Topiramate is an antiepileptic agent that can be given alone or as adjunctive treatment. It is used for generalised tonic-clonic seizures and partial onset seizures. Topiramate is also indicated for migraine prophylaxis.\(^1\)

**START AT A LOW DOSE AND TITRATE TO EFFECT**

For optimum benefit, it is recommended that topiramate should be initiated using a low dose, followed by slow titration to an effective dose. For all indications, dose titration should be guided by clinical outcome.\(^2\)

The recommended starting dose for newly diagnosed epilepsy or migraine prophylaxis is 25mg at night for one week. The dose should then be gradually increased each week, as tolerated, in increments of 25mg until an effective dose is reached. Some patients may require longer intervals between dose adjustments if side effects, such as drowsiness, become troublesome.\(^2\)

For migraine prophylaxis, some patients will experience relief at just 50mg per day; others may require up to 200mg per day (in two divided doses). Patients with epilepsy usually require higher doses than for migraine; the optimal dose differs depending on whether topiramate is used as a monotherapy or add-on therapy. Refer to the datasheet for more detailed dosing information and for recommended doses in children.\(^3\)

Patients with renal disease or hepatic impairment may require a lower dose of topiramate; half the regular starting and maintenance dose is usually recommended.\(^2\) It generally takes longer to reach plasma steady state levels in patients with renal impairment.

**Note:** If topiramate needs to be discontinued, withdrawal must be done gradually because there is an elevated risk of seizures following rapid withdrawal regardless of whether the patient has a history of seizures or not.

**ADVISE PATIENTS TO REPORT OCULAR PAIN OR VISUAL IMPAIRMENT**

Inform patients to report any symptoms of acute decreased visual acuity or ocular pain. Topiramate is associated with a syndrome that presents as acute myopia and which may progress to secondary angle closure glaucoma; this applies to paediatric patients as well as adults.

Visual symptoms typically occur within one month of initiating topiramate. If pain or visual impairment occurs, topiramate should be discontinued as soon as possible, and the patient referred to an ophthalmologist for advice.\(^2\)

Elevated intraocular pressure can lead to permanent loss of vision if left untreated.\(^1\)

**ENCOURAGE ADEQUATE FLUID INTAKE ESPECIALLY DURING EXERCISE OR WARM TEMPERATURES**

Decreased sweating and an increase in body temperature especially after exposure to elevated environmental temperatures, have been reported with topiramate use. All patients taking topiramate should be informed about the likelihood of increased body temperature, especially during hot weather, and to ensure adequate hydration.\(^1\)

Take special care with children and patients who are taking other medicines that predispose them to dehydration and decreased sweating eg anticholinergic medicines.\(^1,2\)

**Note:** Patients taking topiramate are at increased risk of renal stone formation (nephrolithiasis), which can be compounded if patients are dehydrated or are in hot climates.\(^1\) This risk is further increased if other medicines that predispose to renal stone formation are used concurrently eg corticosteroids.

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\(^{3}\) continued
BE AWARE OF EMERGING OR WORSENING DEPRESSION OR SUICIDALITY

Although the overall risk is small, all patients taking antiepileptic medications should be monitored for notable changes in behaviour that could indicate the emergence or worsening of suicidal thoughts or depression. An analysis of 11 antiepileptic medicines, including topiramate, revealed that patients had approximately twice the risk of suicidal thoughts and behaviour (0.43%) compared with those taking placebo (0.22%). These thoughts and behaviours occurred as early as one week after starting medication, and continued throughout the 24-week study. Psychiatric and behavioural disturbances that have been observed with topiramate are generally dose-related.

Note: Topiramate has been reported to have negative effects on cognition. Lower doses and slower dose titrations appear to be associated with fewer adverse cognitive effects.

EDUCATE PATIENTS ABOUT CONTRACEPTION

Women using combined oral hormonal contraceptives and high-dose topiramate (greater than 200mg daily), may be at an increased risk of breakthrough bleeding and possible contraceptive failure because of induction of ethinylestradiol metabolism. Be aware that contraceptive efficacy can be decreased even in the absence of breakthrough bleeding. When prescribing an oral contraceptive, consider initial therapy with an agent containing at least 35 micrograms of ethinylestradiol. Further, topiramate is classified as pregnancy category D, so is considered to be teratogenic. Although there are no studies using topiramate in pregnant women, data from pregnancy registries indicate that there is an increased risk of congenital malformation.

All women of child bearing potential receiving antiepileptic medicines should receive pregnancy counselling and folic acid 5mg per day. Women with epilepsy who are planning a pregnancy should be referred for specialist advice; the combined input of a neurologist and an obstetrician is usually required.

Migraine

If migraine attacks are frequent, assess the patient for potential provoking factors such as stress, sleep deprivation, alcohol, or pharmacological triggers eg nitrates and combined oral contraceptives.

Preventive treatment for migraine should be considered for patients who report:
- at least two attacks a month
- an increasing frequency of headaches
- significant disability despite receiving treatment for migraine attacks or who cannot tolerate treatment for migraine attacks

Options for prophylaxis include beta-blockers (such as propranolol, atenolol, metoprolol, nadolol, and timolol), or topiramate. Unapproved options include tricyclic antidepressants, sodium valproate and gabapentin.

A Cochrane review of 17 studies concluded that topiramate is effective for the prophylaxis of episodic migraine in adults, and was reasonably well tolerated. Further, guidance from NICE recommends that either topiramate or propranolol can be offered for prophylactic treatment of migraine according to patient preference, comorbidities and risk of adverse events.

continued
REFERENCES


10. Carville S. Diagnosis and Management of headaches in young people and adults: summary of NICE guidance. British Medical Journal 2012,345:e5765 [www.bmj.com/content/345/bmj.e5765#ref-7](http://www.bmj.com/content/345/bmj.e5765#ref-7) [Accessed 07-10-13]

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