


A close-up photograph of a woman's face, her eyes closed and her hands pressed against her temples, conveying a sense of intense pain or discomfort. Overlaid on her face is a semi-transparent anatomical diagram of the human brain, with a specific area in the posterior region highlighted in a vibrant red color. Several smaller, semi-transparent purple circles are scattered across the top of the image, some containing faint, abstract patterns. The overall lighting is dramatic, with strong highlights and deep shadows, emphasizing the texture of her skin and the intensity of her expression.

The role of
**triptans in the
treatment of migraine**
in adults

Paracetamol or a non-steroidal anti-inflammatory drug (NSAID) can be used first-line for pain relief in acute migraine. A triptan can then be trialled if this was not successful. Combination treatment with a triptan and paracetamol or NSAID may be required for some patients. Most triptans are similarly effective, so choice is usually based on formulation, e.g. a non-oral preparation may be more suitable for patients with nausea or vomiting. To avoid medication overuse headache, triptan use should not exceed ten or more days per month.

Migraine is a condition characterised by attacks of moderate to severe, throbbing headache, which is usually unilateral. This is often associated with other symptoms, including nausea, vomiting, photophobia or phonophobia. Approximately one-third of patients with migraines also experience a preceding aura. Worldwide, approximately one in every seven people are affected by migraines, which are often associated with significant personal and socioeconomic impact.¹ In the Global Burden of Disease Survey 2010, migraine was ranked as the third most prevalent disorder and the seventh-highest specific cause of disability.²

 For information on diagnosing migraine, see:

National Institute for Health and Care Excellence (NICE) Guideline: Headaches. Diagnosis and management of headaches in young people and adults, 2012. Available from: www.nice.org.uk

British Association for the Study of Headache (BASH) Guidelines for the diagnosis and management of migraine, tension-type headache, cluster headache, medication-overuse headache, 2010. Available from: www.bash.org.uk


"Headache in primary care", BPJ 7 (Aug, 2007), available from: www.bpac.org.nz

A stepwise approach to managing migraine: triptans are appropriate at step two

There are a number of treatment guidelines for acute migraine, all of which differ slightly in their recommended approach (see the NICE and BASH guidelines).^{3,4} Most algorithms, however, recommend stepwise treatment, with triptans usually tried after paracetamol and NSAIDs.

A reasonable approach is:

- Step 1:** Over-the-counter analgesics (paracetamol, NSAIDs)
- Step 2:** Triptan
- Step 3:** Combination treatment with a triptan and an NSAID
 - +/- anti-emetic (prochlorperazine, metoclopramide) at any step

 Recommended doses for these medicines can be found in Tables 2 and 3.

NICE guidelines recommend considering an anti-emetic in addition to other acute treatment for migraine, even in the absence of nausea and vomiting.⁴

Non-oral preparations can be offered to patients who have tried oral preparations and found them ineffective or intolerable, e.g. buccal prochlorperazine, diclofenac suppositories, subcutaneous sumatriptan or intranasal zolmitriptan.⁴

Ergotamine and opioids are generally not recommended for the treatment of patients with acute migraine (Page 35).⁴

N.B. Triptans are not used to treat patients with rarer types of migraine, such as hemiplegic, basilar or ophthalmoplegic migraine.⁵ This is because theoretical concerns about the safety of using a medicine with vasoconstrictor effects in patients with focal migraine mean that these patient groups were not included in clinical trials.

Triptans available in New Zealand

Currently there are four triptans available in New Zealand: sumatriptan, rizatriptan, naratriptan and zolmitriptan. These have slightly differing pharmacokinetic and pharmacodynamic profiles (Table 1). Almotriptan, eletriptan and frovatriptan are other triptans available internationally, however, they are not currently available in New Zealand.⁶


Choice of triptan can be guided by a patient's symptoms

As all triptans have similar effectiveness (see: "How effective are triptans at relieving migraine", Page 32), it is appropriate to choose a triptan based on patient preference. Patients often prefer oral treatment, and oral sumatriptan is an acceptable first choice.¹⁴

