
NEFAZODONE (Serzone) Fact Sheet [G]

Bottom Line:

Nefazodone was once popular due to the lack of sexual side effects, but is now rarely used due to rare hepatic effects.

FDA Indications:

Major depression.

Off-Label Uses:

Anxiety; insomnia.

Dosage Forms:

Tablets (G): 50 mg, 100 mg, 150 mg, 200 mg, 250 mg.

Dosage Guidance:

Start 50–100 mg BID, increase in 50–100 mg/day increments weekly. Usual dose 300–500 mg/day; maximum 600 mg/day divided BID.

Monitoring: LFTs, BP.

Cost: \$\$

Side Effects:

- Most common: Nausea, somnolence, dry mouth, dizziness, lightheadedness, constipation, blurred vision, confusion; less orthostasis than trazodone.
- Serious but rare: Black box warning for hepatic toxicity; 1/200,000 to 1/300,000 risk (three to four times general incidence); cases of severe hepatotoxicity resulting in death or need for transplant have been reported; seems to occur early in treatment; not necessarily associated with increased LFTs.
- Pregnancy/breastfeeding: Limited data suggest safe in pregnancy; considered safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Norepinephrine and serotonin reuptake inhibitor and 5-HT₂ antagonist.
- Metabolized by CYP3A4; potent inhibitor of CYP3A4; t_{1/2}: 2–4 hours.
- Caution with CYP3A4 inhibitors, inducers, and substrates. Avoid MAOIs and other serotonergic agents.

Clinical Pearls:

- Similar to trazodone in chemical structure, but less sedating.
- Minimal sexual side effects.
- If patient tolerates, may be used QHS rather than BID to minimize daytime sedation and improve nighttime sleep.
- Avoid in patients with active liver disease or elevated LFTs; monitor all patients for symptoms of hepatic impairment (jaundice, anorexia, GI complaints, lethargy). If patient is symptomatic or LFTs increase to three or more times upper limit of normal, discontinue and monitor patient; do not re-treat.

Fun Fact:

After the drug was removed from the market in Canada and Europe, the nonprofit organization Public Citizen sued the FDA for failing to remove it from the US market. The suit was later withdrawn, but the manufacturer of the branded product Serzone stopped production due to weak sales; generic sales continue.