

# The Medical Letter®

## on Drugs and Therapeutics

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### ▶ Comparison Table: Triptans

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Drug	Almotriptan	Eletriptan	Frovatriptan	Naratriptan	Rizatriptan	Sumatriptan <sup>1</sup>	Zolmitriptan
Brand Name (Manufacturer)	Axert (no longer manufactured)	Relpax (Pfizer)	Frova (Endo)	Amerge (no longer manufactured)	Maxalt, Maxalt MLT (Organon)	Imitrex (GSK) Onzetra Xsail (Avanir) Tosymra (Upsher-Smith) <sup>17</sup> Zembrace SymTouch (Upsher-Smith)	Zomig (Amneal)
Generic Available	Yes	Yes	Yes	Yes	Yes	Yes – for <i>Imitrex</i> products only	Yes
Route of Administration	Oral	Oral	Oral	Oral	Oral	Oral; Nasal; SC	Oral; Nasal
Formulations	6.25, 12.5 mg tabs	20, 40 mg tabs	2.5 mg tabs	1, 2.5 mg tabs	5, 10 mg tabs, ODTs	<i>Imitrex</i> and generics – Oral: 25, 50, 100 mg tabs SC: 4, 6 mg/0.5 mL auto-injector pen and refill cartridge, vials <sup>2</sup> Nasal: 5, 20 mg/0.1 mL nasal spray <i>Onzetra Xsail</i> : 11 mg nasal powder caps <i>Tosymra</i> : 10-mg single-use nasal spray <i>Zembrace SymTouch</i> : 3 mg/0.5 mL SC auto-injector	Oral: 2.5, 5 mg tabs and 2.5, 5 mg ODTs <sup>3</sup> Nasal: 2.5, 5 mg/0.1 mL nasal spray
Onset of Action	30-60 min	30-60 min	~2 hrs	1-3 hrs	30-60 min	Tablets: 30-60 min SC: ~10 min Nasal: 10-15 min	Tablets: 30-60 min Nasal: 10-15 min
Elimination Half-life	3-4 hrs	~4 hrs	~26 hrs	~6 hrs	2-3 hrs	~2-2.5 hrs	2-3 hrs
Usual Adult Dosage	6.25 or 12.5 mg PO; can be repeated after 2 hrs	20 or 40 mg PO; can be repeated after 2 hrs	2.5 mg PO with fluids; can be repeated after 2 hrs	2.5 mg PO; can be repeated after 4 hrs	5 or 10 mg PO; can be repeated after 2 hrs	Oral: 50 or 100 mg PO; can be repeated after 2 hrs <sup>4</sup> SC: <i>Imitrex</i> , and generics <sup>4</sup> : 6 mg SC; can be repeated after 1 hr <i>Zembrace SymTouch</i> : 3 mg SC; can be repeated after 1 hr Nasal spray: <i>Imitrex</i> , and generics: 5, 10, or 20 mg intranasally; can be repeated after 2 hrs <i>Tosymra</i> : 10 mg intranasally; can be repeated after 1 hr Nasal powder: 22 mg intranasally; can be repeated after 2 hrs	2.5 or 5 mg PO or intranasally; can be repeated after 2 hrs
Max Daily Adult Dose	25 mg	80 mg	7.5 mg	5 mg	30 mg	Oral: 200 mg SC: 12 mg Nasal spray: <i>Imitrex</i> , and generics: 40 mg <i>Tosymra</i> : 30 mg Nasal powder: 44 mg	10 mg
Adult Dosage for Renal Impairment	Severe (CrCl 10-30 mL/min): 6.25 mg starting dose	No dosage adjustment needed	No dosage adjustment needed	Severe (CrCl <15 mL/min): contraindicated Mild-moderate: 1 mg starting dose (max 2.5 mg/day)	No dosage adjustment needed	No dosage adjustment needed	No dosage adjustment needed