Table 1: Triptans – formulations and number needed to treat (NNT)^{7,8}

Triptan	Formulations available	Onset of action	NNT for two hours pain free response vs placebo	Drug interactions
Sumatriptan	Subcutaneous injection 6 mg; tablet 50 mg, 100 mg	Subcutaneous 15 minutes; oral 30 minutes	2.3 (subcutaneous)	MAOIs (avoid use within 14 days); ergotamine, other triptans (within 24 hours)
			6.1 (50 mg tablet)	
			4.7 (100 mg tablet)	
Rizatriptan	Orally disintegrating tablet 10 mg; wafer 10 mg (NS)	0.5 – 1 hour	3.1	MAOIs (avoid use within 14 days); propranolol (increased bioavailability of rizatriptan – do not use concurrently because there is no lower strength rizatriptan tablet available in New Zealand); ergotamine, other triptans (within 24 hours)
Zolmitriptan	Nasal spray 5 mg (NS)	10 – 15 minutes	4.3	MAOIs (avoid use within 14 days); CYP1A2 inhibitor medicines (e.g. ciprofloxacin); ergotamine, other triptans (within 24 hours)
Naratriptan	Tablet 2.5 mg (NS)	1 – 3 hours	8.2	Ergotamine, other triptans (within 24 hours)

Key: NNT= number needed to treat; NS=Not subsidised; CI=confidence interval; MAOI=monoamine oxidase inhibitor

 **Subsidy:** For current subsidy information consult the New Zealand Formulary or the Pharmaceutical Schedule. At present the tablet and subcutaneous injections of sumatriptan are subsidised, as is the orally disintegrating rizatriptan tablet. The other triptans are not currently subsidised. Zolmitriptan nasal spray and sumatriptan 50 mg tablets are available without prescription as pharmacist-only medicines.

Vomiting and nausea may restrict oral treatment for some patients and in these cases, an alternative form of treatment such as subcutaneous sumatriptan (6 mg) or intranasal zolmitriptan (5 mg) are appropriate choices.^{4,16} Subcutaneous sumatriptan may be the best choice for patients who have rapidly developing migraines or for patients with nausea or vomiting that develop early in the migraine.¹⁴

“Melt” preparations dissolve on the tongue and are only absorbed after swallowing.¹⁶ They may be useful for people who find drinking water intolerable during a migraine or who are unable to swallow tablets, but are not usually suitable if vomiting is problematic.³

There is evidence that patients who do not respond to one triptan may respond to another.¹⁵ Therefore, it is reasonable to try an alternative triptan for a subsequent attack if one proves to be ineffective.¹⁶ In particular, patients who do not respond to oral triptans should be encouraged to try subcutaneous sumatriptan.¹⁴

Prescribing triptans and monitoring use

A triptan should be taken early during a migraine attack but not during the aura phase

Triptans are most effective if taken early in a migraine attack while the pain is still mild.⁷ Triptans should not be taken during the aura phase of a migraine because:

1. Trials in which triptans were administered in the aura phase showed no significant benefit of triptan use over placebo.⁷
2. There are concerns around distinguishing migraine aura from early stroke symptoms, particularly in patients with complex aura presentations.⁷

Do not repeat the dose of triptan if not responding to first dose

Individual advice varies for the different triptans but in general patients should not repeat the dose of a triptan if there is no relief of migraine after the first dose. The dose can be repeated

Table 2: Triptan dose and instructions⁵

N.B. If there is no response to the first dose, patients should not take a second dose for the same attack

Triptan	Dose	Instructions
Sumatriptan	Oral: 50 mg (some patients may require 100 mg)	Dose may be repeated after at least two hours if migraine recurs; maximum 300 mg in 24 hours
	Subcutaneous: 6 mg	Dose may be repeated once after at least one hour if migraine recurs; maximum 12 mg in 24 hours
Rizatriptan	Oral: 10 mg	Dose may be repeated after at least two hours if migraine recurs; maximum 30 mg in 24 hours. If prescribing the wafer formulation, advise patient that it should be placed on the tongue and allowed to dissolve.
Zolmitriptan	Intranasal: 5 mg into one nostril	Dose may be repeated after at least two hours if migraine recurs; maximum 10 mg in 24 hours. N.B. this advice is from the UK datasheet for zolmitriptan nasal spray; the New Zealand datasheet does not include information about repeat dosing.
Naratriptan	Oral: 2.5 mg	Dose may be repeated after at least four hours if migraine recurs; maximum 5 mg in 24 hours.

