered by subcutaneous injection  
374 to male and female rats prior to and throughout the mating period, there was no evidence of  
375 impaired fertility at doses up to 60 mg/kg/day. When sumatriptan (5, 50, or 500 mg/kg/day) was  
376 administered orally to male and female rats prior to and throughout the mating period, there was  
377 a treatment-related decrease in fertility secondary to a decrease in mating in animals treated with  
378 doses greater than 5 mg/kg/day. It is not clear whether this finding was due to an effect on males  
379 or females or both.

380 Fertility studies of sumatriptan using the intranasal route have not been conducted.

### 381 **13.2 Animal Toxicology and/or Pharmacology**

382 Corneal Opacities: Dogs receiving oral sumatriptan developed corneal opacities and  
383 defects in the corneal epithelium. Corneal opacities were seen at the lowest dose tested,  
384 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium  
385 were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and  
386 no-effect doses were not established.

## 387 **14 CLINICAL STUDIES**

388 The efficacy of IMITREX Nasal Spray in the acute treatment of migraine headaches was  
389 demonstrated in 8, randomized, double-blind, placebo-controlled trials, of which 5 used the  
390 recommended dosing regimen and used the marketed formulation. Patients enrolled in these 5  
391 trials were predominately female (86%) and Caucasian (95%), with a mean age of 41 years  
392 (range of 18 to 65 years). Patients were instructed to treat a moderate to severe headache.  
393 Headache response, defined as a reduction in headache severity from moderate or severe pain to

394 mild or no pain, was assessed up to 2 hours after dosing. Associated symptoms such as nausea,  
 395 photophobia, and phonophobia were also assessed. Maintenance of response was assessed for up  
 396 to 24 hours postdose. A second dose of IMITREX Nasal Spray or other medication was allowed  
 397 2 to 24 hours after the initial treatment for recurrent headache. The frequency and time to use of  
 398 these additional treatments were also determined. In all trials, doses of 10 and 20 mg were  
 399 compared with placebo in the treatment of 1 to 3 migraine attacks. Patients received doses as a  
 400 single spray into 1 nostril. In 2 trials, a 5-mg dose was also evaluated.

401 In all 5 trials utilizing the market formulation and recommended dosage regimen, the  
 402 percentage of patients achieving headache response 2 hours after treatment was significantly  
 403 greater among patients receiving IMITREX Nasal Spray at all doses (with one exception)  
 404 compared with those who received placebo. In 4 of the 5 trials, there was a statistically  
 405 significant greater percentage of patients with headache response at 2 hours in the 20-mg group  
 406 when compared with the lower dose groups (5 and 10 mg). There were no statistically significant  
 407 differences between the 5- and 10-mg dose groups in any trial. The results from the 5 controlled  
 408 clinical trials are summarized in Table 2. Note that, in general, comparisons of results obtained in  
 409 trials conducted under different conditions by different investigators with different samples of  
 410 patients are ordinarily unreliable for purposes of quantitative comparison.

411

412 **Table 2. Percentage of Patients With Headache Response (No or Mild Pain) 2 Hours**  
 413 **Following Treatment**

	<b>IMITREX Nasal Spray 5 mg</b>	<b>IMITREX Nasal Spray 10 mg</b>	<b>IMITREX Nasal Spray 20 mg</b>	<b>Placebo</b>
Trial 1	49% <sup>a</sup> (n = 121)	46% <sup>a</sup> (n = 112)	64% <sup>a,b,c</sup> (n = 118)	25% (n = 63)
Trial 2	Not applicable	44% <sup>a</sup> (n = 273)	55% <sup>a,b</sup> (n = 277)	25% (n = 138)
Trial 3	Not applicable	54% <sup>a</sup> (n = 106)	63% <sup>a</sup> (n = 202)	35% (n = 100)
Trial 4	Not applicable	43% (n = 106)	62% <sup>a,b</sup> (n = 215)	29% (n = 112)
Trial 5 <sup>d</sup>	45% <sup>a</sup> (n = 296)	53% <sup>a</sup> (n = 291)	60% <sup>a,c</sup> (n = 286)	36% (n = 198)

414 <sup>a</sup> P<0.05 in comparison with placebo.

415 <sup>b</sup> P<0.05 in comparison with 10 mg.

