

Imitrex Tablets
Sumatriptan succinate
NDA 020132/S-028

FDA Approved Labeling Text November 2013

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_{1B/1D}) receptor agonist (triptan) indicated for acute treatment of migraine with or without aura in adults. (1)

Limitations of Use:

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

DOSAGE AND ADMINISTRATION

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

DOSAGE FORMS AND STRENGTHS

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

CONTRAINDICATIONS

- History of coronary artery disease or coronary artery vasospasm (4)
- Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders (4)
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine (4)
- Peripheral vascular disease (4)
- Ischemic bowel disease (4)
- Uncontrolled hypertension (4)
- Recent (within 24 hours) use of another 5-HT₁ agonist (e.g., another 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.

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[®] 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.

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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-hydroxytryptamine₁
51 (5-HT₁) 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-naive 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

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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-HT₁ 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-HT₁ agonists, and some have resulted in fatalities. In a number of cases, it appears
91 possible that the cerebrovascular events were primary, the 5-HT₁ 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-HT₁ agonist, rule out a vasospastic reaction before receiving additional IMITREX
105 Tablets.

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106 Reports of transient and permanent blindness and significant partial vision loss have been
107 reported with the use of 5-HT₁ agonists. Since visual disorders may be part of a migraine attack,
108 a causal relationship between these events and the use of 5-HT₁ 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-HT₁
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

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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

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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.

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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-HT₁ Agonists**

193 Because their vasospastic effects may be additive, co-administration of IMITREX
194 Tablets and other 5-HT₁ 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/m² 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/m² basis) and 0.75 mg/kg/day,
217 respectively.

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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/m² 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/m² 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/m² 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**

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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.

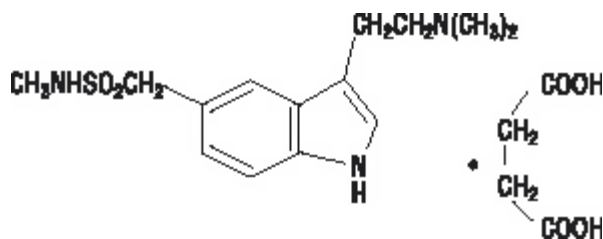
274 The elimination half-life of sumatriptan is approximately 2.5 hours [see Clinical
275 Pharmacology (12.3)], and therefore monitoring of patients after overdose with IMITREX
276 Tablets should continue for at least 12 hours or while symptoms or signs persist.

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_{1B/1D} 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



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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_{1B/1D} receptors. Sumatriptan
297 presumably exerts its therapeutic effects in the treatment of migraine headache through agonist
298 effects at the 5-HT_{1B/1D} 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_{max} of 5 and 16 ng/mL
315 following dosing with a 5- and 20-mg intranasal dose, respectively. The mean C_{max} 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_{max} is similar during a migraine attack and during a migraine-free period, but
319 the T_{max} 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

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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}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.

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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/m² 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

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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% ^a	67% ^a	61% ^{a,b}	78% ^{a,b}	62% ^{a,b}	79% ^{a,b}	27%	38%
	(n = 298)		(n = 296)		(n = 296)		(n = 94)	
Trial 2	52% ^a	70% ^a	50% ^a	68% ^a	56% ^a	71% ^a	26%	38%
	(n = 66)		(n = 62)		(n = 66)		(n = 65)	
Trial 3	52% ^a	65% ^a	54% ^a	72% ^a	57% ^a	78% ^a	17%	19%

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

422 ^a $P < 0.05$ in comparison with placebo.

423 ^b $P < 0.05$ in comparison with 25 mg.