How effective are triptans at relieving migraine?

The evidence shows that triptans are effective in reducing the pain associated with acute migraine. There is little difference in efficacy between different types of triptans.

Recent systematic reviews of the effectiveness of sumatriptan concluded that sumatriptan (oral and subcutaneous) was superior to placebo for all efficacy outcomes.^{9,10} For oral sumatriptan 50 mg versus placebo, the number needed to treat (NNT) was 6.1 for pain-free response at two hours. For oral sumatriptan 100 mg, the NNT was 4.7 and for subcutaneous sumatriptan 6 mg, the NNT was 2.3 for the same outcome.^{9,10}

Other reviews have found that all triptans are superior to placebo, with small differences in efficacy between the various triptans.^{11,12} A study in 2002 found that rizatriptan, zolmitriptan, almotriptan, eletriptan and frovatriptan were therapeutically similar to 100 mg oral sumatriptan, but naratriptan was marginally less effective.¹² A more recent review in 2013 found that eletriptan (not available in New Zealand) appeared to be the most effective triptan at relieving pain at two and 24 hours.¹¹ Rizatriptan appeared to be the second most favourable treatment and was effective at two hours but did not have the same efficacy at 24 hours. Oral sumatriptan 100 mg was the third most effective treatment at two hours and appeared to maintain efficacy at 24 hours.¹¹

The mechanism of action of triptans

Triptans are selective 5-hydroxytryptamine (5-HT) receptor agonists with high affinity for 5-HT_{1B} and 5-HT_{1D} receptors.¹³ Stimulation of the 5-HT_{1B} receptors on smooth muscle cells of blood vessels causes cranial vasoconstriction. This was originally thought to be the main mechanism of action of triptans in relieving migraine.¹³ 5-HT_{1D} receptors lie on the perivascular trigeminal nerve terminals and in the dorsal horn. It is thought that stimulation of these receptors blocks the release of vasoactive peptides from trigeminal neurons and of neurotransmitters in the dorsal horn, which convey nociceptive information to the thalamus.¹³

after two to four hours if there was initial relief from the migraine and it has then reoccurred (Table 2).

Avoid using triptans for \geq ten days per month

Medication overuse headache can result from excessive use of analgesics used to treat headache, including the use of triptans for migraine. To avoid this, triptans should not be used for more than (or equal to) ten days per month on a regular basis.³ It is also recommended that paracetamol and NSAIDs should not be taken for headache on more than 15 days per month.³ Most guidelines advise that codeine and other opioids should not be used to treat migraine or other primary headache disorders, because of high rates of medication overuse headache with these preparations.

Medication overuse headache may manifest as a tension-type daily headache or migraine-like attacks. Headaches often improve within two months following the withdrawal of the overused medicine, although symptoms typically initially worsen before this improvement is seen.^{2,7}

Withdrawing triptans

There are a number of different strategies to manage withdrawal of triptans in people who have overused this medicine. Most involve the abrupt withdrawal of the triptan and the use of other medicines to cover symptoms after the triptan is withdrawn, e.g. headache, nausea and vomiting.

The following medicines may be used for withdrawal symptoms:¹⁷


- Naproxen 250 mg, three times daily or 500 mg, twice daily, or as required. Treatment may be continued for three to four weeks (some experts recommend only two to three weeks).
- Prednisone 60 – 100 mg tapered over five to six days; there is less evidence that this is effective for medication overuse headache
- Metoclopramide or domperidone can be used as required for nausea and vomiting

The patient should be reviewed after two to three weeks to ensure withdrawal has been achieved. Prophylactic medicines for migraine may be required, e.g. beta-blockers. Triptans may need to be reintroduced for acute migraine, but the patient should be advised to avoid using them for more than two days per week.¹⁷

A study of 98 patients with medication overuse headache found that following triptan withdrawal, the mean duration of

headache was 4.1 days, and overall improvement in associated symptoms, e.g. nausea, vomiting, sleep disturbance, occurred within 7 – 10 days.¹⁸

Referral to a Neurologist is sometimes useful for patients who are unable to successfully withdraw from overused medicine.

