Vortioxetine (Trintellix®)

(Brintellix was re-named Trintellix in June 2016 to avoid name confusion)

Indication: Indicated for the treatment of major depressive disorder (MDD), FDA approved September, 2013

Mechanism of action

- Not fully understood, considered a new multimodal antidepressant with antagonist properties at 5-HT3A and 5-HT7 receptors, partial agonist properties at 5-HT1B receptors, agonist properties at 5-HT1A receptors, and potent inhibition of the serotonin reuptake transporter
- Preclinical data suggest that these multiple effects on numerous serotonin receptors result in regional increases in noradrenaline and dopamine as well as glutamatergic transmission

Dosage and administration

- Initially 10 mg PO Q day without regard to meals
- Dose can be increased to 20 mg/d, as tolerated. Consider 5 mg/d if higher doses are intolerable
- Max recommended dose in CYP2D6 poor metabolizers: 10 mg/d

Discontinuing treatment: Can be discontinued abruptly, however, transient AEs such as headache and muscle tension were experienced by patients on vortioxetine 15 mg/d or 20 mg/d. To avoid adverse reactions, consider reducing dose to 10 mg/d for one week prior to discontinuation

How supplied: 5 mg, 10 mg, 15 mg, and 20 mg IR tablets

Warnings and Precautions

- Risk of Serotonin syndrome when taken alone or co-administered with other serotonergic agents
- May increase the risk of bleeding particularly if used with aspirin, NSAIDs, warfarin or other anticoagulants
- Activation of Mania/Hypomania can occur with antidepressant treatment (screen patients for bipolar disorder)
- SIADH and hyponatremia
- Black Box Warning: Suicidal thoughts and behaviors

Contraindications: Hypersensitivity to vortioxetine or any component of the formulation; use of MAO inhibitors (concurrently or within 21 days of discontinuing vortioxetine or within 14 days of discontinuing the MAO inhibitor); initiation of vortioxetine in a patient receiving linezolid or intravenous methylene blue

Adverse Reactions

- AEs occurring in ≥5% and at least twice the rate of placebo: Nausea, constipation, and vomiting
- AEs occurring in ≥2% of patients and at least 2% greater than the placebo group (table below)

References available upon request

January 27, 2014

Note: Brintellix was renamed Trintellix in June 2016 to avoid name confusion

System Organ Class Preferred Term	BRINTELLIX 5 mg/day N=1013 %	BRINTELLIX 10 mg/day N=699 %	BRINTELLIX 15 mg/day N=449 %	BRINTELLIX 20 mg/day N=455 %	Placebo N=1621 %
Gastrointestinal disorders					
Nausea	21	26	32	32	9
Diarrhea	7	7	10	7	6
Dry mouth	7	7	6	8	6
Constipation	3	5	6	6	3
Vomiting	3	5	6	6	1
Flatulence	1	3	2	1	1
Nervous system disorders					
Dizziness	6	6	8	9	6
Psychiatric disorders					
Abnormal dreams	<1	<1	2	3	1
Skin and subcutaneous tissue disorders					
Pruritus*	1	2	3	3	1

*includes pruritus generalized

- **Sexual dysfunction:** Incidence* of patients that developed treatment-emergent sexual dysfunction in any fixed dose group (table below)

	BRINTELLIX 5 mg/day N=65:67†	BRINTELLIX 10 mg/day N=94:86†	BRINTELLIX 15 mg/day N=57:67†	BRINTELLIX 20 mg/day N=67:59†	Placebo N=135:162†
Females	22%	23%	33%	34%	20%
Males	16%	20%	19%	29%	14%

*Incidence based on number of subjects with sexual dysfunction during the study / number of subjects without sexual dysfunction at baseline. Sexual dysfunction was defined as a subject scoring any of the following on the ASEX scale at two consecutive visits during the study: 1) total score ≥19; 2) any single item ≥5; 3) three or more items each with a score ≥4

†Sample size for each dose group is the number of patients (females:males) without sexual dysfunction at baseline

Pharmacokinetics

- Steady state plasma concentrations achieved within two weeks
- Half-life ~ 66 hours indicating that rebound and withdrawal phenomena after missing doses or stopping the medication are unlikely
- Hepatic (mild or moderate) or renal impairment (mild, moderate, severe and ESRD) did not appear to affect vortioxetine clearance

DDI

- Concomitant use of strong CYP2D6 inhibitor (eg. bupropion, fluoxetine, paroxetine, or quinidine): Reduce vortioxetine dose by half
- Concomitant use of strong CYP inducer (eg. rifampin, carbamazepine, or phenytoin) for more than 14 days: Consider increasing vortioxetine dose (max recommended dose: 3 times the original dose)

Use in specific populations

- Pregnancy Category C: May cause fetal harm based on animal data

References available upon request
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- Nursing Mothers: Discontinue vortioxetine or nursing
- Not evaluated for use in pediatric patients

Formulary status: PA required
Please contact BHRS Pharmacy Services for additional information

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