

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) injection, for subcutaneous 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)
- Acute treatment of cluster headache in adults (1)

Limitations of Use:

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

DOSAGE AND ADMINISTRATION

- For subcutaneous use only. (2.1)
- Acute treatment of migraine: 1- to 6-mg Single dose. (2.1)
- Acute treatment of cluster headache: 6-mg Single dose. (2.1)
- Maximum dose in a 24-hour period: 12 mg, Separate doses by at least 1 hour. (2.1)
- Patients receiving doses other than 4 or 6 mg: Use the 6-mg single-dose vial. (2.3)

DOSAGE FORMS AND STRENGTHS

- Injection: 4- and 6-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose Pen (3)
- Injection: 6-mg single-dose vial (3)

CONTRAINDICATIONS

- Coronary artery disease or coronary 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)

- Current or recent (past 2 weeks) use of monoamine oxidase-A inhibitor (4)
- Known hypersensitivity to sumatriptan (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 ischemia and infarction events, 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)
- Increase in blood pressure: Monitor blood pressure. (5.8)
- Anaphylactic/anaphylactoid reactions: Discontinue IMITREX if occurs (5.9)
- Seizures: Use with caution in patients with epilepsy or a lowered seizure threshold. (5.10)

ADVERSE REACTIONS

Most common adverse reactions (≥5% and > placebo) were injection site reactions, tingling, dizziness/vertigo, warm/hot sensation, burning sensation, feeling of heaviness, pressure sensation, flushing, feeling of tightness, and numbness (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)
- Geriatric use: A cardiovascular evaluation is recommended in those who have other cardiovascular risk factors prior to receiving IMITREX. (8.5)

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

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1 FULL PRESCRIBING INFORMATION

2 1 INDICATIONS AND USAGE

3 IMITREX[®] Injection is indicated in adults for (1) the acute treatment of migraine, with or
4 without aura, and (2) the acute treatment of cluster headache.

5 Limitations of Use:

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

10 2 DOSAGE AND ADMINISTRATION

11 2.1 Dosing Information

12 The maximum single recommended adult dose of IMITREX Injection for the acute
13 treatment of migraine or cluster headache is 6 mg injected subcutaneously. For the treatment of
14 migraine, if side effects are dose limiting, lower doses (1 to 5 mg) may be used [*see Clinical*
15 *Studies (14.1)*]. For the treatment of cluster headache, the efficacy of lower doses has not been
16 established.

17 The maximum cumulative dose that may be given in 24 hours is 12 mg, two 6-mg
18 injections separated by at least 1 hour. A second 6-mg dose should only be considered if some
19 response to a first injection was observed.

20 2.2 Administration Using the IMITREX STATdose Pen[®]

21 An autoinjector device (IMITREX STATdose Pen) is available for use with 4- and 6-mg
22 prefilled syringe cartridges. With this device, the needle penetrates approximately 1/4 inch (5 to
23 6 mm). The injection is intended to be given subcutaneously, and intramuscular or intravascular
24 delivery must be avoided. Instruct patients on the proper use of IMITREX STATdose Pen and
25 direct them to use injection sites with an adequate skin and subcutaneous thickness to
26 accommodate the length of the needle.

27 2.3 Administration of Doses of IMITREX Other Than 4 or 6 mg

28 In patients receiving doses other than 4 or 6 mg, use the 6-mg single-dose vial; do not use
29 the IMITREX STATdose Pen. Visually inspect the vial for particulate matter and discoloration
30 before administration. Do not use if particulates and discolorations are noted.

31 3 DOSAGE FORMS AND STRENGTHS

- 32 • Injection: 4- and 6-mg single-dose prefilled syringe cartridges for use with the IMITREX
33 STATdose Pen
- 34 • Injection: 6-mg single-dose vial

35 4 CONTRAINDICATIONS

36 IMITREX Injection is contraindicated in patients with:

- 37 • Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or
38 documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina
39 [*see Warnings and Precautions (5.1)*].
- 40 • Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory
41 conduction pathway disorders [*see Warnings and Precautions (5.2)*].
- 42 • History of stroke or transient ischemic attack (TIA) because these patients are at a higher risk
43 of stroke [*see Warnings and Precautions (5.4)*].
- 44 • History of hemiplegic or basilar migraine.
- 45 • Peripheral vascular disease [*see Warnings and Precautions (5.5)*].
- 46 • Ischemic bowel disease [*see Warnings and Precautions (5.5)*].
- 47 • Uncontrolled hypertension [*see Warnings and Precautions (5.8)*].
- 48 • Recent (i.e., within 24 hours) use of ergotamine-containing medication, ergot-type
49 medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine₁
50 (5-HT₁) agonist [*see Drug Interactions (7.1, 7.3)*].
- 51 • Concurrent administration of an MAO-A inhibitor or recent (within 2 weeks) use of an
52 MAO-A inhibitor [*see Drug Interactions (7.2) and Clinical Pharmacology (12.3)*].
- 53 • Known hypersensitivity to sumatriptan [*see Warnings and Precautions (5.9) and Adverse
54 Reactions (6.2)*].
- 55 • Severe hepatic impairment [*see Clinical Pharmacology (12.3)*].

56 **5 WARNINGS AND PRECAUTIONS**

57 **5.1 Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina**

58 The use of IMITREX Injection is contraindicated in patients with ischemic or vasospastic
59 CAD. There have been rare reports of serious cardiac adverse reactions, including acute
60 myocardial infarction, occurring within a few hours following administration of IMITREX
61 Injection. Some of these reactions occurred in patients without known CAD. 5-HT₁ agonists,
62 including IMITREX Injection, may cause coronary artery vasospasm (Prinzmetal's angina), even
63 in patients without a history of CAD.

64 Perform a cardiovascular evaluation in triptan-naive patients who have multiple
65 cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong
66 family history of CAD) prior to receiving IMITREX Injection. If there is evidence of CAD or
67 coronary artery vasospasm, IMITREX Injection is contraindicated. For patients with multiple
68 cardiovascular risk factors who have a negative cardiovascular evaluation, consider
69 administering the first dose of IMITREX Injection in a medically supervised setting and
70 performing an electrocardiogram (ECG) immediately following IMITREX Injection. For such
71 patients, consider periodic cardiovascular evaluation in intermittent long-term users of IMITREX
72 Injection.

73 Evaluate patients with signs or symptoms suggestive of angina following IMITREX
74 Injection for the presence of CAD or Prinzmetal's angina before receiving additional doses of
75 IMITREX Injection.

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 Injection if these disturbances occur.
80 IMITREX Injection is 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 As with other 5-HT₁ agonists, sensations of tightness, pain, pressure, and heaviness in the
84 precordium, throat, neck, and jaw commonly occur after treatment with IMITREX Injection and
85 are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at
86 high cardiac risk. The use of IMITREX Injection is contraindicated in patients shown to have
87 CAD and those with Prinzmetal's variant 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 Injection if a
95 cerebrovascular event occurs.

96 As with other acute migraine therapies, before treating headaches in patients not
97 previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms,
98 exclude other potentially serious neurological conditions. IMITREX Injection is contraindicated
99 in patients with a history of stroke or TIA.

100 **5.5 Other Vasospasm Reactions**

101 5-HT₁ agonists, including IMITREX Injection, may cause non-coronary vasospastic
102 reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction
103 (presenting with abdominal pain and bloody diarrhea), splenic infarction, and Raynaud's
104 syndrome. Until further evaluation, IMITREX Injection is contraindicated in patients who
105 experience symptoms or signs suggestive of non-coronary vasospasm reaction following the use
106 of any 5-HT₁ agonist.