 For further information, see: “Medication overuse headache: when the cure becomes the cause”, *BPJ* 16 (Sept, 2008).

Safety and precautions with triptans

Cardiovascular safety

All triptans are associated with “triptan sensations”, which are symptoms of burning, tingling, or tightness in the face, neck, limbs or chest. Chest pressure may be alarming for the patient, however, in most cases it is not associated with ECG changes or other evidence of decreased myocardial perfusion.¹⁴ To improve tolerability, the triptan dose may be lowered in patients who are very sensitive to the adverse effects.¹⁴

There have been reports of serious cardiovascular events, including death, associated with triptan use. Most of these cases were linked to patients having prior cardiovascular risk factors. Patients with multiple cardiac risk factors may require cardiac evaluation before triptans are initiated.¹⁵

Triptans are contraindicated in people with uncontrolled or severe hypertension, ischaemic heart disease, or previous myocardial infarction, stroke or coronary vasospasm (including Prinzmetal’s angina) due to their vasoconstrictive effect.⁵

Safety in pregnancy and breastfeeding

Migraines are approximately three times more common among females than males, with an average age of onset of 18 years. The peak prevalence of migraine in females occurs between ages 25 and 55 years, making the safety of triptans in pregnancy and breastfeeding a potentially significant issue.¹⁹

Sumatriptan can be considered for the acute treatment of migraine in pregnant women if clinically indicated (see: “Management of acute migraine in pregnancy”). It is the triptan with the most evidence of use during pregnancy because it has been available for longer than other triptans. A large number of studies have confirmed that sumatriptan exposure during any stage of pregnancy has not been associated with an increased risk of major malformations.²⁰ Other triptans require more study. There is also no compelling evidence of other adverse

Management of acute migraine in pregnancy

There is no clear evidence that migraines are a significant risk factor for adverse outcomes during pregnancy, however, recent population-based studies have found a possible link suggesting that pregnant women with migraines may be more at risk of pregnancy-induced hypertension and pre-eclampsia.² Many women with a history of migraine report that the incidence of their migraines decreases during pregnancy, especially in the second and third trimesters. This is thought to be due to sustained oestrogen levels.² However, in women who do get migraines during pregnancy it is important that they are offered appropriate and adequate treatment to avoid adverse effects on maternal wellbeing, e.g. sleep deprivation, poor nutrition (due to vomiting and nausea) and increased stress.²⁰

Paracetamol is recommended first-line for the acute treatment of migraine in pregnant women. Sumatriptan can be considered as a second-line option, depending on the need for treatment balanced against the risk. NSAIDs (ibuprofen is preferred) may be considered in the second trimester, but should be avoided in the first and third trimesters, and are generally only used in pregnant women if their benefit outweighs the risk.⁵

