

and eletriptan are, on a population basis, the most efficacious of the triptans. Sumatriptan and zolmitriptan have similar rates of efficacy as well as time to onset, with an advantage of having multiple formulations, whereas almotriptan has a similar rate of efficacy to sumatriptan and is better tolerated, and frovatriptan and naratriptan are somewhat slower in onset and are also well tolerated. Clinical efficacy appears to be related more to the $t_{\max}$ (time to peak plasma level) than to the potency, half-life, or bioavailability. This observation is consistent with a large body of data indicating that faster-acting analgesics are more effective than slower-acting ones.

Unfortunately, monotherapy with a selective oral 5-HT_{1B/1D} receptor agonist does not result in rapid, consistent, and complete relief of migraine in all patients. Triptans are generally not effective in migraine with aura unless given after the aura is completed and the headache initiated. Side effects are common, although often mild and transient. Moreover, 5-HT_{1B/1D} receptor agonists are contraindicated in individuals with a history, symptoms, or signs of ischemic cardiac, cerebrovascular, or peripheral vascular syndromes. Recurrence of headache, within the usual time course of an attack, is another important limitation of triptan use and occurs at least occasionally in most patients. Evidence from randomized controlled trials shows that coadministration of a longer-acting NSAID, naproxen 500 mg, with sumatriptan will augment the initial effect of sumatriptan and, importantly, reduce rates of headache recurrence.

Ergotamine preparations offer a nonselective means of stimulating 5-HT₁ receptors. A nonnauseating dose of ergotamine should be sought because a dose that provokes nausea is too high and may intensify head pain. Oral (excluding sublingual) formulations of ergotamine also contain 100 mg caffeine (theoretically to enhance ergotamine absorption and possibly to add additional analgesic activity). The average oral ergotamine dose for a migraine attack is 2 mg. Because the clinical studies demonstrating the efficacy of ergotamine in migraine predated the clinical trial methodologies used with the triptans, it is difficult to assess the comparative efficacy of ergotamine versus the triptans. In general, with use of ergotamine there appears to be a much