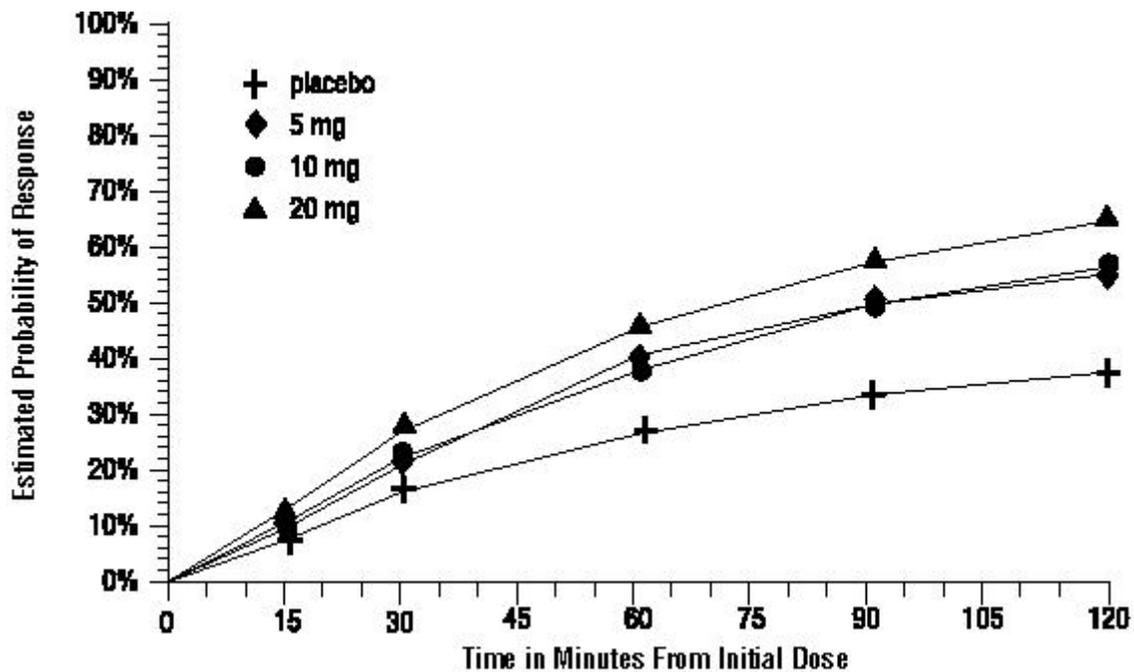
416 <sup>c</sup> P<0.05 in comparison with 5 mg.

417 <sup>d</sup> Data are for attack 1 only of multi-attack trial for comparison.

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The estimated probability of achieving an initial headache response over the 2 hours following treatment is depicted in Figure 1.

**Figure 1. Estimated Probability of Achieving Initial Headache Response Within 120 Minutes<sup>a</sup>**



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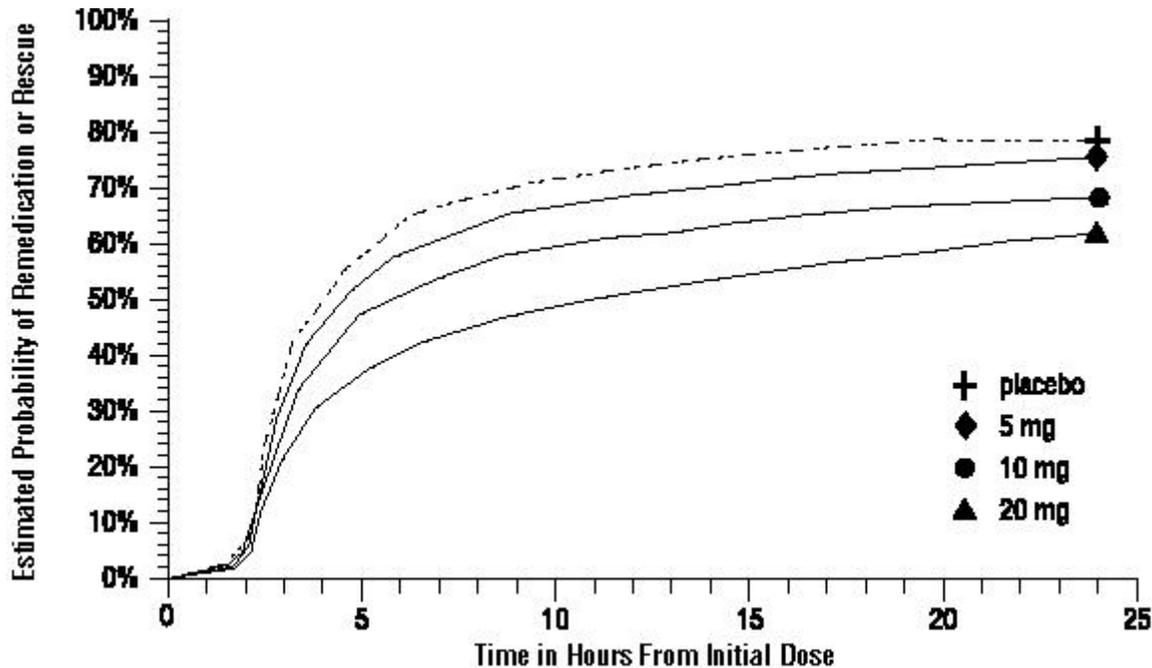
<sup>a</sup> The figure shows the probability over time of obtaining headache response (no or mild pain) following treatment with intranasal sumatriptan. The averages displayed are based on pooled data from the 5 clinical controlled trials providing evidence of efficacy. Kaplan-Meier plot with patients not achieving response within 120 minutes censored to 120 minutes.

