TIAGABINE

THERAPEUTICS

Brands
• Gabitril

Generic?
Yes

Class
• Antiepileptic drug (AED)

Commonly Prescribed for
(FDA approved in bold)
• Partial seizures in adults and children age 12 or older
• Temporal lobe epilepsy (children and adults)
• Panic disorder

How the Drug Works
• Enhances activity of GABA by binding to sites associated with GABA uptake into presynaptic neurons, allowing more GABA to be available to bind to receptors on postsynaptic cells

How Long Until It Works
• Seizures – should decrease by 2 weeks

If It Works
• Seizures – goal is the remission of seizures. Continue as long as effective and well-tolerated. Consider tapering and slowly stopping after 2 years without seizures

If It Doesn’t Work
• Increase to highest tolerated dose
• Epilepsy: consider changing to another agent, adding a second agent or referral for epilepsy surgery evaluation

Best Augmenting Combos for Partial Response or Treatment-Resistance
• Epilepsy: titration and combination regimen depends on whether the patient is on an enzyme-inducing drug or not

Tests
• No regular blood tests are recommended

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
• CNS AEs are probably caused by excess GABA effect

Notable AEs
• Confusion, stuttering, muscle tremor, dizziness, sedation, paresthesias (usually doses > 8 mg/day), abdominal pain
• Less commonly, behavioral symptoms such as amnesia, extreme confusion, or seizures or seizure-like symptoms

Life-Threatening or Dangerous AEs
• Can precipitate seizure in some patients (rare)
• Severe rash (rare) including Stevens-Johnson syndrome
• Falls producing accidental injury

Weight Gain
• Common

Sedation
• Common

What to Do About AEs
• Decreasing dose may improve CNS AEs, especially weakness and sedation
• Titrate more slowly

Best Augmenting Agents for AEs
• Initially dose at night to avoid sedation

DOSING AND USE

Usual Dosage Range
• Epilepsy: 16–56 mg/day

Dosage Forms
• Tablets: 2 mg, 4 mg, 12 mg, 16 mg

How to Dose
• For adults on enzyme-inducing AEDs (phenytoin, carbamazepine, primidone, phenobarbital), start at 4 mg. Increase dose by 4–8 mg in 1 week and continue to
increase by 4–8 mg/week as needed, to a maximum of 56 mg daily. At final doses give in divided doses 2–4 times daily.
- In patients not on enzyme-inducing AEDs, give only half the dose and titrate more slowly.

### Dosing Tips
- Food and specifically fats slow absorption rate but not the extent of absorption. Most patients take with food.
- Titrate slowly in patients not on enzyme-inducing AEDs.

### Overdose
- Somnolence, weakness, agitation, confusion, depression, respiratory depression, and myoclonus have been reported. Rarely precipitates non-convulsive status epilepticus.

### Long-Term Use
- Safe for long-term use.

### Habit Forming
- No.

### How to Stop
- Taper slowly.
- Abrupt withdrawal can lead to seizures in patients with epilepsy.

### Pharmacokinetics
- Elimination half-life is 2–5 hours in patients on inducing AEDs, but 7–9 hours in others. Most drug is metabolized by CYP-450 3A system. Bioavailability is about 90% and drug is 96% protein bound.

### Drug Interactions
- Carbamazepine, phenytoin, phenobarbital, and primidone increase clearance of tiagabine by about 60%.
- Use with other highly protein-bound drug may increase free levels and drug effect.
- Valproate may slightly increase free tiagabine levels and tiagabine causes a slight decrease in valproate concentrations. Usually not clinically relevant.

### Other Warnings/Precautions
- CNS AEs increase when used with other CNS depressants.

### Do Not Use
- Hypersensitivity to drug.

### SPECIAL POPULATIONS

#### Renal Impairment
- No known effects.

#### Hepatic Impairment
- Lower dose, as patients with moderate disease have reduced clearance by 60%.

#### Cardiac Impairment
- No known effects.

#### Elderly
- May need lower dose.

#### Children and Adolescents
- For children age 12–18 on enzyme-inducing AEDs (phenytoin, carbamazepine, primidone, phenobarbital), start at 4 mg. Increase dose to 8 mg in 1 week and continue to increase by 4–8 mg/week as needed, to a maximum of 32 mg daily. At final doses, give in divided doses 2–4 times daily.
- In children not on enzyme-inducing AEDs, give only half the dose and titrate more slowly.

#### Pregnancy
- Risk category C. Multiple malformations in animals. Use only if benefits of using drug outweigh potential risk to fetus.
- Supplementation with 0.4 mg of folic acid before and during pregnancy is recommended.

#### Breast Feeding
- Some drug is found in mother’s breast milk.
- Generally recommendations are to discontinue drug or bottle feed.
TIAGABINE (continued)

**THE ART OF NEUROPHARMACOLOGY**

**Potential Advantages**

- Useful for partial seizures, especially with coexisting panic disorder

**Potential Disadvantages**

- Depression and cognitive impairment. Does not treat generalized epilepsies

**Primary Target Symptoms**

- Seizure frequency and severity

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**Pearls**

- Contraindicated in generalized epilepsy and may precipitate non-convulsive status epilepticus.
- There are reports of patients with spike-wave discharges who experience exacerbations of EEG abnormalities which correlate with cognitive or neuropsychological reactions on tiagabine.

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**Suggested Reading**