107 Reports of transient and permanent blindness and significant partial vision loss have been
108 reported with the use of 5-HT₁ agonists. Since visual disorders may be part of a migraine attack,
109 a causal relationship between these events and the use of 5-HT₁ agonists have not been clearly
110 established.

111 **5.6 Medication Overuse Headache**

112 Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, combination of
113 drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse
114 headache). Medication overuse headache may present as migraine-like daily headaches, or as a
115 marked increase in frequency of migraine attacks. Detoxification of patients, including

116 withdrawal of the overused drugs, and treatment of withdrawal symptoms (which often includes
117 a transient worsening of headache) may be necessary.

118 **5.7 Serotonin Syndrome**

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

128 **5.8 Increase in Blood Pressure**

129 Significant elevation in blood pressure, including hypertensive crisis with acute
130 impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT₁
131 agonists, including patients without a history of hypertension. Monitor blood pressure in patients
132 treated with IMITREX. IMITREX Injection is contraindicated in patients with uncontrolled
133 hypertension.

134 **5.9 Anaphylactic/Anaphylactoid Reactions**

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

139 **5.10 Seizures**

140 Seizures have been reported following administration of sumatriptan. Some have
141 occurred in patients with either a history of seizures or concurrent conditions predisposing to
142 seizures. There are also reports in patients where no such predisposing factors are apparent.
143 IMITREX Injection should be used with caution in patients with a history of epilepsy or
144 conditions associated with a lowered seizure threshold.

145 **6 ADVERSE REACTIONS**

146 The following adverse reactions are discussed in more detail in other sections of the
147 labeling:

- 148 • Myocardial ischemia, myocardial infarction, and Prinzmetal's angina [see *Warnings and*
149 *Precautions (5.1)*]
- 150 • Arrhythmias [see *Warnings and Precautions (5.2)*]
- 151 • Chest, throat, neck, and/or jaw pain/tightness/pressure [see *Warnings and Precautions (5.3)*]
- 152 • Cerebrovascular events [see *Warnings and Precautions (5.4)*]
- 153 • Other vasospasm reactions [see *Warnings and Precautions (5.5)*]
- 154 • Medication overuse headache [see *Warnings and Precautions (5.6)*]

- 155 • Serotonin syndrome [see Warnings and Precautions (5.7)]
- 156 • Increase in blood pressure [see Warnings and Precautions (5.8)]
- 157 • Anaphylactic/anaphylactoid reactions [see Warnings and Precautions (5.9)]
- 158 • Seizures [see Warnings and Precautions (5.10)]

159 **6.1 Clinical Trials Experience**

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

163 **Migraine Headache:** Table 1 lists adverse reactions that occurred in 2 US
 164 placebo-controlled clinical trials in migraine subjects [Studies 2 and 3, see Clinical Studies
 165 (14.1)] following either a single 6-mg dose of IMITREX Injection or placebo. Only reactions
 166 that occurred at a frequency of 2% or more in groups treated with IMITREX Injection 6 mg and
 167 that occurred at a frequency greater than the placebo group are included in Table 1.

168
 169 **Table 1. Adverse Reactions Reported by at Least 2% of Subjects and at a Greater**
 170 **Frequency Than Placebo in 2 Placebo-Controlled Migraine Clinical Trials (Studies 2**
 171 **and 3)^a**

Adverse Reaction	Percent of Subjects Reporting	
	IMITREX Injection 6 mg Subcutaneous (n = 547)	Placebo (n = 370)
Atypical sensations	42	9
Tingling	14	3
Warm/hot sensation	11	4
Burning sensation	7	<1
Feeling of heaviness	7	1
Pressure sensation	7	2
Feeling of tightness	5	<1
Numbness	5	2
Feeling strange	2	<1
Tight feeling in head	2	<1
Cardiovascular		
Flushing	7	2
Chest discomfort	5	1
Tightness in chest	3	<1
Pressure in chest	2	<1
Ear, nose, and throat		
Throat discomfort	3	<1
Discomfort: nasal cavity/sinuses	2	<1
Injection site reaction ^b	59	24

Miscellaneous		
Jaw discomfort	2	0
Musculoskeletal		
Weakness	5	<1
Neck pain/stiffness	5	<1
Myalgia	2	<1
Neurological		
Dizziness/vertigo	12	4
Drowsiness/sedation	3	2
Headache	2	<1
Skin		
Sweating	2	1

172 ^a The sum of the percentages cited is greater than 100% because subjects may have
173 experienced more than 1 type of adverse reaction. Only reactions that occurred at a
174 frequency of 2% or more in groups treated with IMITREX Injection and occurred at a
175 frequency greater than the placebo groups are included.

176 ^b Includes injection site pain, stinging/burning, swelling, erythema, bruising, bleeding.

177

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

181 **Cluster Headache:** In the controlled clinical trials assessing the efficacy of IMITREX
182 Injection as a treatment for cluster headache [Studies 4 and 5, *see Clinical Studies (14.2)*], no
183 new significant adverse reactions were detected that had not already been identified in trials of
184 IMITREX in subjects with migraine.

185 Overall, the frequency of adverse reactions reported in the trials of cluster headache was
186 generally lower than in the migraine trials. Exceptions include reports of paresthesia (5%
187 IMITREX, 0% placebo), nausea and vomiting (4% IMITREX, 0% placebo), and bronchospasm
188 (1% IMITREX, 0% placebo).

189 **Other Adverse Reactions:** In the paragraphs that follow, the frequencies of less
190 commonly reported adverse reactions are presented. Reaction frequencies were calculated as the
191 number of subjects reporting a reaction divided by the total number of subjects (N = 6,218)
192 exposed to subcutaneous IMITREX Injection. All reported reactions are included except those
193 already listed in the previous table. Reactions are further classified within body system
194 categories and enumerated in order of decreasing frequency using the following definitions:
195 frequent are defined as those occurring in at least 1/100 subjects, infrequent are those occurring
196 in 1/100 to 1/1,000 subjects, and rare are those occurring in fewer than 1/1,000 subjects.

197 ***Cardiovascular:*** Infrequent were hypertension, hypotension, bradycardia, tachycardia,
198 palpitations, and syncope. Rare was arrhythmia.

199 ***Gastrointestinal:*** Frequent was abdominal discomfort.

200 *Musculoskeletal:* Frequent were muscle cramps.
201 *Neurological:* Frequent was anxiety. Infrequent were mental confusion, euphoria,
202 agitation, tremor. Rare were myoclonia, sleep disturbance, and dystonia.
203 *Respiratory:* Infrequent was dyspnea.
204 *Skin:* Infrequent were erythema, pruritus, and skin rashes.
205 *Miscellaneous:* Infrequent was “serotonin agonist effect”.

206 Adverse Events Observed With Other Formulations of IMITREX: The following
207 adverse events occurred in clinical trials with IMITREX[®] Tablets and IMITREX[®] Nasal Spray.
208 Because the reports include events observed in open and uncontrolled trials, the role of
209 IMITREX in their causation cannot be reliably determined. All reported events are included
210 except those already listed, those too general to be informative, and those not reasonably
211 associated with the use of the drug.

212 *Cardiovascular:* Angina, cerebrovascular lesion, heart block, peripheral cyanosis,
213 phlebitis, thrombosis.

214 *Gastrointestinal:* Abdominal distention and colitis.

215 *Neurological:* Convulsions, hallucinations, syncope, suicide, and twitching.

216 *Miscellaneous:* Edema, hypersensitivity, swelling of extremities, and swelling of
217 face.