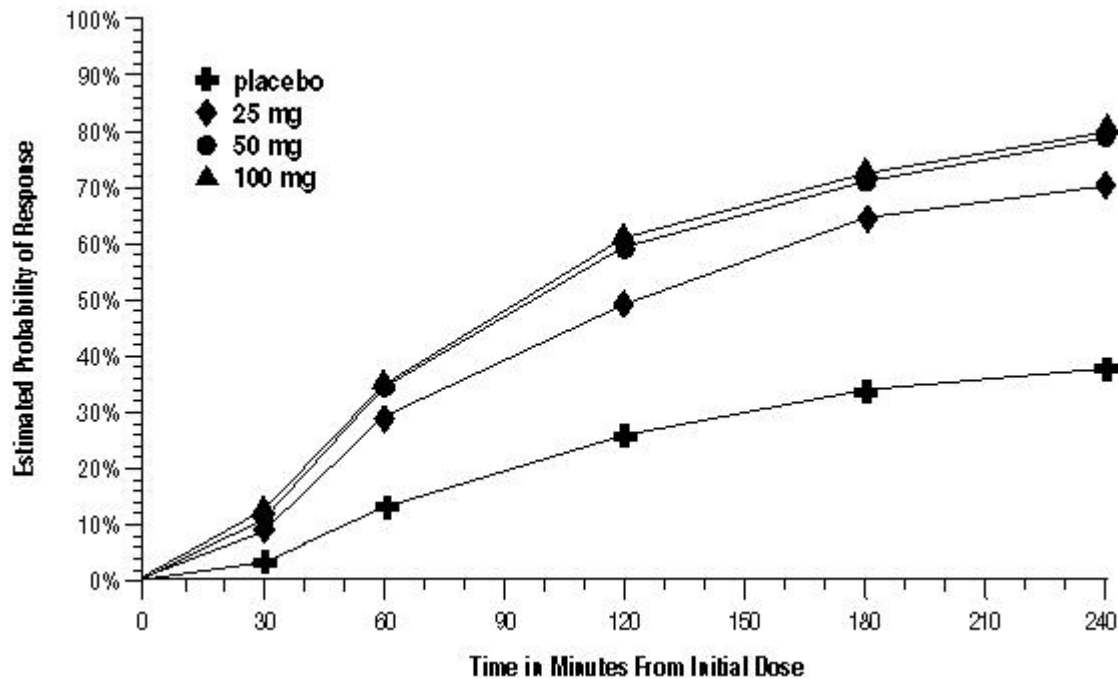
424

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^a**

430



431

432 ^a 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

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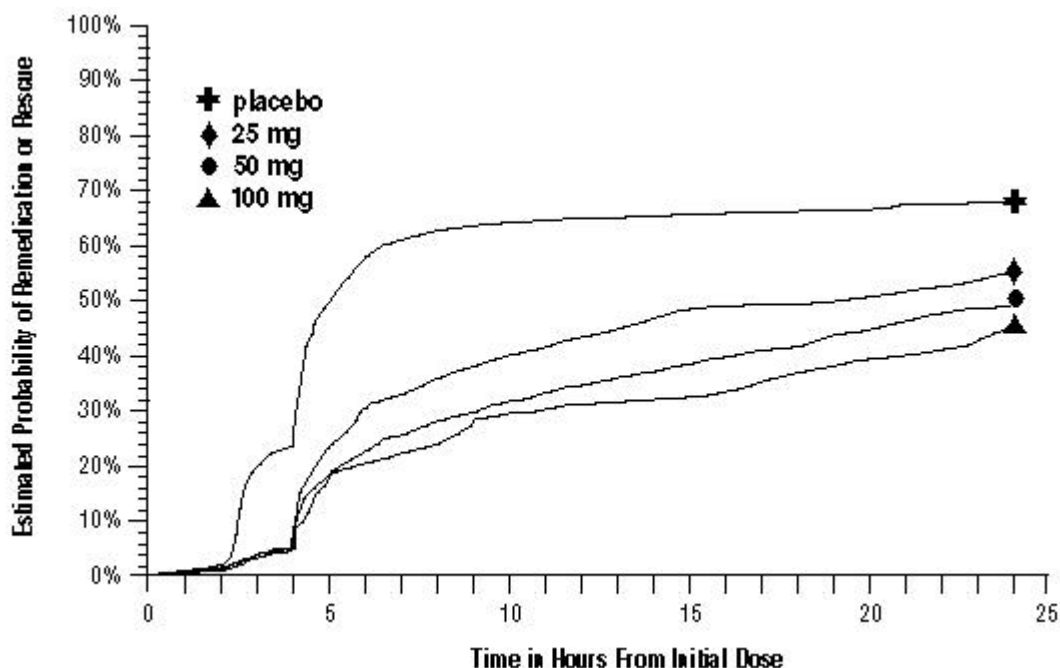
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443 for pain relief in the form of a second dose of study treatment or other medication. The estimated
444 probability of patients taking a second dose or other medication for migraine over the 24 hours
445 following the initial dose of study treatment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

450



451

452 ^a 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 remediation 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.

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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 “T” 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

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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

522

IMITREX[®] (IM-i-trex)

523

(sumatriptan succinate)

524

Tablets

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.**

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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)

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- 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[®])
- 576 • eletriptan (RELPAX[®])
- 577 • frovatriptan (FROVA[®])
- 578 • naratriptan (AMERGE[®])
- 579 • rizatriptan (MAXALT[®], MAXALT-MLT[®])
- 580 • sumatriptan and naproxen (TREXIMET[®])
- 581 • ergotamines (CAFERGOT[®], ERGOMAR[®], MIGERGOT[®])
- 582 • dihydroergotamine (D.H.E. 45[®], MIGRANAL[®])
- 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.

