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

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

Includes pruritus generalized

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

<table>
<thead>
<tr>
<th></th>
<th>BRINTELLIX 5 mg/day N=65:67†</th>
<th>BRINTELLIX 10 mg/day N=94:86‡</th>
<th>BRINTELLIX 15 mg/day N=57:67†</th>
<th>BRINTELLIX 20 mg/day N=67:59‡</th>
<th>Placebo N=135:162‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>22%</td>
<td>23%</td>
<td>33%</td>
<td>34%</td>
<td>20%</td>
</tr>
<tr>
<td>Males</td>
<td>16%</td>
<td>20%</td>
<td>19%</td>
<td>29%</td>
<td>14%</td>
</tr>
</tbody>
</table>

*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

January 27, 2014
• 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