
VORTIOXETINE (Trintellix) Fact Sheet

Bottom Line:

Vortioxetine is a newer “multimodal” antidepressant with diverse effects on neurotransmitters. Recent data suggest that vortioxetine may have pro-cognitive effects and may be less likely to cause sexual side effects than SSRIs. It is reasonable to try the drug in patients who have complained of SSRI-induced sexual dysfunction. A high prevalence of nausea and the high brand-name price tag are negative factors to consider.

FDA Indications:

Major depression.

Off-Label Uses:

Generalized anxiety disorder; other anxiety disorders.

Dosage Forms:

Tablets: 5 mg, 10 mg, 20 mg.

Dosage Guidance:

Start 10 mg QD; ↑ to 20 mg QD as tolerated. Consider 5 mg/day for those unable to tolerate higher doses (eg, due to nausea). May be taken in the morning or night.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$\$\$\$

Side Effects:

- Most common: Nausea, constipation, vomiting, sexual side effects, dry mouth, headache.
- Serious but rare: Serotonergic antidepressants have been rarely associated with bruising or bleeding.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Multimodal antidepressant.
- Metabolized primarily through CYP2D6 and, to a lesser extent, via 3A4/5, 2C9/19, 2A6, 2C8, and 2B6; t_{1/2}: 66 hours.
- Avoid use with MAOIs, other serotonergic medications. Use lower doses in presence of potent 2D6 inhibitors.

Clinical Pearls:

- Vortioxetine is a “multimodal” antidepressant or a “serotonin modulator and stimulator.” This means it has effects on several receptor sites. Like SSRIs, it is a serotonin reuptake inhibitor, but it also is an agonist at 5-HT_{1A} receptors, a partial agonist at 5-HT_{1B} receptors, and an antagonist at 5-HT_{3A}, 5-HT_{1D}, and 5-HT₇ receptors.
- The Trintellix labeling was updated twice in 2018. First, data from studies examining cognitive functioning in patients treated for depression were included to note improved processing speed with vortioxetine. The second update was made to include head-to-head data showing greater improvement in treatment-emergent sexual side effects when patients were switched from SSRI to vortioxetine over escitalopram.
- The degree of cognitive improvement seen with vortioxetine has been compared to that of caffeine from a shot of espresso. Whether or how much that results in functional improvement remains to be seen.
- Negative findings in some studies were attributed to dose being too low (5–10 mg/day). Higher-dose studies showed vortioxetine to be as effective as both duloxetine and agomelatine, an antidepressant approved in Europe.
- Compared to SSRIs, vortioxetine has more GI side effects, including nausea, vomiting, diarrhea, and constipation. This may mean that some patients won't be able to get beyond 5 or 10 mg per day.
- Two studies looked at vortioxetine for cognitive symptoms in perimenopausal depression. One found benefits and the other did not, but both were small observational studies, not randomized and with no placebo group.

Fun Fact:

The original brand name of vortioxetine, Brintellix, was apparently crafted to subliminally suggest that the drug helps cognition (“**bring intelligence**”). It was changed to Trintellix in 2016 because of reports of dispensing errors between Brintellix and Brilinta, the antiplatelet medication ticagrelor.