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Comparison Table: Triptans (continued)							
Drug	Almotriptan	Eletriptan	Frovatriptan	Naratriptan	Rizatriptan	Sumatriptan <sup>1</sup>	Zolmitriptan
Adult Dosage for Hepatic Impairment	6.25 mg starting dose (max 12.5 mg/day)	Severe <sup>5</sup> : not recommended	Severe <sup>5</sup> : caution recommended	Severe: contraindicated Mild-moderate: 1 mg starting dose (max 2.5 mg/day)	No dosage adjustment needed	Mild-moderate (oral): max single dose 50 mg Severe (oral, intranasal, and SC): contraindicated	Moderate-severe (oral): 1.25 mg (max 5 mg/day) Moderate-severe (intranasal): not recommended
Adult Dosage-Adjustment for Drug Interactions	With a strong CYP3A4 inhibitor <sup>6</sup> : 6.25 mg starting dose (max 12.5 mg/day); avoid strong CYP3A4 inhibitors in patients with renal or hepatic impairment	With a strong CYP3A4 inhibitor: avoid use within 72 hrs of treatment	No dosage adjustment needed	No dosage adjustment needed	With propranolol: only the 5 mg dose is recommended (max 15 mg/day)	No dosage adjustment needed	With cimetidine: 2.5 mg (max 5 mg/day)
Usual Pediatric Dosage	12-17 yrs: 6.25 or 12.5 mg PO; can be repeated after 2 hrs	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	6-17 yrs: 5 mg (<40 kg) or 10 mg (≥40 kg)	Not FDA-approved for pediatric use	Oral: not FDA-approved for pediatric use Nasal: (≥12 yrs): 2.5 or 5 mg intranasally; can be repeated after 2 hrs
Max Pediatric Dose	25 mg/day	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	The efficacy and safety of redosing within 24 hrs have not been established	Not FDA-approved for pediatric use	10 mg/day
Pediatric Dosage for Renal Impairment	Severe (CrCl 10-30 mL/min): 6.25 mg starting dose (max 12.5 mg/day)	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	No dosage adjustment needed	Not FDA-approved for pediatric use	No dosage adjustment needed
Pediatric Dosage for Hepatic Impairment	6.25 mg starting dose (max 12.5 mg/day)	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	No dosage adjustment needed	Not FDA-approved for pediatric use	Moderate-severe: not recommended
Pediatric Dosage Adjustment for Drug Interactions	With a strong CYP3A4 inhibitor: 6.25 mg starting dose (max 12.5 mg/day); avoid strong CYP3A4 inhibitors in patients with renal or hepatic impairment	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	With propranolol: avoid concurrent use (<40 kg); only a single 5 mg dose is recommended (≥40 kg)	Not FDA-approved for pediatric use	With cimetidine: 2.5 mg (max 5 mg/day)
Class Adverse Effects	Tingling, flushing, dizziness, drowsiness, fatigue, and heaviness or tightness in the chest (can occur with any triptan, but most frequently with SC sumatriptan); angina, myocardial infarction, cardiac arrhythmia, stroke, seizure, and death have occurred very rarely with triptans <sup>7</sup> ; peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction, and Raynaud phenomenon have also occurred						
Other Adverse Effects	Most common (≥1%): nausea, dry mouth, paresthesia	Most common (≥5%): asthenia, nausea, dizziness, somnolence	Most common (≥2%): dizziness, headache, paresthesia, dry mouth, dyspepsia, fatigue, hot or cold sensation, chest pain, skeletal pain, flushing	Most common (≥2%): paresthesia, nausea, dizziness, drowsiness, throat or neck pain/pressure	Most common (≥5%): asthenia/fatigue, somnolence, pain or pressure sensation, dizziness	Most common (≥2%): paresthesia, warm/cold sensation, chest/neck/throat/jaw pain, tightness, or pressure, vertigo, fatigue SC: burning at injection site, adverse effects more likely with SC formulation Intranasal: abnormal taste, nasal discomfort, rhinorrhea, rhinitis	Most common (≥5%): neck/throat/jaw pain, tightness, or pressure, dizziness, paresthesia, asthenia, somnolence, warm/cold sensation, nausea, heaviness sensation, dry mouth Intranasal: abnormal taste
Class Drug Interactions	A triptan should generally not be used within 24 hours of another triptan or an ergot because vasoconstriction could be additive; cases of serotonin syndrome reported with SSRIs and SNRIs, but risk is likely low <sup>8</sup>						
Other Drug Interactions	CYP3A4 inhibitors <sup>6</sup> can increase serum concentrations; dose adjustment is recommended	Propranolol can increase serum concentrations CYP3A4 inhibitors <sup>6</sup> can increase serum concentrations; contraindicated for use within 72 hours of treatment with a strong CYP3A4 inhibitor	Propranolol can increase serum concentrations	None	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor Propranolol can increase serum concentrations; dosage adjustment is recommended	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor Propranolol and cimetidine can increase serum concentrations; dosage adjustment recommended with cimetidine