218 **6.2 Postmarketing Experience**

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

225 Blood: Hemolytic anemia, pancytopenia, thrombocytopenia.

226 Ear, Nose, and Throat: Deafness.

227 Eye: Ischemic optic neuropathy, retinal artery occlusion, retinal vein thrombosis.

228 Neurological: Central nervous system vasculitis, cerebrovascular accident, serotonin
229 syndrome, subarachnoid hemorrhage.

230 Non-Site Specific: Angioedema, cyanosis, temporal arteritis.

231 Skin: Exacerbation of sunburn, hypersensitivity reactions (allergic vasculitis, erythema,
232 pruritus, rash, shortness of breath, urticaria), photosensitivity. Following subcutaneous
233 administration of IMITREX, pain, redness, stinging, induration, swelling, contusion,
234 subcutaneous bleeding, and, on rare occasions, lipoatrophy (depression in the skin) or
235 lipohypertrophy (enlargement or thickening of tissue) have been reported.

236 Urogenital: Acute renal failure.

237 **7 DRUG INTERACTIONS**

238 **7.1 Ergot-Containing Drugs**

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

243 **7.2 Monoamine Oxidase-A Inhibitors**

244 MAO-A inhibitors increase systemic exposure by 2-fold. Therefore, the use of IMITREX
245 Injection in patients receiving MAO-A inhibitors is contraindicated [*see Clinical Pharmacology*
246 (12.3)].

247 **7.3 Other 5-HT₁ Agonists**

248 Because their vasospastic effects may be additive, coadministration of IMITREX
249 Injection and other 5-HT₁ agonists (e.g., triptans) within 24 hours of each other is
250 contraindicated.

251 **7.4 Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine 252 Reuptake Inhibitors and Serotonin Syndrome**

253 Cases of serotonin syndrome have been reported during coadministration of triptans and
254 SSRIs, or SNRIs, SNRIs, TCAs, and MAO inhibitors [*see Warnings and Precautions (5.7)*].

255 **8 USE IN SPECIFIC POPULATIONS**

256 **8.1 Pregnancy**

257 Pregnancy Category C: There are no adequate and well-controlled trials of IMITREX
258 Injection in pregnant women. IMITREX Injection should be used during pregnancy only if the
259 potential benefit justifies the potential risk to the fetus.

260 When sumatriptan was administered intravenously to pregnant rabbits daily throughout
261 the period of organogenesis, embryoletality was observed at doses at or close to those
262 producing maternal toxicity. These doses were less than the maximum recommended human
263 dose (MRHD) of 12 mg/day on a mg/m² basis. Oral administration of sumatriptan to rabbits
264 during organogenesis was associated with increased incidences of fetal vascular and skeletal
265 abnormalities. The highest no-effect dose for these effects was 15 mg/kg/day. The intravenous
266 administration of sumatriptan to pregnant rats throughout organogenesis at doses that are
267 approximately 10 times the MRHD on a mg/m² basis, did not produce evidence of
268 embryoletality. The subcutaneous administration of sumatriptan to pregnant rats prior to and
269 throughout pregnancy did not produce evidence of embryoletality or teratogenicity.

270 **8.3 Nursing Mothers**

271 It is not known whether sumatriptan is excreted in human breast milk following
272 subcutaneous administration. Because many drugs are excreted in human milk, and because of
273 the potential for serious adverse reactions in nursing infants from IMITREX, a decision should
274 be made whether to discontinue nursing or to discontinue the drug, taking into account the
275 importance of the drug to the mother.

276 **8.4 Pediatric Use**

277 Safety and effectiveness of IMITREX Injection in pediatric patients under 18 years of
278 age have not been established; therefore, IMITREX Injection is not recommended for use in
279 patients under 18 years of age.

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

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

292 Postmarketing experience documents that serious adverse reactions have occurred in the
293 pediatric population after use of subcutaneous, oral, and/or intranasal IMITREX. These reports
294 include reactions similar in nature to those reported rarely in adults, including stroke, visual loss,
295 and death. A myocardial infarction has been reported in a 14-year-old male following the use of
296 oral IMITREX; clinical signs occurred within 1 day of drug administration. Since clinical data to
297 determine the frequency of serious adverse reactions in pediatric patients who might receive
298 subcutaneous, oral, or intranasal IMITREX are not presently available, the use of IMITREX in
299 patients under 18 years of age is not recommended.

300 **8.5 Geriatric Use**

301 Clinical trials of IMITREX Injection did not include sufficient numbers of subjects aged
302 65 and over to determine whether they respond differently from younger subjects. Other reported
303 clinical experience has not identified differences in responses between the elderly and younger
304 subjects. In general, dose selection for an elderly patient should be cautious, usually starting at
305 the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or
306 cardiac function and of concomitant disease or other drug therapy.

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

310 **10 OVERDOSAGE**

311 No gross overdoses in clinical practice have been reported. Coronary vasospasm was
312 observed after intravenous administration of IMITREX Injection [*see Contraindications (4)*].
313 Overdoses would be expected from animal data (dogs at 0.1 g/kg, rats at 2 g/kg) to possibly
314 cause convulsions, tremor, inactivity, erythema of the extremities, reduced respiratory rate,

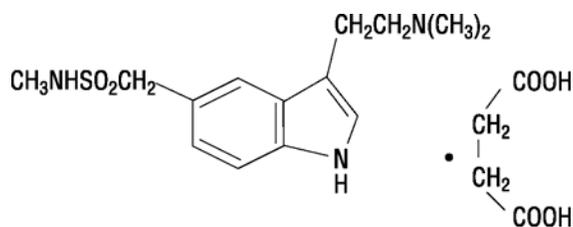
315 cyanosis, ataxia, mydriasis, injection site reactions (desquamation, hair loss, and scab formation),
316 and paralysis.

317 The elimination half-life of sumatriptan is about 2 hours [see *Clinical Pharmacology*
318 (12.3)], and therefore monitoring of patients after overdose with IMITREX Injection should
319 continue for at least 10 hours or while symptoms or signs persist.

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

322 11 DESCRIPTION

323 IMITREX Injection contains sumatriptan succinate, a selective 5-HT_{1B/1D} receptor
324 agonist. Sumatriptan succinate is chemically designated as 3-[2-(dimethylamino)ethyl]-N-
325 methyl-indole-5-methanesulfonamide succinate (1:1), and it has the following structure:
326



327
328
329 The empirical formula is C₁₄H₂₁N₃O₂S•C₄H₆O₄, representing a molecular weight of
330 413.5. Sumatriptan succinate is a white to off-white powder that is readily soluble in water and in
331 saline.

332 IMITREX Injection is a clear, colorless to pale yellow, sterile, nonpyrogenic solution for
333 subcutaneous injection. Each 0.5 mL of IMITREX Injection 8 mg/mL solution contains 4 mg of
334 sumatriptan (base) as the succinate salt and 3.8 mg of sodium chloride, USP in Water for
335 Injection, USP. Each 0.5 mL of IMITREX Injection 12 mg/mL solution contains 6 mg of
336 sumatriptan (base) as the succinate salt and 3.5 mg of sodium chloride, USP in Water for
337 Injection, USP. The pH range of both solutions is approximately 4.2 to 5.3. The osmolality of
338 both injections is 291 mOsmol.

339 12 CLINICAL PHARMACOLOGY

340 12.1 Mechanism of Action

341 Sumatriptan binds with high affinity to human cloned 5-HT_{1B/1D} receptors. IMITREX
342 presumably exerts its therapeutic effects in the treatment of migraine headache by binding to
343 5-HT_{1B/1D} receptors located on intracranial blood vessels and sensory nerves of the trigeminal
344 system.