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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?**

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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

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- 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.

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710 For more information, go to 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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723 GlaxoSmithKline group of companies. The other brands listed are trademarks of
724 their respective owners and are not trademarks of GlaxoSmithKline. The makers of
725 these brands are not affiliated with and do not endorse GlaxoSmithKline or its
726 products.

727

728



729

730 GlaxoSmithKline

731 Research Triangle Park, NC 27709

732

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734

735 Month Year

736 IMT: xPIL

Imitrex Nasal Spray
Sumatriptan
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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_{1B/1D}) receptor agonist (triptan) indicated for acute treatment of migraine with or without aura in adults. (1)

Limitations of Use:

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

DOSAGE AND ADMINISTRATION

- Single dose of 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-HT₁ 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.

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[®] 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)*]

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- 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-hydroxytryptamine₁
40 (5-HT₁) 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-HT₁ agonists. Discontinue IMITREX Nasal Spray if these disturbances

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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-HT₁ agonists, and some have resulted in fatalities. In a number of cases, it appears
79 possible that the cerebrovascular events were primary, the 5-HT₁ 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-HT₁ 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-HT₁ agonists. Since visual disorders may be part of a migraine attack,
96 a causal relationship between these events and the use of 5-HT₁ 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.

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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-HT₁
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

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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

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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

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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-HT₁ Agonists**

190 Because their vasospastic effects may be additive, co-administration of IMITREX Nasal
191 Spray and other 5-HT₁ 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

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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.

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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.

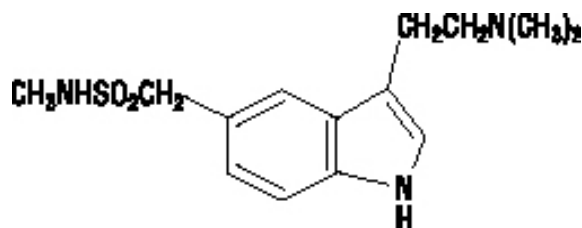
266 The elimination half-life of sumatriptan is approximately 2 hours [see Clinical
267 Pharmacology (12.3)], and therefore monitoring of patients after overdose with IMITREX Nasal
268 Spray should continue for at least 10 hours or while symptoms or signs persist.

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_{1B/1D} 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 C₁₄H₂₁N₃O₂S, 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.

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285 **12 CLINICAL PHARMACOLOGY**

286 **12.1 Mechanism of Action**

287 Sumatriptan binds with high affinity to human cloned 5-HT_{1B/1D} receptors. Sumatriptan
288 presumably exerts its therapeutic effects in the treatment of migraine headache through agonist
289 effects at the 5-HT_{1B/1D} 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_{max} following a 6-mg subcutaneous injection is 71 ng/mL (range: 49 to 110 ng/mL). The
306 mean C_{max} 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

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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.

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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

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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**

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

414 ^a $P < 0.05$ in comparison with placebo.

415 ^b $P < 0.05$ in comparison with 10 mg.

416 ^c $P < 0.05$ in comparison with 5 mg.

417 ^d Data are for attack 1 only of multi-attack trial for comparison.

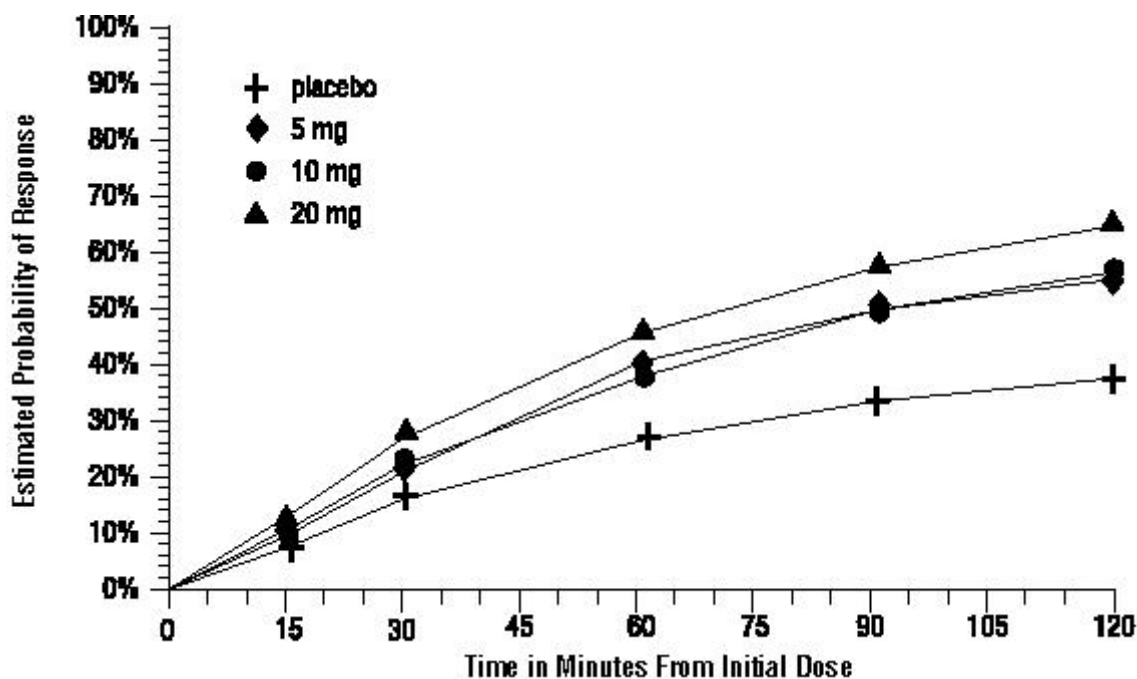
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The estimated probability of achieving an initial headache response over the 2 hours following treatment is depicted in Figure 1.

