

## The Bulletin from the Clinical Pharmacist

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### Zonisamide

Zonisamide is a broad-spectrum anti-seizure medication (ASM) chemically classified as a **1,2-benzisoxazole derivative**, a unique sulfonamide compound unrelated to other antiepileptic drugs. Zonisamide may even be more cost-effective and show slightly higher probabilities of achieving a seizure-free state compared to levetiracetam.

**Pharmacological Class:** 1,2-benzisoxazole derivative; Sulfonamide anticonvulsant.

**Therapeutic Class:** Antiepileptic Drug (AED) / Antiseizure Medication (ASM).

#### Mechanism of Action (MOA):

- **Ion Channel Blockade:** Primarily blocks voltage-dependent **sodium channels** and **T-type calcium channels**, suppressing neuronal hyper-synchronization.
- **Neurotransmitter Modulation:** May inhibit presynaptic glutamate release and allosterically enhance GABAergic function.
- **Carbonic Anhydrase Inhibition:** It is a weak carbonic anhydrase inhibitor; however, this is not believed to be its primary antiepileptic mechanism.

#### Therapeutic Uses and Outcomes

**Indications:** Adjunctive therapy for **partial-onset (focal) seizures** in adults and children aged 16+ (U.S.) and potentially as low as 6 years and for Generalized tonic-clonic seizures, Lennox-Gastaut syndrome, infantile spasms, and myoclonic seizures. It has also been investigated for migraine prophylaxis, Parkinson's disease (motor symptoms), and neuropathic pain.

#### Clinical Outcomes:

- **Responder Rate:** Studies show a **40%–80%** responder rate ( $\geq 50\%$  seizure reduction) in focal epilepsy.
- **Retention:** Demonstrates high long-term retention rates (e.g.,  $\sim 60\%$  at 2 years), indicating sustained effectiveness and tolerability.

#### Available Formulation

Oral Tablet: 100 mg (Brand name: Zonegran)

Category	Information/ Dosing details
<b>Dosing</b>	Oral, initially 100mg per day. Dose may be increased 200mg per day after 2 weeks. Further dosage increases to 300mg and 400mg per day can be made with minimum of 2 weeks between adjustments. <b>Note:</b> Doses of 300mg per day and higher are associated with increased side effects.
<b>Geriatric dosing</b>	Begin dosing at the low end of the dosing range

#### Warning and precautions:

Anticonvulsant should not be discontinued abruptly because of the possibility of increasing seizure frequency, therapy should be withdrawn gradually to minimize the potential of increased seizure frequency, unless safety concerns require a more rapid withdrawal.

**Side effects:**

More Common side effects	Less common side effects
Continuing ringing or buzzing (or) unexplained noise in ears.	Acid or sour stomach
Difficulty with memory	Bad, unusual unpleasant taste in stomach
Unusual drowsiness	Bleeding gums
Diarrhea, Sleepiness	Difficulty with speaking and thinking
Hyperammonemia	Tingling, burning or prickly feelings on skin.
Ataxia, weight loss, reduce seating.	Irritation in mouth

**Inpatient use of Zonisamide:**

During the review period, several inpatients were prescribed Zonisamide (50 – 100 mg, primarily at bedtime) for seizure prophylaxis and management of neurological conditions, including Post-traumatic head injury with intracranial hemorrhage, diffuse axonal injury, post-craniotomy status following space-occupying lesion excision, suspected autoimmune encephalitis, and seizure disorders.