VENLAFAXINE (Effexor, Effexor XR) Fact Sheet [G]

Bottom Line:
Venlafaxine is probably somewhat more effective than SSRIs for depression, but its side effect disadvantages, such as blood pressure elevation and discontinuation symptoms, relegate it to second-line use. Venlafaxine's active metabolite, desvenlafaxine, may be preferred by some over the parent compound—see our desvenlafaxine fact sheet in this chapter.

FDA Indications:
Major depression; social anxiety disorder; generalized anxiety disorder; panic disorder.

Off-Label Uses:
PTSD; PMDD; vasomotor symptoms of menopause; diabetic peripheral neuropathy.

Dosage Forms:
- **Tablets (G):** 25 mg, 37.5 mg, 50 mg, 75 mg, 100 mg (scored).
- **ER tablets (G):** 37.5 mg, 75 mg, 112.5 mg, 150 mg, 225 mg.
- **ER capsules (G):** 37.5 mg, 75 mg, 150 mg.

Dosage Guidance:
- Depression:
  Start 75 mg/day in two or three divided doses or as XR once daily; ↑ dose by 75 mg/day at intervals of four or more days; max 375 mg/day (divided TID) or 225 mg/day XR given once daily. IR may be switched to nearest equivalent daily dose of XR QD.
- Anxiety:
  XR: Start 75 mg QD, ↑ by 75 mg/day at weekly intervals; max 225 mg/day; for panic disorder, to minimize exacerbation of panic, start 37.5 mg QD, ↑ to 75 mg QD after one week then by 75 mg/day at weekly intervals; max 225 mg/day.

Monitoring: Periodic blood pressure.

Cost: $

Side Effects:
- Most common: Anorexia, constipation, dizziness, dry mouth, nausea, nervousness, somnolence, sweating, sexual side effects, headache, insomnia.
- Serious but rare: Sustained, dose-related hypertension reported. May cause hyponatremia or SIADH; use with caution in patients who are volume depleted, elderly, or taking diuretics.
- Pregnancy/breastfeeding: Less data than other antidepressants; considered safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Serotonin and norepinephrine reuptake inhibitor.
- Metabolized primarily through CYP2D6 to O-desmethylvenlafaxine (ODV), major active metabolite (an SNRI, marketed as Pristiq), and also by CYP3A4; t ½: 5 hours (11 hours for ODV).
- Avoid use with MAOIs, other serotonergic agents. Caution with CYP2D6 or 3A4 inhibitors, which may increase venlafaxine levels. Inhibits CYP2D6.

Clinical Pearls:
- For patients with nausea, start at lower dose, titrate more slowly, and give with food.
- May cause false-positive PCP in urine drug screen.
- Increase in blood pressure much more likely in doses >225 mg/day.
- Significant discontinuation syndrome, even with XR formulation.
- Theoretically functions as an SSRI in low doses (75 mg/day) and as an SNRI in moderate doses (150–225 mg/day), and affects all monoamines in high doses (>225 mg/day).
- No additional benefit seen with doses >225 mg/day in moderately depressed outpatients, but patients with more severe depression may respond to higher doses (350 mg/day).

Fun Fact:
Venlafaxine is structurally related to the atypical opioid analgesic tramadol (Ultram, itself a serotonergic agent), but not to any other antidepressant drugs.