Figure 1. Estimated Probability of Achieving Initial Headache Response Within 120 Minutes^a



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^a 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.

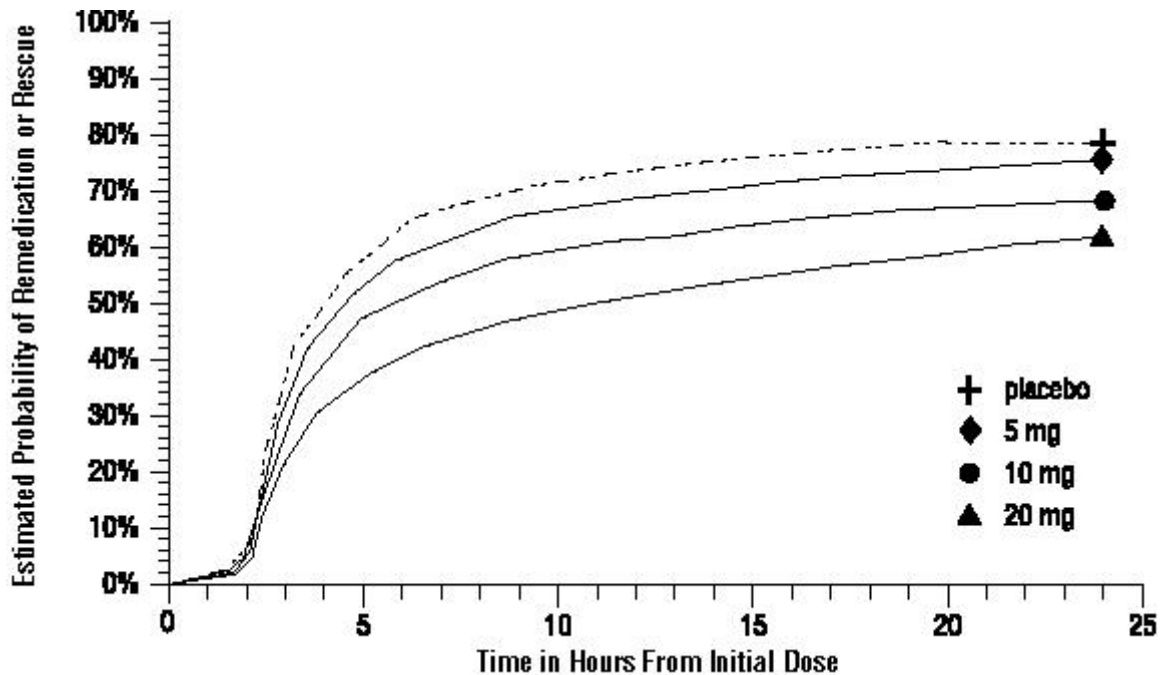
For patients with migraine-associated nausea, photophobia, and phonophobia at baseline, there was a lower incidence of these symptoms at 2 hours following administration of IMITREX Nasal Spray compared with placebo.

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.

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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^a**
444



445 ^a 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 remedication
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.

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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.

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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



506

507 GlaxoSmithKline

508 Research Triangle Park, NC 27709

509

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511

512 IMN:xPI

513

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

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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

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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[®])
 - 568 • eletriptan (RELPA[®])
 - 569 • frovatriptan (FROVA[®])

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

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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:

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- 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.

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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 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.

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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.

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Month Year

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