345 Current theories proposed to explain the etiology of migraine headache suggest that
346 symptoms are due to local cranial vasodilatation and/or to the release of sensory neuropeptides
347 (including substance P and calcitonin gene-related peptide) through nerve endings in the
348 trigeminal system. The therapeutic activity of IMITREX for the treatment of migraine and
349 cluster headaches is thought to be due to the agonist effects at the 5-HT_{1B/1D} receptors on

350 intracranial blood vessels (including the arterio-venous anastomoses) and sensory nerves of the
351 trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory
352 neuropeptide release.

353 **12.2 Pharmacodynamics**

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

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

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

363 **12.3 Pharmacokinetics**

364 Absorption and Bioavailability: The bioavailability of sumatriptan via subcutaneous site
365 injection to 18 healthy male subjects was $97\% \pm 16\%$ of that obtained following intravenous
366 injection.

367 After a single 6-mg subcutaneous manual injection into the deltoid area of the arm in 18
368 healthy males (age: 24 ± 6 years, weight: 70 kg), the maximum serum concentration (C_{\max}) of
369 sumatriptan was (mean \pm standard deviation) 74 ± 15 ng/mL and the time to peak concentration
370 (T_{\max}) was 12 minutes after injection (range: 5 to 20 minutes). In this trial, the same dose injected
371 subcutaneously in the thigh gave a C_{\max} of 61 ± 15 ng/mL by manual injection versus $52 \pm$
372 15 ng/mL by autoinjector techniques. The T_{\max} or amount absorbed was not significantly altered
373 by either the site or technique of injection.

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

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

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

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

386 Following a 6-mg subcutaneous injection into the deltoid area of the arm, the systemic
387 clearance of sumatriptan was $1,194 \pm 149$ mL/min and the terminal half-life was $115 \pm$
388 19 minutes.

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

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

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

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

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

407 **13 NONCLINICAL TOXICOLOGY**

408 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

409 Carcinogenesis: In carcinogenicity studies, rats and mice were given sumatriptan by
410 oral gavage. Mice were dosed for 78 weeks and rats were dosed for 104 weeks. Average
411 exposures achieved in mice receiving the highest dose were approximately 110 times the
412 exposure attained in humans after the maximum recommended single dose of 6 mg. The highest
413 dose to rats was approximately 260 times the maximum single dose of 6 mg on a mg/m^2 basis.
414 There was no evidence of an increase in tumors in either species related to sumatriptan
415 administration.

416 Mutagenesis: Sumatriptan was not mutagenic in the presence or absence of metabolic
417 activation when tested in 2 gene mutation assays (the Ames test and the in vitro mammalian
418 Chinese hamster V79/HGPRT assay). It was not clastogenic in 2 cytogenetics assays (the in vitro
419 human lymphocyte assay and the in vivo rat micronucleus assay).

420 Impairment of Fertility: A fertility study (Segment I) by the subcutaneous route, during
421 which male and female rats were dosed daily with sumatriptan prior to and throughout the
422 mating period, has shown no evidence of impaired fertility at doses equivalent to approximately
423 100 times the maximum recommended single human dose of 6 mg on a mg/m^2 basis. However,
424 following oral administration, a treatment-related decrease in fertility, secondary to a decrease in
425 mating, was seen for rats treated with 50 and 500 mg/kg/day. The no-effect dose for this finding
426 was approximately 8 times the maximum recommended single human dose of 6 mg on a mg/m^2

427 basis. It is not clear whether the problem is associated with the treatment of males or females or
428 both.

429 **13.2 Animal Toxicology and/or Pharmacology**

430 Corneal Opacities: Dogs receiving oral sumatriptan developed corneal opacities and
431 defects in the corneal epithelium. Corneal opacities were seen at the lowest dosage tested,
432 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium
433 were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and
434 no-effect doses were not established; however, the relative exposure at the lowest dose tested
435 was approximately 5 times the human exposure after a 100-mg oral dose or 3 times the human
436 exposure after a 6-mg subcutaneous dose.

437 Melanin Binding: In rats with a single subcutaneous dose (0.5 mg/kg) of radiolabeled
438 sumatriptan, the elimination half-life of radioactivity from the eye was 15 days, suggesting that
439 sumatriptan and its metabolites bind to the melanin of the eye. The clinical significance of this
440 binding is unknown.

441 **14 CLINICAL STUDIES**

442 **14.1 Migraine**

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

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

451

452 **Table 2. Proportion of Subjects With Migraine Relief and Incidence of Adverse Events by**
453 **Time and by IMITREX Dose in Study 1**

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

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

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

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

Table 3. Proportion of Subjects With Pain Relief and Relief of Migraine Symptoms After 1 and 2 Hours of Treatment in Studies 2 and 3

1-Hour Data	Study 2		Study 3	
	Placebo (n = 190)	IMITREX 6 mg (n = 384)	Placebo (n = 180)	IMITREX 6 mg (n = 350)
Subjects with pain relief (grade 0/1)	18%	70% ^a	26%	70% ^a
Subjects with no pain	5%	48% ^a	13%	49% ^a
Subjects without nausea	48%	73% ^a	50%	73% ^a
Subjects without photophobia	23%	56% ^a	25%	58% ^a
Subjects with little or no clinical disability ^b	34%	76% ^a	34%	76% ^a
2-Hour Data	Study 2		Study 3	
	Placebo ^c	IMITREX 6 mg ^d	Placebo ^c	IMITREX 6 mg ^d
Subjects with pain relief (grade 0/1)	31%	81% ^a	39%	82% ^a
Subjects with no pain	11%	63% ^a	19%	65% ^a
Subjects without nausea	56%	82% ^a	63%	81% ^a
Subjects without photophobia	31%	72% ^a	35%	71% ^a
Subjects with little or no clinical disability ^b	42%	85% ^a	49%	84% ^a

468 ^a $P < 0.05$ versus placebo.
 469 ^b A successful outcome in terms of clinical disability was defined prospectively as ability to
 470 work mildly impaired or ability to work and function normally.
 471 ^c Includes subjects that may have received an additional placebo injection 1 hour after the initial
 472 injection.
 473 ^d Includes subjects that may have received an additional 6 mg of IMITREX Injection 1 hour
 474 after the initial injection.
 475

476 IMITREX Injection also relieved photophobia, phonophobia (sound sensitivity), nausea,
 477 and vomiting associated with migraine attacks. Similar efficacy was seen when subjects
 478 self-administered IMITREX Injection using the IMITREX STATdose Pen.

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

482 **14.2 Cluster Headache**

483 The efficacy of IMITREX Injection in the acute treatment of cluster headache was
 484 demonstrated in 2 randomized, double-blind, placebo-controlled, 2-period crossover trials
 485 (Studies 4 and 5). Subjects aged 21 to 65 years were enrolled and were instructed to treat a
 486 moderate to very severe headache within 10 minutes of onset. Headache relief was defined as a
 487 reduction in headache severity to mild or no pain. In both trials, the proportion of individuals
 488 gaining relief at 10 or 15 minutes was significantly greater among subjects receiving 6 mg of
 489 IMITREX Injection compared with those who received placebo (see Table 4).

