

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Zonisamide

Zonisamide (Zonegran®) is an antiepileptic drug that has been used for many years around the world but has only recently become available in Australia. It is listed as an Authority benefits prescription on the Pharmaceutical Benefits Scheme, subsidised for the treatment of partial epileptic seizures not controlled satisfactorily by other anti-epileptic drugs

Zonisamide is a sulphonamide agent and its exact mechanism of action is unclear. Studies have shown efficacy as an adjunct treatment in partial epilepsy, and it may also be effective as monotherapy. Whilst zonisamide reduces the frequency of seizures more than placebo, few patients become seizure free. The longest randomised controlled clinical trial had a maintenance stage of only 18 weeks, so long term efficacy is unclear. Its use has also been investigated in the treatment of bipolar disorder, obesity and parkinsonism.

Adverse reactions

Zonisamide is a sulphonamide derivative and so is contraindicated for patients with a sulpha allergy. Some of the adverse reactions reported include the expected CNS adverse effects such as drowsiness, dizziness and confusion. Other common adverse effects include weight loss, nephrolithiasis and gastrointestinal disturbances. Rare but serious adverse effects include serious skin reactions such as Stevens-Johnson syndrome, metabolic acidosis and hyperthermia.

Interactions

Drugs that induce or inhibit CYP3A4 may interact with zonisamide. Other epileptics including carbamazepine, phenytoin and phenobarbitone reduce the half life of zonisamide and valproate has also been reported to reduce the half life but to a lesser extent. Drugs that are known to cause hyperthermia and increase the risk of developing renal calculi should be avoided (to decrease the risk of adverse effects developing). Carbonic anhydrase inhibitors can increase the risk of developing metabolic acidosis and so should not be taken with zonisamide.

Dosing

Zonisamide has a complicated dosing initiation regimen: the recommended starting dose is 25 mg twice daily; increase after one week to 50 mg twice daily and then at weekly intervals by up to 50 mg twice daily according to response. The usual maintenance dose is 300-500 mg daily in one or two doses. A slower up titration of dose is recommended in renal impairment and mild to moderate hepatic impairment, and the manufacturer recommends avoiding this drug for those with severe hepatic impairment. In some patients not taking carbamazepine or phenytoin a lower dose may be effective. As with all anti-epileptics withdrawal of zonisamide should be gradual to avoid precipitating an increase in frequency of seizures.

Zonisamide is Australian category D in pregnancy and is excreted into breast milk.

Monitoring

Serum bicarbonate should be measured at baseline and periodically during treatment. Monitor for decreased sweating and hyperthermia, especially in hot weather. Patients should be counselled to maintain adequate hydration (especially if there is a history of kidney stones).

Acknowledgment – This E-Bulletin is based on work by Ruth Wilton, Senior Pharmacist, DATIS, RGH

FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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