Zonisamide

Zonegran

Zonisamide is a sulfonamide anticonvulsant.

Initiate therapy with 100mg PO q PM× 2 wks, then increase dose by 100 mg/d q 2 wks up to 400 mg/d. Bioavailability is not affected by food. Steady state is achieved within 14 days of dosage changes. Supplied : 100mg capsules.

Indications

approved for use as an adjunctive therapy in adults with partial seizures; infantile spasm, mixed seizure types of Lennox–Gastaut syndrome, myoclonic, and generalized tonic clonic seizure.

Zonisamide is approved in the United States,United Kingdom, and Australia for adjunctive treatment of partial seizures in adults and in Japan for both adjunctive and monotherapy for partial seizures (simple, complex, secondarily generalized), generalized (tonic, tonic-clonic (grand mal), and atypical absence) and combined seizures.

For epilepsy, most studies have used oral zonisamide in daily doses ranging from 200 to 600 milligrams/day, divided in 2 daily doses, adjusted to maintain serum levels of 15 to 40 micrograms/milliliter.

In an open-label trial zonisamide attenuated the symptoms of tardive dyskinesia.

It has also been studied for obesity with significant positive effects on body weight and there are three ongoing clinical trials for this indication. It is to be sold, when combined with bupropion, under the brand name Empatic.

Zonisamide has been studied for and used as a migraine preventative medication, and has also been shown to be effective in some cases of neuropathic pain.

It has also been used off-label by psychiatrists as a mood stabilizer to treat bipolar depression.

Adverse effects

Long-term anti-seizure drug therapy with zonisamide, sultiam, lacosamide, clobazam, and rufinamide from prepubertal to adulthood causes apoptosis and disruption of folliculogenesis in the ovarian follicles of nonepileptic rats [1)]

Very common (>10% incidence) adverse effects include:

Anorexia

Somnolence

Dizziness

Agitation Irritability

Confusional state

Depression

Diplopia

Memory impairment

Decreased bicarbonate

Common (1-10% incidence) adverse effects include:

Ecchymosis

Hypersensitivity

Affect lability

Anxiety

Insomnia

Psychotic disorder

Bradyphrenia

Disturbance in attention

Nystagmus

Paraesthesia

Speech disorder

Tremor

Abdominal pain

Constipation

Diarrhoea

Dyspepsia

Nausea

Rash

Pruritus

Alopecia

Nephrolithiasis

Fatigue

Influenza-like illness

Pyrexia

Oedema peripheral

Weight loss

Zonisamide and other carbonic anhydrase inhibitors such as topiramate, furosemide, and hydrochlorothiazide have been known to interfere with amobarbital, which has led to inadequate anesthetization during the Wada test.

Zonisamide may also interact with other carbonic anhydrase inhibitors to increase the potential for metabolic acidosis.

Additionally, the metabolism of zonisamide is inhibited by ketoconazole, ciclosporin, miconazole, fluconazole and carbamazepine (in descending order of inhibition) due to their effects on the CYP3A4 enzyme.

Zonisamide is an antiseizure drug chemically classified as a sulfonamide and unrelated to other antiseizure agents. The precise mechanism by which zonisamide exerts its antiseizure effect is unknown, although it is believed that the drug blocks sodium and T-type calcium channels, which leads to the suppression of neuronal hypersynchronization (that is, seizure-form activity).

It is also known to be a weak carbonic anhydrase inhibitor (similarly to the anticonvulsant, acetazolamide). It is also known to modulate GABAergic and glutamatergic neurotransmission.

Variable, yet relatively rapid rate of absorption with a time to peak concentration of 2.8-3.9 hours. Food has no effect on the bioavailability of zonisamide.

Zonisamide is metabolized mostly by the CYP3A4 isoenzyme, but also CYP3A7 and CYP3A5, to 2-(sulphamoylacetyl)-phenol via reductive cleavage of the 1,2-benzisoxazole ring.

Zonisamide was discovered by Uno and colleagues in 1972 and launched by Dainippon Sumitomo Pharma (formerly Dainippon Pharmaceutical) in 1989 as Excegran in Japan.

It was marketed by Élan in the United States starting in 2000 as Zonegran, before Élan transferred their interests in zonisamide to Eisai Co., Ltd. in 2004.

Eisai also markets Zonegran in Asia (China, Taiwan, and fourteen others) and Europe (starting in Germany and the United Kingdom) [2)].

There is no high level evidence to support any particular current agents for use in infants with seizures. For focal seizures, levetiracetam is effective (strong evidence); for generalized seizures, weak evidence supports levetiracetam, valproate, lamotrigine, topiramate, and clobazam; for Dravet syndrome, strong evidence supports that stiripentol is effective (in combination with valproate and clobazam), whereas weak evidence supports that topiramate, zonisamide, valproate, bromide, and

the ketogenic diet are possibly effective; and for Ohtahara syndrome, there is weak evidence that most antiepileptic drugs are poorly effective [3].

Results may provide an experimental basis for the use of ZNS-M as a clinically applicable therapeutic drug for the treatment of spinal cord injury SCI in the future [4].

1)
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2)
https://en.wikipedia.org/wiki/Zonisamide
3)
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