490
 491 **Table 4. Proportion of Subjects With Cluster Headache Relief by Time in Studies 4 and 5**

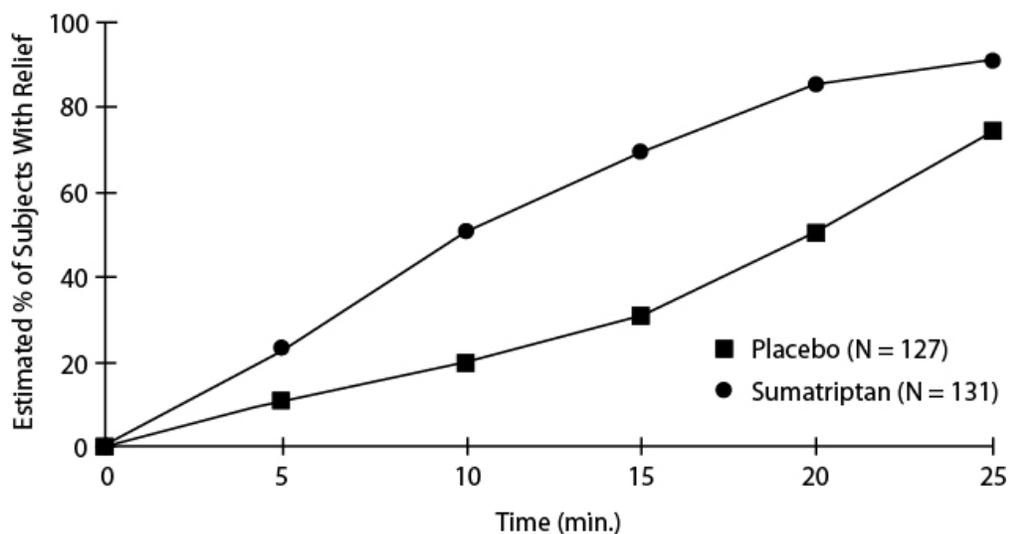
	Study 4		Study 5	
	Placebo (n = 39)	IMITREX 6 mg (n = 39)	Placebo (n = 88)	IMITREX 6 mg (n = 92)
Subjects with pain relief (no/mild)				
5 Minutes post-injection	8%	21%	7%	23% ^a
10 Minutes post-injection	10%	49% ^a	25%	49% ^a
15 Minutes post-injection	26%	74% ^a	35%	75% ^a

492 ^a $P < 0.05$.
 493 (n = Number of headaches treated.)

494
 495 An estimate of the cumulative probability of a subject with a cluster headache obtaining
 496 relief after being treated with either IMITREX Injection or placebo is presented in Figure 1.
 497

498 **Figure 1. Time to Relief of Cluster Headache from Time of Injection^a**

499



500

501 ^a The figure uses Kaplan-Meier (product limit) Survivorship Plot. Subjects taking rescue
502 medication were censored at 15 minutes.

503

504 The plot was constructed with data from subjects who either experienced relief or did not
505 require (request) rescue medication within a period of 2 hours following treatment. As a
506 consequence, the data in the plot are derived from only a subset of the 258 headaches treated
507 (rescue medication was required in 52 of the 127 placebo-treated headaches and 18 of the 131
508 headaches treated with IMITREX Injection).

509 Other data suggest that treatment with IMITREX Injection is not associated with an
510 increase in early recurrence of headache and has little effect on the incidence of later-occurring
511 headaches (i.e., those occurring after 2, but before 18 or 24 hours).

512 **16 HOW SUPPLIED/STORAGE AND HANDLING**

513 IMITREX Injection contains sumatriptan (base) as the succinate salt and is supplied as a
514 clear, colorless to pale yellow, sterile, nonpyrogenic solution as follows:

515 Prefilled Syringe and/or Autoinjector Pen: Each pack contains a Patient Information and Patients
516 Instructions for Use leaflet.

- 517 • IMITREX STATdose System[®], 4 mg, containing 1 IMITREX STATdose Pen, 2 prefilled
518 single-dose syringe cartridges, and 1 carrying case (NDC 0173-0739-00).
- 519 • IMITREX STATdose System, 6 mg, containing 1 IMITREX STATdose Pen, 2 prefilled
520 single-dose syringe cartridges, and 1 carrying case (NDC 0173-0479-00).
- 521 • Two 4-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose System
522 (NDC 0173-0739-02).
- 523 • Two 6-mg single-dose prefilled syringe cartridges for use with IMITREX STATdose System
524 (NDC 0173-0478-00).

525 Single-Dose Vial:

- 526 • IMITREX Injection single-dose vial (6 mg/0.5 mL) in cartons containing 5 vials (NDC 0173-
527 0449-02).

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

529 **17 PATIENT COUNSELING INFORMATION**

530 See FDA-approved patient labeling (Patient Information and Instructions for Use).

531 **17.1 Risk of Myocardial Ischemia and/or Infarction, Prinzmetal's Angina, Other**
532 **Vasospasm-Related Events, Arrhythmias, and Cerebrovascular Events**

533 Inform patients that IMITREX Injection may cause serious cardiovascular side effects
534 such as myocardial infarction or stroke. Although serious cardiovascular events can occur
535 without warning symptoms, patients should be alert for the signs and symptoms of chest pain,
536 shortness of breath, irregular heartbeat, significant rise in blood pressure, weakness, and slurring
537 of speech and should ask for medical advice when observing any indicative sign or symptoms.
538 Patients should be apprised of the importance of this follow-up [*see Warnings and Precautions*
539 (5.1, 5.2, 5.4, 5.5, 5.8)].

540 **17.2 Anaphylactic/Anaphylactoid Reactions**

541 Inform patients that anaphylactic/anaphylactoid reactions have occurred in patients
542 receiving IMITREX Injection. Such reactions can be life threatening or fatal. In general,
543 anaphylactic reactions to drugs are more likely to occur in individuals with a history of
544 sensitivity to multiple allergens [*see Warnings and Precautions* (5.9)].

545 **17.3 Medication Overuse Headache**

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

549 **17.4 Pregnancy**

550 Inform patients that IMITREX Injection should not be used during pregnancy unless the
551 potential benefit justifies the potential risk to the fetus [*see Use in Specific Populations* (8.1)].

552 **17.5 Nursing Mothers**

553 Advise patients to notify their healthcare provider if they are breastfeeding or plan to
554 breastfeed [*see Use in Specific Populations* (8.3)].

555 **17.6 Ability To Perform Complex Tasks**

556 Since migraines or treatment with IMITREX Injection may cause somnolence and
557 dizziness, instruct patients to evaluate their ability to perform complex tasks during migraine
558 attacks and after administration of IMITREX Injection.

559 **17.7 Serotonin Syndrome**

560 Patients should be cautioned about the risk of serotonin syndrome with the use of
561 IMITREX Injection or other triptans, particularly during combined use with SSRIs, SNRIs,
562 TCAs, and MAO inhibitors [*see Warnings and Precautions* (5.7) and *Drug Interactions* (7.4)].

563 **17.8 How to Use IMITREX Injection**

564 Provide patients instruction on the proper use of IMITREX Injection if they are able to
565 self-administer IMITREX Injection in medically unsupervised situation.

566 Inform patients that the needle in the IMITREX STATdose Pen penetrates approximately
567 1/4 of an inch (5 to 6 mm). Inform patients that the injection is intended to be given
568 subcutaneously and intramuscular or intravascular delivery should be avoided. Instruct patients
569 to use injection sites with an adequate skin and subcutaneous thickness to accommodate the
570 length of the needle.

571
572 IMITREX, IMITREX STATdose Pen, and IMITREX STATdose System are registered
573 trademarks of GlaxoSmithKline.

574
575



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577 GlaxoSmithKline
578 Research Triangle Park, NC 27709

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581
582

583 **Patient Information**
584 **IMITREX[®] (IM-i-trex)**
585 **(sumatriptan succinate)**
586 **Injection**

587
588 Read this Patient Information before you start taking IMITREX and each time you get a refill.
589 There may be new information. This information does not take the place of talking with your
590 healthcare provider about your medical condition or treatment.