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For patients with migraine-associated nausea, photophobia, and phonophobia at baseline, there was a lower incidence of these symptoms at 2 hours following administration of IMITREX Nasal Spray compared with placebo.

Two to 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.

441 **Figure 2. The Estimated Probability of Patients Taking a Second Dose or Other**  
 442 **Medication for Migraine Over the 24 Hours Following the Initial Dose of Study**  
 443 **Treatment<sup>a</sup>**  
 444



445 <sup>a</sup> Kaplan-Meier plot based on data obtained in the 3 clinical controlled trials providing  
 446 evidence of efficacy with patients not using additional treatments censored to 24 hours.  
 447 Plot also includes patients who had no response to the initial dose. No remediation  
 448 was allowed within 2 hours postdose.  
 449  
 450

451 There is evidence that doses above 20 mg do not provide a greater effect than 20 mg.  
 452 There was no evidence to suggest that treatment with sumatriptan was associated with an  
 453 increase in the severity of recurrent headaches. The efficacy of IMITREX Nasal Spray was  
 454 unaffected by presence of aura; duration of headache prior to treatment; gender, age, or weight of  
 455 the subject; or concomitant use of common migraine prophylactic drugs (e.g., beta-blockers,  
 456 calcium channel blockers, tricyclic antidepressants). There were insufficient data to assess the  
 457 impact of race on efficacy.

458 **16 HOW SUPPLIED/STORAGE AND HANDLING**

459 IMITREX Nasal Spray 5 mg (NDC 0173-0524-00) and 20 mg (NDC 0173-0523-00) are  
 460 each supplied in boxes of 6 nasal spray devices. Each unit dose spray supplies 5 mg and 20 mg,  
 461 respectively, of sumatriptan.

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

463 **17 PATIENT COUNSELING INFORMATION**

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

465 Risk of Myocardial Ischemia and/or Infarction, Prinzmetal's Angina, Other  
466 Vasospasm-Related Events, Arrhythmias, and Cerebrovascular Events: Inform patients  
467 that IMITREX Nasal Spray may cause serious cardiovascular side effects such as myocardial  
468 infarction or stroke. Although serious cardiovascular events can occur without warning  
469 symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath,  
470 irregular heartbeat, significant rise in blood pressure, weakness, and slurring of speech and  
471 should ask for medical advice if any indicative sign or symptoms are observed. Apprise patients  
472 of the importance of this follow-up [*see Warnings and Precautions (5.1, 5.2, 5.4, 5.5, 5.8)*].

473 Anaphylactic/Anaphylactoid Reactions: Inform patients that  
474 anaphylactic/anaphylactoid reactions have occurred in patients receiving IMITREX Nasal Spray.  
475 Such reactions can be life threatening or fatal. In general, anaphylactic reactions to drugs are  
476 more likely to occur in individuals with a history of sensitivity to multiple allergens [*see*  
477 *Contraindications (4) and Warnings and Precautions (5.10)*].

478 Concomitant Use With Other Triptans or Ergot Medications: Inform patients that  
479 use of IMITREX Nasal Spray within 24 hours of another triptan or an ergot-type medication  
480 (including dihydroergotamine or methysergide) is contraindicated [*see Contraindications (4) and*  
481 *Drug Interactions (7.1, 7.3)*].

482 Serotonin Syndrome: Caution patients about the risk of serotonin syndrome with the  
483 use of IMITREX Nasal Spray or other triptans, particularly during combined use with SSRIs,  
484 SNRIs, TCAs, and MAO inhibitors [*see Warnings and Precautions (5.7) and Drug Interactions*  
485 *(7.4)*].

