
DESVENLAFAXINE (Pristiq) Fact Sheet [G]

Bottom Line:

Desvenlafaxine is the active metabolite of venlafaxine, and it has some minor advantages in terms of drug interactions, ease of dosing, and longer half-life. One disadvantage is lack of FDA approval for anxiety disorders. At least for depression, since desvenlafaxine is now available in a low-cost generic version, some clinicians prefer it over venlafaxine XR.

FDA Indications:

Major depression.

Off-Label Uses:

Fibromyalgia; vasomotor symptoms of menopause; generalized anxiety disorder (GAD); social anxiety disorder; panic disorder; PTSD; PMDD.

Dosage Forms:

ER tablets (G): 25 mg, 50 mg, 100 mg.

Dosage Guidance:

Start 50 mg QD, usually best in the morning due to risk of insomnia. Some patients require increase to 100 mg QD, but dosing above this is not recommended as it only increases side effects without being more efficacious.

Monitoring: Periodic blood pressure.

Cost: \$

Side Effects:

- Most common: Nausea, dizziness, insomnia, excessive sweating, constipation, dry mouth, somnolence, decreased appetite, anxiety, sexual side effects.
- Serious but rare: Dose-related increases in systolic and diastolic blood pressure (as likely with desvenlafaxine as venlafaxine). Monitor BP regularly, and if increases are sustained, consider reducing dose or discontinuing.
- Pregnancy/breastfeeding: Less data than other antidepressants; considered safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Serotonin and norepinephrine reuptake inhibitor.
- Active metabolite of venlafaxine, metabolized primarily through conjugation and oxidation via CYP3A4 (minor). Minimally inhibits CYP2D6; $t_{1/2}$: 11 hours.
- Avoid use with MAOIs, other serotonergic medications. Not likely to cause other clinically significant interactions.

Clinical Pearls:

- Potential advantages vs venlafaxine: not significantly metabolized by 2D6, so less concern about drug interactions; less dosage titration needed (starting dose is usually effective, occasionally need to increase to 100 mg daily); longer half-life (11 vs six hours), so potentially less severe discontinuation syndrome.
- Potential disadvantages vs venlafaxine: FDA approval limited to major depression (vs major depression plus GAD, panic disorder, and social anxiety disorder for venlafaxine); flat dose-response curve.
- Desvenlafaxine has not been shown to be any more effective than venlafaxine.
- Recent low-cost generic versions of desvenlafaxine make it about as cheap as venlafaxine.
- Desvenlafaxine is available in two forms: a succinate salt (Pristiq) and a base (Khedezla). Aside from small differences in half-life, there is no difference between these products—all efficacy studies were based on the original Pristiq studies.

Fun Fact:

Desvenlafaxine's manufacturer withdrew its application for approval in the European Union, where regulatory bodies had said that desvenlafaxine was likely less effective than venlafaxine with no advantages in terms of safety and tolerability.