591
592 **What is the most important information I should know about IMITREX?**

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

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

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

- 597 • discomfort in the center of your chest that lasts for more than a few minutes, or that goes
598 away and comes back
- 599 • severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- 600 • pain or discomfort in your arms, back, neck, jaw, or stomach
- 601 • shortness of breath with or without chest discomfort

- 602 • breaking out in a cold sweat
- 603 • nausea or vomiting
- 604 • feeling lightheaded

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

- 607 • have high blood pressure
- 608 • have high cholesterol levels
- 609 • smoke
- 610 • are overweight
- 611 • have diabetes
- 612 • have a family history of heart disease

613

614 **What is IMITREX?**

615 IMITREX is a prescription medicine used to treat acute migraine headaches with or without aura
616 and acute cluster headaches in adults who have been diagnosed with migraine or cluster
617 headaches.

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

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

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

621

622 **Who should not take IMITREX?**

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

- 624 • heart problems or a history of heart problems
- 625 • narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular
626 disease)
- 627 • uncontrolled high blood pressure
- 628 • hemiplegic migraines or basilar migraines. If you are not sure if you have these types of
629 migraines, ask your healthcare provider.
- 630 • had a stroke, transient ischemic attacks (TIAs), or problems with your blood circulation
- 631 • taken any of the following medicines in the last 24 hours:
 - 632 • almotriptan (AXERT[®])
 - 633 • eletriptan (RELPA[®])
 - 634 • frovatriptan (FROVA[®])
 - 635 • naratriptan (AMERGE[®])
 - 636 • rizatriptan (MAXALT[®], MAXALT-MLT[®])
 - 637 • sumatriptan and naproxen (TREXIMET[®])

- 638 • ergotamines (CAFERGOT[®], ERGOMAR[®], MIGERGOT[®])
639 • dihydroergotamine (D.H.E. 45[®], MIGRANAL[®])

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

- 641 • an allergy to sumatriptan or any of the ingredients in IMITREX. See the end of this leaflet for
642 a complete list of ingredients in IMITREX.

643

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

645 Before you take IMITREX, tell your healthcare provider about all of your medical conditions,
646 including if you:

- 647 • have high blood pressure
648 • have high cholesterol
649 • have diabetes
650 • smoke
651 • are overweight
652 • have heart problems or family history of heart problems or stroke
653 • have liver problems
654 • have had epilepsy or seizures
655 • are not using effective birth control
656 • become pregnant while taking IMITREX
657 • are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk and may harm
658 your baby. Talk with your healthcare provider about the best way to feed your baby if you
659 take IMITREX.

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

662 Using IMITREX with certain other medicines can affect each other, causing serious side effects.

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

- 664 • selective serotonin reuptake inhibitors (SSRIs)
665 • serotonin norepinephrine reuptake inhibitors (SNRIs)
666 • tricyclic antidepressants (TCAs)
667 • monoamine oxidase inhibitors (MAOIs)

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

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

671

672 **How should I take IMITREX?**

- 673 • Certain people should take their first dose of IMITREX in their healthcare provider’s office
674 or in another medical setting. Ask your healthcare provider if you should take your first dose
675 in a medical setting.
- 676 • Use IMITREX exactly as your healthcare provider tells you to use it.
- 677 • Your healthcare provider may change your dose. Do not change your dose without first
678 talking with your healthcare provider.
- 679 • For adults, the usual dose is a single injection given just below the skin.
- 680 • You should give an injection as soon as the symptoms of your headache start, but it may be
681 given at any time during a migraine attack.
- 682 • If you did not get any relief after the first injection, do not give a second injection without
683 first talking with your healthcare provider.
- 684 • You can take a second injection 1 hour after the first injection, but not sooner, if your
685 headache came back after your first injection.
- 686 • Do not take more than 12 mg in a 24-hour period.
- 687 • If you use too much IMITREX, call your healthcare provider or go to the nearest hospital
688 emergency room right away.
- 689 • You should write down when you have headaches and when you take IMITREX so you can
690 talk with your healthcare provider about how IMITREX is working for you.

691

692 **What should I avoid while taking IMITREX?**

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

695

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

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

699 These serious side effects include:

- 700 • changes in color or sensation in your fingers and toes (Raynaud’s syndrome)
- 701 • stomach and intestinal problems (gastrointestinal and colonic ischemic events). Symptoms of
702 gastrointestinal and colonic ischemic events include:
- 703 • sudden or severe stomach pain
- 704 • stomach pain after meals
- 705 • weight loss
- 706 • nausea or vomiting
- 707 • constipation or diarrhea
- 708 • bloody diarrhea
- 709 • fever
- 710 • problems with blood circulation to your legs and feet (peripheral vascular ischemia).
711 Symptoms of peripheral vascular ischemia include:

- 712 • cramping and pain in your legs or hips
- 713 • feeling of heaviness or tightness in your leg muscles
- 714 • burning or aching pain in your feet or toes while resting
- 715 • numbness, tingling, or weakness in your legs
- 716 • cold feeling or color changes in 1 or both legs or feet
- 717 • medication overuse headaches. Some people who use too many IMITREX injections may
- 718 have worse headaches (medication overuse headache). If your headaches get worse, your
- 719 healthcare provider may decide to stop your treatment with IMITREX.
- 720 • serotonin syndrome. Serotonin syndrome is a rare but serious problem that can happen in
- 721 people using IMITREX, especially if IMITREX is used with anti-depressant medicines
- 722 called SSRIs or SNRIs.

723 Call your healthcare provider right away if you have any of the following symptoms of
724 serotonin syndrome:

- 725 • mental changes such as seeing things that are not there (hallucinations), agitation, or
- 726 coma
- 727 • fast heartbeat
- 728 • changes in blood pressure
- 729 • high body temperature
- 730 • tight muscles
- 731 • trouble walking
- 732 • seizures. Seizures have happened in people taking IMITREX who have never had seizures
- 733 before. Talk with your healthcare provider about your chance of having seizures while you
- 734 take IMITREX.

735 The most common side effects of IMITREX include:

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

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

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

746 Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-
747 800-FDA-1088.

748

749 **How should I store IMITREX Injection?**

- 750 • Store IMITREX between 36°F to 86°F (2°C to 30°C).
751 • Store your medicine away from light.
752 • Keep your medicine in the packaging or carrying case provided with it.

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

754

755 **General information about the safe and effective use of IMITREX**

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

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

763 For more information, go to www.gsk.com or call 1-888-825-5249.

764

765 **What are the ingredients in IMITREX Injection?**

766 Active ingredient: sumatriptan succinate

767 Inactive ingredients: sodium chloride, water for injection

768

769 This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug
770 Administration.

771

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775 GlaxoSmithKline or its products.

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780 Research Triangle Park, NC 27709

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783

784 September 2012

785

1 **Patient Information**
2 **IMITREX® (IM-i-trex)**
3 **(sumatriptan succinate)**
4 **Injection**
5

6 Read this Patient Information before you start taking IMITREX and each time you
7 get a refill. There may be new information. This information does not take the place
8 of talking with your healthcare provider about your medical condition or treatment.
9

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

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

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

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

- 15 • discomfort in the center of your chest that lasts for more than a few minutes, or
16 that goes away and comes back
- 17 • severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- 18 • pain or discomfort in your arms, back, neck, jaw, or stomach
- 19 • shortness of breath with or without chest discomfort
- 20 • breaking out in a cold sweat
- 21 • nausea or vomiting
- 22 • feeling lightheaded

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

- 25 • have high blood pressure
- 26 • have high cholesterol levels
- 27 • smoke
- 28 • are overweight
- 29 • have diabetes
- 30 • have a family history of heart disease

31
32 **What is IMITREX?**

33 IMITREX is a prescription medicine used to treat acute migraine headaches with or
34 without aura and acute cluster headaches in adults who have been diagnosed with
35 migraine or cluster headaches.