486 Medication Overuse Headache: Inform patients that use of acute migraine drugs for  
487 10 or more days per month may lead to an exacerbation of headache and encourage patients to  
488 record headache frequency and drug use (e.g., by keeping a headache diary) [*see Warnings and*  
489 *Precautions (5.6)*].

490 Pregnancy: Inform patients that IMITREX Nasal Spray should not be used during  
491 pregnancy unless the potential benefit justifies the potential risk to the fetus [*see Use in Specific*  
492 *Populations (8.1)*].

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

495 Ability to Perform Complex Tasks: Treatment with IMITREX Nasal Spray may cause  
496 somnolence and dizziness; instruct patients to evaluate their ability to perform complex tasks  
497 after administration of IMITREX Nasal Spray.

498 Local Irritation: Inform patients that they may experience local irritation of their nose and  
499 throat. The symptoms will generally resolve in less than 2 hours.

500 How to Use IMITREX Nasal Spray: Provide patients instruction on the proper use of  
501 IMITREX Nasal Spray. Caution patients to avoid spraying the contents of the device in their  
502 eyes.

503

504 IMITREX is a registered trademark of the GlaxoSmithKline group of companies.

505



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507 GlaxoSmithKline

508 Research Triangle Park, NC 27709

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511

512 IMN:xPI

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**Patient Information**  
**IMITREX® (IM-i-trex)**  
**(sumatriptan)**  
**Nasal Spray**

514

515

516

517

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

521

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

523 **IMITREX can cause serious side effects, including:**

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

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

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

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

- 537 • have high blood pressure
- 538 • have high cholesterol levels
- 539 • smoke
- 540 • are overweight
- 541 • have diabetes
- 542 • have a family history of heart disease

543

#### 544 **What is IMITREX?**

545 IMITREX is a prescription medicine used to treat acute migraine headaches with or  
546 without aura in adults.

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

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

552 It is not known if IMITREX is safe and effective to treat cluster headaches.

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

554

#### 555 **Who should not use IMITREX?**

##### 556 **Do not use IMITREX if you have:**

- 557 • heart problems or a history of heart problems
- 558 • narrowing of blood vessels to your legs, arms, stomach, or kidneys (peripheral  
559 vascular disease)
- 560 • uncontrolled high blood pressure
- 561 • severe liver problems
- 562 • hemiplegic migraines or basilar migraines. If you are not sure if you have these  
563 types of migraines, ask your healthcare provider.
- 564 • had a stroke, transient ischemic attacks (TIAs), or problems with your blood  
565 circulation
- 566 • taken any of the following medicines in the last 24 hours:
  - 567 • almotriptan (AXERT<sup>®</sup>)
  - 568 • eletriptan (RELPAX<sup>®</sup>)
  - 569 • frovatriptan (FROVA<sup>®</sup>)

- 570 • naratriptan (AMERGE<sup>®</sup>)
- 571 • rizatriptan (MAXALT<sup>®</sup>, MAXALT-MLT<sup>®</sup>)
- 572 • sumatriptan and naproxen (TREXIMET<sup>®</sup>)
- 573 • ergotamines (CAFERGOT<sup>®</sup>, ERGOMAR<sup>®</sup>, MIGERGOT<sup>®</sup>)
- 574 • dihydroergotamine (D.H.E. 45<sup>®</sup>, MIGRANAL<sup>®</sup>)

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

- 576 • an allergy to sumatriptan or any of the ingredients in IMITREX. See below for a
- 577 complete list of ingredients in IMITREX.

578

579 **What should I tell my healthcare provider before using IMITREX?**

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

- 582 • have high blood pressure
- 583 • have high cholesterol
- 584 • have diabetes
- 585 • smoke
- 586 • are overweight
- 587 • have heart problems or family history of heart problems or stroke
- 588 • have kidney problems
- 589 • have liver problems
- 590 • have had epilepsy or seizures
- 591 • are not using effective birth control
- 592 • become pregnant while taking IMITREX
- 593 • are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk  
594 and may harm your baby. Talk with your healthcare provider about the best way  
595 to feed your baby if you use IMITREX.