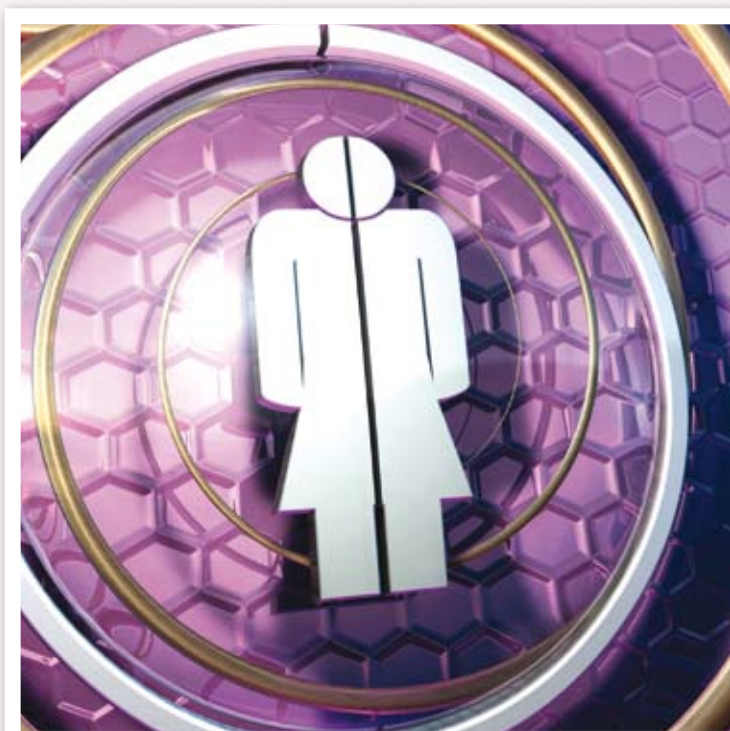


Table 3: Other pharmacological options for the treatment of migraine in adults^{5,29}

Drug class	Drug name	Dose and instructions
Analgesics	Paracetamol	1 g every 4–6 hours, no more than 4 doses in 24 hours
	Aspirin	600 – 900 mg every 4–6 hours, no more than 4 doses in 24 hours
	Ibuprofen	200 – 400 mg every 4–6 hours, no more than 2.4 g in 24 hours
	Naproxen	750 mg at onset, followed if necessary by a further 250 – 500 mg at least 1 hour after initial dose, no more than 1250 mg in first 24 hours; if ongoing migraine relief required, 250 mg every 6 – 8 hours as necessary, no more than 4 doses in 24 hours (or a maximum of 1 g daily) Naproxen sodium*: 825 mg at onset, followed if necessary by a further 275 – 550 mg at least 30 minutes after the initial dose. Maximum 1375 mg (5 tablets) in 24 hours * not subsidised, can be purchased over-the-counter (Naprogenic, Sonaflam)
	Diclofenac	Diclofenac sodium (oral): immediate release 50 – 75 mg at onset, repeated after 2 hours if necessary and then after 4 – 6 hours, no more than 200 mg in first 24 hours; if ongoing migraine relief required, modified release 75 mg once or twice daily as necessary, no more than 150 mg in 24 hours Diclofenac sodium (rectal): 100 mg at onset, repeated up after 2 hours if necessary by 100 mg rectally, up to 200 mg on the first day if required; if ongoing migraine relief required, 50 mg as necessary up to 3 times daily, no more than 150 mg in 24 hours Diclofenac potassium (oral)*: 50 mg at onset, repeated after 2 hours if necessary and then after 4 – 6 hours, maximum 150 mg in 24 hours * not subsidised, can be purchased over-the-counter (Voltaren Rapid)
Anti-emetics	Domperidone	10 mg, up to 3 doses in 24 hours
	Metoclopramide	10 mg, up to 3 doses in 24 hours. Do not prescribe for longer than 5 days (risk of neurological adverse events – see NZF for further details)
	Prochlorperazine	Oral tablets: 20 mg at outset, repeated if necessary by 10 mg 2 hours later; if ongoing anti-emetic required, 5–10 mg as necessary up to 3 times daily. Buccal tablets: 3 – 6 mg, up to 2 doses in 24 hours
Combination drugs	Paracetamol and metoclopramide (Paramax)*	Paracetamol (500 mg) + metoclopramide (5 mg): two tablets should be taken at the onset of the attack, repeated four-hourly as required; no more than 6 doses in 24 hours * Paramax to be delisted on 1 November 2014 due to supplier discontinuation.

pregnancy outcomes from exposure to sumatriptan during pregnancy,²¹ although some evidence suggests that triptan use later in pregnancy is associated with a slightly increased risk of complications, especially pre-term birth, atonic uterus and haemorrhage during labour (due to 5-HT effects on uterine blood vessels and platelet aggregation).^{22, 23}

Data regarding the use of triptans during breastfeeding is limited, but sumatriptan is considered compatible with breastfeeding.^{5, 20} In one study of five women who received subcutaneous sumatriptan, infants received approximately 3.5% of the weight-adjusted maternal dose through breast milk.²⁴ Given the low oral bioavailability of sumatriptan, the dose that infants would receive following a mother taking intermittent doses of oral sumatriptan is expected to be even lower.