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

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

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

40

41 **Who should not take IMITREX?**

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

- 43 • heart problems or a history of heart problems
- 44 • narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral
- 45 vascular disease)
- 46 • uncontrolled high blood pressure
- 47 • hemiplegic migraines or basilar migraines. If you are not sure if you have these
- 48 types of migraines, ask your healthcare provider.
- 49 • had a stroke, transient ischemic attacks (TIAs), or problems with your blood
- 50 circulation
- 51 • taken any of the following medicines in the last 24 hours:
 - 52 • almotriptan (AXERT[®])
 - 53 • eletriptan (RELPAX[®])
 - 54 • frovatriptan (FROVA[®])
 - 55 • naratriptan (AMERGE[®])
 - 56 • rizatriptan (MAXALT[®], MAXALT-MLT[®])
 - 57 • sumatriptan and naproxen (TREXIMET[®])
 - 58 • ergotamines (CAFERGOT[®], ERGOMAR[®], MIGERGOT[®])
 - 59 • dihydroergotamine (D.H.E. 45[®], MIGRANAL[®])

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

- 61 • an allergy to sumatriptan or any of the ingredients in IMITREX. See the end of
- 62 this leaflet for a complete list of ingredients in IMITREX.

63

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

65 Before you take IMITREX, tell your healthcare provider about all of your medical

66 conditions, including if you:

- 67 • have high blood pressure
- 68 • have high cholesterol
- 69 • have diabetes
- 70 • smoke
- 71 • are overweight
- 72 • have heart problems or family history of heart problems or stroke
- 73 • have liver problems
- 74 • have had epilepsy or seizures
- 75 • are not using effective birth control

- 76 • become pregnant while taking IMITREX
77 • are breastfeeding or plan to breastfeed. IMITREX passes into your breast milk
78 and may harm your baby. Talk with your healthcare provider about the best way
79 to feed your baby if you take IMITREX.

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

82 Using IMITREX with certain other medicines can affect each other, causing serious
83 side effects.

84 **Especially tell your healthcare provider if** you take anti-depressant medicines
85 called:

- 86 • selective serotonin reuptake inhibitors (SSRIs)
- 87 • serotonin norepinephrine reuptake inhibitors (SNRIs)
- 88 • tricyclic antidepressants (TCAs)
- 89 • monoamine oxidase inhibitors (MAOIs)

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

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

94

95 **How should I take IMITREX?**

- 96 • Certain people should take their first dose of IMITREX in their healthcare
97 provider's office or in another medical setting. Ask your healthcare provider if
98 you should take your first dose in a medical setting.
- 99 • Use IMITREX exactly as your healthcare provider tells you to use it.
- 100 • Your healthcare provider may change your dose. Do not change your dose
101 without first talking with your healthcare provider.
- 102 • For adults, the usual dose is a single injection given just below the skin.
- 103 • You should give an injection as soon as the symptoms of your headache start,
104 but it may be given at any time during a migraine attack.
- 105 • If you did not get any relief after the first injection, do not give a second
106 injection without first talking with your healthcare provider.
- 107 • You can take a second injection 1 hour after the first injection, but not sooner, if
108 your headache came back after your first injection.
- 109 • Do not take more than 12 mg in a 24-hour period.
- 110 • If you use too much IMITREX, call your healthcare provider or go to the nearest
111 hospital emergency room right away.

- 112 • You should write down when you have headaches and when you take IMITREX
113 so you can talk with your healthcare provider about how IMITREX is working for
114 you.

115

116 **What should I avoid while taking IMITREX?**

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

120

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

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

124 These serious side effects include:

- 125 • changes in color or sensation in your fingers and toes (Raynaud’s syndrome)
- 126 • stomach and intestinal problems (gastrointestinal and colonic ischemic events).

127 Symptoms of gastrointestinal and colonic ischemic events include:

- 128 • sudden or severe stomach pain
- 129 • stomach pain after meals
- 130 • weight loss
- 131 • nausea or vomiting
- 132 • constipation or diarrhea
- 133 • bloody diarrhea
- 134 • fever

- 135 • problems with blood circulation to your legs and feet (peripheral vascular
136 ischemia). Symptoms of peripheral vascular ischemia include:

- 137 • cramping and pain in your legs or hips
- 138 • feeling of heaviness or tightness in your leg muscles
- 139 • burning or aching pain in your feet or toes while resting
- 140 • numbness, tingling, or weakness in your legs
- 141 • cold feeling or color changes in 1 or both legs or feet

- 142 • medication overuse headaches. Some people who use too many IMITREX
143 injections may have worse headaches (medication overuse headache). If your
144 headaches get worse, your healthcare provider may decide to stop your
145 treatment with IMITREX.

- 146 • serotonin syndrome. Serotonin syndrome is a rare but serious problem that can
147 happen in people using IMITREX, especially if IMITREX is used with
148 anti-depressant medicines called SSRIs or SNRIs.

149 Call your healthcare provider right away if you have any of the following
150 symptoms of serotonin syndrome:

- 151 • mental changes such as seeing things that are not there (hallucinations),
- 152 agitation, or coma
- 153 • fast heartbeat
- 154 • changes in blood pressure
- 155 • high body temperature
- 156 • tight muscles
- 157 • trouble walking
- 158 • seizures. Seizures have happened in people taking IMITREX who have never had
- 159 seizures before. Talk with your healthcare provider about your chance of having
- 160 seizures while you take IMITREX.

161 The most common side effects of IMITREX include:

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

168 Tell your healthcare provider if you have any side effect that bothers you or that

169 does not go away.

170 These are not all the possible side effects of IMITREX. For more information, ask

171 your healthcare provider or pharmacist.

172 Call your doctor for medical advice about side effects. You may report side effects

173 to FDA at 1-800-FDA-1088.

174

175 **How should I store IMITREX Injection?**

- 176 • Store IMITREX between 36°F to 86°F (2°C to 30°C).
- 177 • Store your medicine away from light.
- 178 • Keep your medicine in the packaging or carrying case provided with it.

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

180

181 **General information about the safe and effective use of IMITREX**

182 Medicines are sometimes prescribed for purposes other than those listed in Patient

183 Information leaflets. Do not use IMITREX for a condition for which it was not

184 prescribed. Do not give IMITREX to other people, even if they have the same

185 symptoms you have. It may harm them.

186 This Patient Information leaflet summarizes the most important information about

187 IMITREX. If you would like more information, talk with your healthcare provider.

188 You can ask your healthcare provider or pharmacist for information about IMITREX
189 that is written for healthcare professionals.