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**Comparison Table: Triptans (continued)**

Drug	Almotriptan	Eletriptan	Frovatriptan	Naratriptan	Rizatriptan	Sumatriptan <sup>1</sup>	Zolmitriptan
Comments	Short-acting: all short-acting oral triptans are similar in their efficacy and speed of onset <sup>9,10</sup>	Short-acting: all short-acting oral triptans are similar in their efficacy and speed of onset <sup>9,10</sup>	Longer-acting: slower onset of action and lower initial response rate than other triptans, but better tolerated <sup>11</sup>	Longer-acting: slower onset of action and lower initial response rate than other triptans, but better tolerated <sup>11</sup>	Short-acting: all short-acting oral triptans are similar in efficacy and speed of onset <sup>9,10</sup> ODTs may be taken without water	Short-acting: all short-acting oral triptans are similar in efficacy and speed of onset <sup>9,10</sup> SC: faster-acting and more effective than other triptans, but more adverse effects Intranasal: faster-acting than oral, but may have unpleasant taste; efficacy partially dependent on GI absorption of swallowed portion of dose	Short-acting: all short-acting oral triptans are similar in efficacy and speed of onset <sup>9,10</sup> Intranasal: faster-acting than oral; unpleasant taste can occur, but may be less common than with sumatriptan <sup>12</sup> ; efficacy partially dependent on GI absorption of swallowed portion of dose ODTs may be taken without water
Cost <sup>13</sup> :	generic: \$33.40	generic: \$13.10 <i>Relpax</i> : 76.90	generic: \$26.20 <i>Frova</i> : 129.70	generic: \$6.10	generic: \$2.10 (tabs) 1.90 (ODTs) <i>Maxalt</i> : 40.70 <i>Maxalt MLT</i> : 36.60	generic: \$1.40 (tabs) 40.10 (vial) <sup>14</sup> 114.10 (auto-injector) 52.90 (nasal spray) <i>Imitrex</i> : 73.50 (tabs) 468.50 (auto-injector) 93.50 (nasal spray) <i>Onzetra Xsail</i> : 86.00 <i>Tosymra</i> : 106.30 <i>Zembrace SymTouch</i> : 188.40	generic: \$5.70 (tabs) 6.50 (ODTs) 69.40 (nasal spray) <i>Zomig</i> : 129.40 <i>Zomig nasal spray</i> : 97.80

ODT = orally disintegrating tablet; SC = subcutaneous; MAO = monoamine oxidase

1. Also available in combination with naproxen (*Treximet* – Pernix). Use of the fixed-dose combination is more effective in relieving moderate or severe migraine pain than either of its components taken alone (S Law et al. Cochrane Database Syst Rev 2016; 4:CD008541).

2. Vials are only available in 6 mg/0.5 mL.

3. ODTs are available generically only.

4. If migraine returns after initial treatment with sumatriptan injection (*Imitrex*, and generics), single doses of sumatriptan tablets can be taken at intervals  $\geq 2$  hours, up to a maximum of 100 mg/day.

5. Use of the drug in severe hepatic impairment has not been evaluated.

6. Inhibitors and inducers of CYP enzymes, P-glycoprotein, and other transporters. Med Lett Drugs Ther 2023 Feb 6 (epub). Available at secure.https://secure.medicalletter.org/TML-article-1669g. Accessed June 12, 2023.

7. G Roberto et al. Cephalalgia 2014; 34:5.

8. PE Rolan. CNS Drugs 2012; 26:949.

9. Short-acting triptans: sumatriptan, almotriptan, eletriptan, rizatriptan, and zolmitriptan.

10. MM Johnston and AM Rapoport. Drugs 2010; 70:1505.

11. V Tullo et al. Neurol Sci 2010; 31:S51.

12. Med Lett Drugs Ther 2004; 46:7.

13. Approximate WAC for one dose at the lowest usual adult dosage. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5,

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14. Cost for one 6 mg/0.5 mL vial.