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

598 IMITREX and certain other medicines can affect each other, causing serious side  
599 effects.

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

- 602 • selective serotonin reuptake inhibitors (SSRIs)
- 603 • serotonin norepinephrine reuptake inhibitors (SNRIs)
- 604 • tricyclic antidepressants (TCAs)
- 605 • monoamine oxidase inhibitors (MAOIs)

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

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

610

611 **How should I use IMITREX?**

- 612 • Certain people should use their first dose of IMITREX in their healthcare  
613 provider's office or in another medical setting. Ask your healthcare provider if  
614 you should use your first dose in a medical setting.
- 615 • Use IMITREX exactly as your healthcare provider tells you to use it.
- 616 • Your healthcare provider may change your dose. Do not change your dose  
617 without first talking with your healthcare provider.
- 618 • If you do not get any relief after your first nasal spray, do not use a second  
619 nasal spray without first talking with your healthcare provider.
- 620 • If your headache comes back after the first nasal spray or you only get some  
621 relief from your headache, you can use a second nasal spray 2 hours after the  
622 first nasal spray.
- 623 • Do not use more than 40 mg of IMITREX Nasal Spray in a 24-hour period.
- 624 • It is not known how using IMITREX Nasal Spray for a long time affects the nose  
625 and throat.
- 626 • If you use too much IMITREX, call your healthcare provider or go to the nearest  
627 hospital emergency room right away.
- 628 • You should write down when you have headaches and when you use IMITREX so  
629 you can talk with your healthcare provider about how IMITREX is working for  
630 you.

631

632 **What should I avoid while using IMITREX?**

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

636

637 **What are the possible side effects of IMITREX?**

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

640 These serious side effects include:

- 641 • changes in color or sensation in your fingers and toes (Raynaud's syndrome)
- 642 • stomach and intestinal problems (gastrointestinal and colonic ischemic events).
- 643 Symptoms of gastrointestinal and colonic ischemic events include:
- 644 • sudden or severe stomach pain
- 645 • stomach pain after meals
- 646 • weight loss
- 647 • nausea or vomiting
- 648 • constipation or diarrhea
- 649 • bloody diarrhea
- 650 • fever
- 651 • problems with blood circulation to your legs and feet (peripheral vascular
- 652 ischemia). Symptoms of peripheral vascular ischemia include:
- 653 • cramping and pain in your legs or hips
- 654 • feeling of heaviness or tightness in your leg muscles
- 655 • burning or aching pain in your feet or toes while resting
- 656 • numbness, tingling, or weakness in your legs
- 657 • cold feeling or color changes in 1 or both legs or feet
- 658 • hives (itchy bumps); swelling of your tongue, mouth, or throat
- 659 • medication overuse headaches. Some people who use too many IMITREX nasal
- 660 sprays may have worse headaches (medication overuse headache). If your
- 661 headaches get worse, your healthcare provider may decide to stop your
- 662 treatment with IMITREX.
- 663 • serotonin syndrome. Serotonin syndrome is a rare but serious problem that can
- 664 happen in people using IMITREX, especially if IMITREX is used with anti-
- 665 depressant medicines called SSRIs or SNRIs.
- 666 Call your healthcare provider right away if you have any of the following
- 667 symptoms of serotonin syndrome:
- 668 • mental changes such as seeing things that are not there (hallucinations),
- 669 agitation, or coma
- 670 • fast heartbeat
- 671 • changes in blood pressure
- 672 • high body temperature
- 673 • tight muscles
- 674 • trouble walking
- 675 • seizures. Seizures have happened in people taking IMITREX who have never had
- 676 seizures before. Talk with your healthcare provider about your chance of having
- 677 seizures while you take IMITREX.

678 The most common side effects of IMITREX Nasal Spray include:

- 679 • unusual or bad taste in your mouth
- 680 • nausea and/or vomiting
- 681 • discomfort of your throat or nose
- 682 • dizziness
- 683 • warm, hot, burning feeling

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

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

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

690

691 **How should I store IMITREX Nasal Spray?**

- 692 • Store IMITREX between 36°F to 86°F (2°C to 30°C).
- 693 • Store your medicine away from light.

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

695

696 **General information about the safe and effective use of IMITREX.**

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

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

705 For more information, go to [www.gsk.com](http://www.gsk.com) or call 1-888-825-5249.

706

707 **What are the ingredients in IMITREX Nasal Spray?**

708 Active ingredient: sumatriptan

709 Inactive ingredients: monobasic potassium phosphate NF, anhydrous dibasic  
710 sodium phosphate USP, sulfuric acid NF, sodium hydroxide NF, and purified water  
711 USP.

712

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

715

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717 GlaxoSmithKline group of companies. The other brands listed are trademarks of  
718 their respective owners and are not trademarks of GlaxoSmithKline. The makers of  
719 these brands are not affiliated with and do not endorse GlaxoSmithKline or its  
720 products.

721



722

723 GlaxoSmithKline

724 Research Triangle Park, NC 27709

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