Medicine interactions

There are several medicine interactions to be aware of when prescribing triptans. Triptans are contraindicated in people either currently taking monoamine oxidase inhibitors (MAOIs) or within two weeks of stopping a MAOI. Clinical evidence suggests that moclobemide approximately doubles the bioavailability of sumatriptan and other MAOIs (phenelzine and tranylcypromine) would be expected to interact in a similar way.^{5, 25}

There is also a potential risk of serotonin syndrome with the concurrent use of triptans in patients taking serotonin reuptake inhibitors (SSRIs), however, this interaction appears to be rare. The American Headache Society advised that the limited evidence provided by case reports does not support limiting the use of triptans with SSRIs or serotonin-noradrenaline reuptake inhibitors.²⁶ If these medicines are used together, monitor patients for signs of serotonin syndrome, e.g. weakness, hyperreflexia and poor co-ordination.⁵ There is also a possible risk of serotonin syndrome with the combination of St John's wort and triptans (one case report in the literature).²⁵

There is a theoretical risk of additive vasoconstriction, and possible significant coronary vasoconstriction, with the combined use of triptans and ergot derivatives (e.g. ergotamine) and the combination is generally contraindicated.²⁵ It is advised to avoid using ergotamine for six hours after using sumatriptan, and to avoid using sumatriptan for 24 hours after using ergotamine.⁵

Propranolol increases the plasma concentration of rizatriptan. International advice is to use a 5 mg dose of rizatriptan and limit the number of doses to two in 24 hours.²⁵ However, New

Zealand does not currently have a 5 mg formulation and the 10 mg formulations available are unable to be halved. Therefore in New Zealand, it may be best to avoid using this combination.

Other treatment options for the relief of acute migraine

Triptans are one of a number of therapeutic options available for the management of migraine. Other treatments that are used to manage migraine include paracetamol, NSAIDs and anti-emetics (see Table 3 for recommended doses). Ergotamine and opioids are not generally recommended.

There is limited evidence that directly compares triptans with other classes of medicines used for treating migraine. Two reviews found that triptans are superior to ergotamine compounds for treating migraine, however, both reviews found no significant difference in the effectiveness of triptans compared with other pharmacological approaches to treating migraine.^{13, 27}

A Cochrane review evaluated the combination of naproxen and sumatriptan to treat migraine. It was concluded that naproxen plus sumatriptan was significantly better than naproxen alone. However, there was only a small benefit when using the combination compared with using sumatriptan alone.²⁸

Ergotamine (combined with caffeine in Cafergot) is an older treatment for migraine that is still occasionally used. Current advice suggests that it is not appropriate to use ergots for migraine as there is evidence that they are not as effective as triptans and they are associated with an increased risk of adverse effects.^{4, 16}

Opioids are also not recommended as they may exacerbate nausea, increase the risk of medication overuse headache, and have the risk of potential addiction.¹³

ACKNOWLEDGEMENT: Thank you to **Dr John Mottershead**, Consultant Neurologist and Clinical Senior Lecturer, Dunedin School of Medicine, University of Otago, Dunedin and **Dr Lynette Murdoch**, General Practitioner and Senior Teaching Fellow, University of Otago, Christchurch for expert review of this article.

References:

1. World Health Organisation (WHO). How common are headaches? WHO, 2014. Available from: www.who.int/features/qa/25/en/ (Accessed Jul, 2014).
2. McGregor E. In the clinic. Migraine. *Ann Intern Med* 2013;159:ITC5–1–16.
3. British Association for the Study of Headache (BASH). Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type headache, cluster headache, medication-overuse headache. 3rd ed. BASH, 2010. Available from: www.bash.org.uk (Accessed Jul, 2014).
4. National Institute for Health and Care Excellence (NICE). Headaches. Diagnosis and management of headaches in young people and adults. NICE, 2012. Available from: www.nice.org.uk (Accessed Jul, 2014).
5. New Zealand Formulary (NZF). NZF v25. 2014. www.nzf.org.nz (Accessed Jul, 2014).
6. Brayfield A (ed). Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Available from: www.medicinescomplete.com (Accessed Jul, 2014).
7. Pringsheim T, Becker WJ. Triptans for symptomatic treatment of migraine headache. *BMJ* 2014;348:g2285.
8. Bird S, Derry S, Moore RA. Zolmitriptan for acute migraine attacks in adults. *Cochrane Database Syst Rev* 2014;5:CD008616.
9. Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. *Cochrane Database Syst Rev* 2012;2:CD008615.
10. Derry CJ, Derry S, Moore RA. Sumatriptan (subcutaneous route of administration) for acute migraine attacks in adults. *Cochrane Database Syst Rev* 2012;2:CD009665.
11. Thorlund K, Mills EJ, Wu P, et al. Comparative efficacy of triptans for the abortive treatment of migraine: a multiple treatment comparison meta-analysis. *Cephalalgia Int J Headache* 2014;34:258–67.
12. Ferrari MD, Goadsby PJ, Roon KI, et al. Triptans (serotonin, 5-HT_{1B/1D} agonists) in migraine: detailed results and methods of a meta-analysis of 53 trials. *Cephalalgia Int J Headache* 2002;22:633–58.
13. Worthington I, Pringsheim T, Gawel MJ. Canadian Headache Society Guideline: acute drug therapy for migraine headache. *Can J Neurol Sci* 2013;40:S1–S80.
14. Loder E. Triptan therapy in migraine. *N Engl J Med* 2010;363:63–70.
15. Gilmore B, Michael M. Treatment of acute migraine headache. *Am Fam Physician* 2011;83:271–80.
16. Clinical Knowledge Summaries (CKS). Migraine. CKS, 2013. Available from: <http://cks.nice.org.uk/migraine> (Accessed Jul, 2014).
17. Management of medication overuse headache. *Drug Ther Bull* 2010;48:2–6.
18. Katsarava Z, Fritsche M, Muessig H, et al. Clinical features of withdrawal headache following overuse of triptans and other headache drugs. *Neurology* 2001;57:1694–8.
19. Ephross SA, Sinclair SM. Final results from the 16-year sumatriptan, naratriptan, and treximet pregnancy registry. *Headache* 2014;[ePub ahead of print].
20. Duong S, Bozzo P, Nordeng H, et al. Safety of triptans for migraine headaches during pregnancy and breastfeeding. *Can Fam Physician* 2010;56:537–9.
21. UK Teratology Information Service (UKTIS). Use of sumatriptan in pregnancy. 2010. Available from: www.uktis.org/docs/sumatriptan.pdf (Accessed Jul, 2014).
22. Källén B, Nilsson E, Otterblad Olausson P. Delivery outcome after maternal use of drugs for migraine: a register study in Sweden. *Drug Saf Int J Med Toxicol Drug Exp* 2011;34:691–703.
23. Nezvalová-Henriksen K, Spigset O, Nordeng H. Triptan exposure during pregnancy and the risk of major congenital malformations and adverse pregnancy outcomes: results from the Norwegian Mother and Child Cohort Study. *Headache* 2010;50:563–75.
24. Wojnar-Horton RE, Hackett LP, Yapp P, et al. Distribution and excretion of sumatriptan in human milk. *Br J Clin Pharmacol* 1996;41:217–21.
25. Baxter K, Preston CL, (eds). *Stockley's Drug Interactions*. London: Pharmaceutical Press Available from: www.medicinescomplete.com (Accessed Jul, 2014).
26. Evans RW, Tepper SJ, Shapiro RE, et al. The FDA alert on serotonin syndrome with use of triptans combined with selective serotonin reuptake inhibitors or selective serotonin-norepinephrine reuptake inhibitors: American Headache Society position paper. *Headache* 2010;50:1089–99.
27. Lipton RB, Bigal ME, Goadsby PJ. Double-blind clinical trials of oral triptans vs other classes of acute migraine medication - a review. *Cephalalgia Int J Headache* 2004;24:321–32.
28. Law S, Derry S, Moore RA. Sumatriptan plus naproxen for acute migraine attacks in adults. *Cochrane Database Syst Rev* 2013;10:CD008541.
29. Australian medicines handbook. Adelaide: Australian Medicines Handbook Pty Ltd, 2011.