190 For more information, go to www.gsk.com or call 1-888-825-5249.

191

192 **What are the ingredients in IMITREX Injection?**

193 Active ingredient: sumatriptan succinate

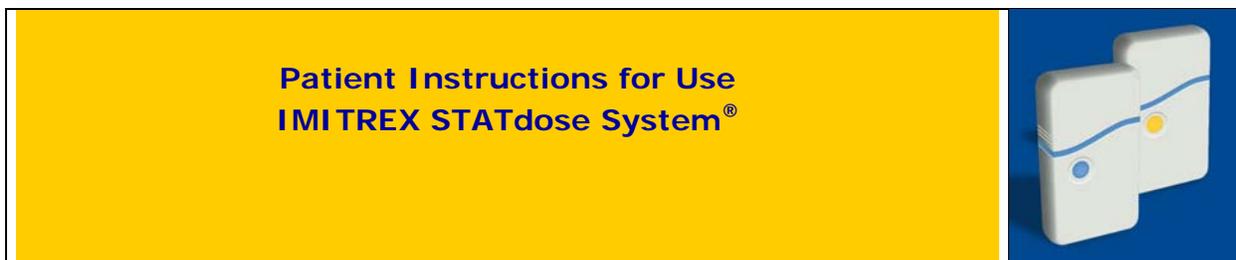
194 Inactive ingredients: sodium chloride, water for injection

195

196 Month Year

197 IMJ: xPPI

198



199 Read this Patient Instructions for Use before you start to use the IMITREX
200 STATdose System. There may be new information. This information does not take
201 the place of talking with your healthcare provider about your medical condition or
202 treatment. You and your healthcare provider should talk about IMITREX Injection
203 when you start taking it and at regular checkups.

204 Keep the IMITREX STATdose System out of the reach of children.

205 **Before you use the IMITREX STATdose System**

206 When you first open the IMITREX STATdose System box, the Cartridge Pack and
207 the IMITREX STATdose Pen® are already in the Carrying Case for your convenience.



208

209 The grey and blue **Carrying Case** is used for
210 storing the unloaded Pen and the Cartridge
211 Pack when they are not being used.

212 The **Cartridge Pack** holds 2 individually
213 sealed **Syringe Cartridges**. Each Syringe
214 Cartridge holds 1 dose of IMITREX®

215 (sumatriptan succinate) Injection. The
216 Cartridge Pack for the 4-mg strength of this

217 medicine is yellow, and the Cartridge Pack for
218 the 6-mg strength is blue (as shown). Refill
219 Cartridge Packs are available.

220 The grey and blue **Pen** is used to automatically inject 1 dose of medicine from a
221 Syringe Cartridge. Do not touch the **Blue Button** until you have pressed the Pen
222 against your skin to give a dose. If you press it at any other time, you might lose a
223 dose. The **Safety Catch** keeps the Pen from accidentally firing until you are ready.
224 The Pen will only work when you slide the grey part of the barrel down to the blue
225 part. Always check to make sure that the white Priming Rod is not sticking out from
226 the end of the Pen (as shown in Figure B) before you load a new Syringe Cartridge.
227 If it is sticking out, you will lose that dose.

How to load the IMITREX STATdose Pen

**Do not load the Pen until you are ready to give yourself an injection.
Do not touch the Blue Button on top of the Pen (see Figure A)
while you are loading the Pen.**



Figure A

240 1. Open the lid of the Carrying Case. The tamper-
241 evident seals over the 2 Syringe Cartridges are
242 labeled "A" and "B" (see Figure A inset).

243 Always use the Syringe Cartridge marked "A"
244 before the one marked "B" to help you keep
245 track of your doses. **Do not use if either**
246 **seal is broken or missing when you first**
247 **open the Carrying Case.**

248 2. Tear off one of the tamper-evident seals (see
249 Figure A). Throw away the seal. Open the lid
250 over the Syringe Cartridge.

251 3. Hold the Pen by the ridges at the top. Take
252 the Pen out of the Carrying Case (see Figure
253 B).

254 Check to make sure the white Priming Rod is
255 not sticking out from the lower end of the Pen
256 (see Figure B inset). If it is sticking out, put
257 the Pen back into the Carrying Case and press
258 down firmly until you feel it click. Take the
259 Pen out of the Carrying Case.



Figure B



260
261

Figure C



262
263

Figure D

264 4. Put the Pen in the Cartridge Pack. Turn it to
265 the right (clockwise) until it will not turn any
266 more (about half a turn) (**see Figure C**).

267
268
269
270
271

272 5. Hold the loaded Pen by the ridges and pull it
273 **straight out (see Figure D)**. You may need
274 to pull hard on the Pen, but this is normal. **Do**
275 **not** press the Blue Button yet.

276 The Pen is now ready to use. **Do not** put the loaded Pen back into the Carrying
277 Case because that will damage the needle.

278 **How to use the IMITREX STATdose Pen to take your medicine**

279 Before injecting your medicine, choose an area with a fatty tissue layer (see Figure
280 E **or** Figure F). Ask your healthcare provider if you have a question about where to
281 inject your medicine.

282 To prepare the area of skin where IMITREX is to be injected, wipe the injection site
283 with an alcohol swab. Do not touch this area again before giving the injection.

284



285
288

Figure E



286
or

Figure F



287

Figure G

289 6. Without pushing the Blue Button, press the loaded Pen firmly against the skin
290 so that the grey barrel slides down toward the blue section that holds the

291 Syringe Cartridge (**see Figure D**). (This releases the Safety Catch that keeps
292 the Pen from firing by mistake until you are ready.)

293 7. Push the Blue Button. Hold the Pen still for **at least 5 seconds**. If the Pen is
294 taken away from the skin too soon, not all the medicine will come out.

295 8. **After 5 seconds**, carefully take the Pen away from your skin. The needle will
296 be showing (**see Figure G**). **Do not touch the needle**.

How to unload the IMITREX STATdose Pen after taking your medicine

298 Right after you take a dose with the Pen, you need to return the used Syringe
299 Cartridge to the Cartridge Pack.



301 Figure H



303 Figure I



305 Figure J

306 9. Push the Pen down into the empty side of the Cartridge Pack as far as it will go
307 (**see Figure H**).

308 10. Turn the Pen to the left (counterclockwise) about half a turn until it is released
309 from the Syringe Cartridge (**see Figure I**).

310 11. Pull the empty Pen out of the Cartridge Pack (**see Figure J**).

311 Because the Pen has now been used, the white Priming Rod will stick out from
312 the lower end of the Pen (**see Figure J**).

313 12. Close the Cartridge Pack lid over the used Syringe Cartridge. When the used
314 Syringe Cartridges are inserted correctly, the Cartridge Pack is a disposable,
315 protective case to help you avoid needle sticks and use the syringes correctly.

316 13. Put the Pen back into the Carrying Case and press it down firmly until you feel
317 it click. Close the Carrying Case lid. This gets the Pen ready for the next use.

318 If the lid will not close, push the Pen down until you feel it click. Then close the
319 lid.

320 **How to take out a used Cartridge Pack**

321 After both Syringe Cartridges have been used, take the Cartridge Pack out of the
322 Carrying Case. **Never reuse or recycle a Syringe Cartridge.**



323
324

Figure K



325
326

Figure L

- 327 14. Open the Carrying Case lid.
- 328 15. Hold the Carrying Case with one hand and press the 2 buttons on either side of
329 the Carrying Case (**see Figure K**).
- 330 16. Gently pull out the Cartridge Pack with the other hand (**see Figure L**).
- 331 17. Throw away the Cartridge Pack or dispose of it as instructed by your healthcare
332 provider. There may be special state and local laws for disposing of used
333 needles and syringes. Always keep out of the reach of children.

334 **How to insert a new Cartridge Pack**

335



336
337

Figure M



338
339

Figure N



340
341

Figure O

- 342 17. Take the new Cartridge Pack out of its box. **Do not take off the**
343 **tamper-evident seals (see Figure M).**
- 344 18. Put the Cartridge Pack in the Carrying Case. Slide it down smoothly (**see**
345 **Figure N**).
- 346 19. The Cartridge Pack will click into place when the 2 buttons show through the
347 holes in the Carrying Case (**see Figure O**). Close the lid.
- 348

349 This Patient Information and Instructions for Use has been approved by the U.S.
350 Food and Drug Administration.

351

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364

365 Month Year

366 IMJ: xPIL