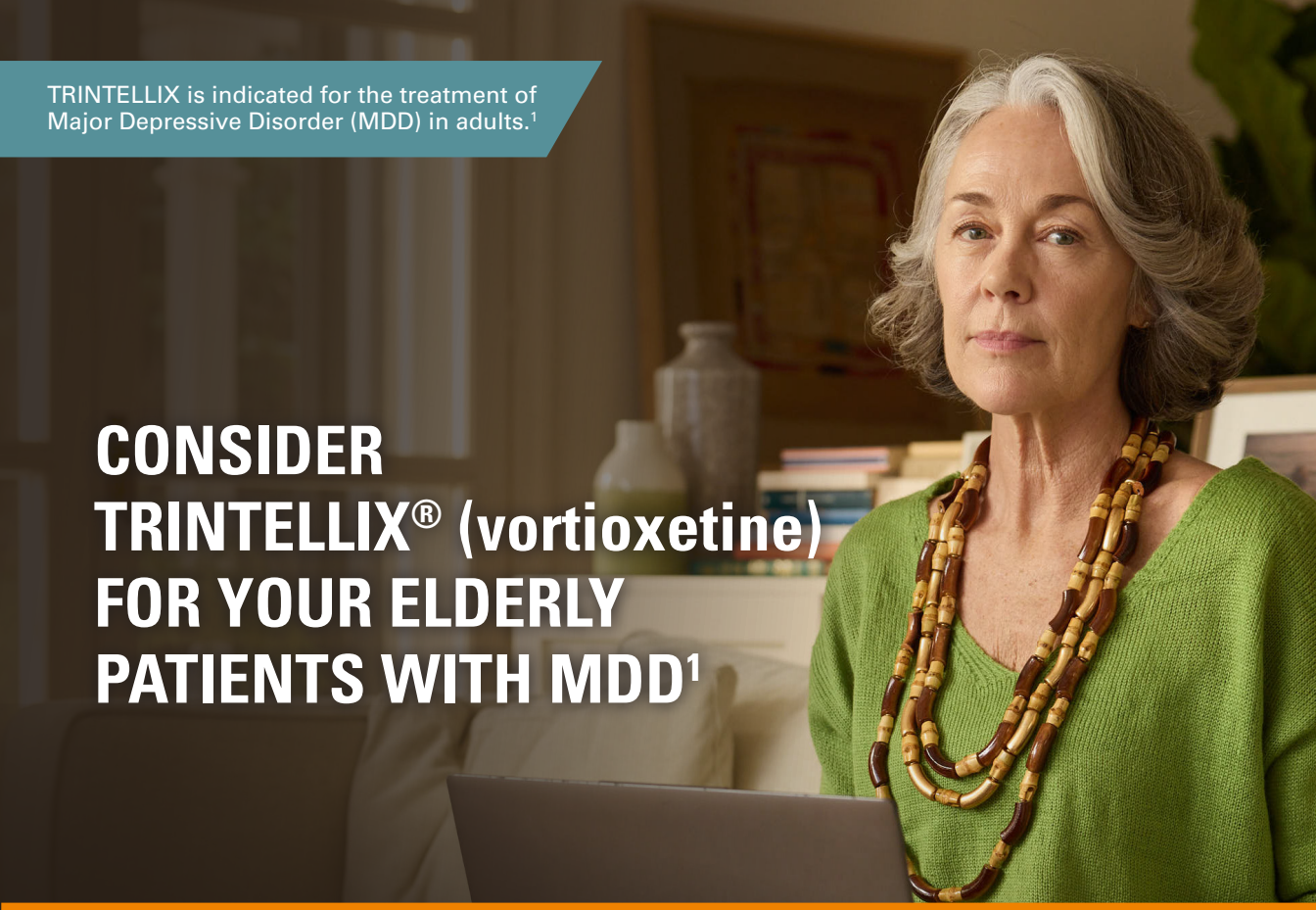
TRINTELLIX is indicated for the treatment of Major Depressive Disorder (MDD) in adults.[1]



CONSIDER TRINTELLIX® (vortioxetine) FOR YOUR ELDERLY PATIENTS WITH MDD[1]

TRINTELLIX RELIEVED THE OVERALL SYMPTOMS OF MDD[1]
Based on MADRS or HAM- D_{24} total scores vs placebo, as shown in six 6- to 8-week studies (5 mg to 20 mg once daily) in MDD, including one in patients aged 64-88.
Two additional studies of the 5-mg dose in the US failed to show effectiveness.

The most common adverse reactions (incidence ≥5% and at least twice the rate of placebo in 6- to 8-week studies) were nausea, constipation, and vomiting.[1]

HAM-D_{24}, Hamilton Depression 24-item Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale.

IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS & BEHAVIORS

- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies.**
- **Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.**
- **TRINTELLIX is not approved for use in pediatric patients.**

Please see additional Important Safety Information throughout this brochure, and click for Full Prescribing Information.

Trintellix
vortioxetine
5mg•10mg•20mg tablets

MEET BETTY, 65

Married | Retired teacher | Has comorbidities

- Diagnosed with MDD prior to age 60 and is currently experiencing a major depressive episode
- Children and grandchildren have noticed she is struggling with the overall symptoms of MDD
- Is stable on an antihypertension treatment
- Concerned about side effects but is seeking comprehensive, monotherapy relief for her MDD

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- **Hypersensitivity:** Hypersensitivity to vortioxetine or any component of the TRINTELLIX formulation. Hypersensitivity reactions including anaphylaxis, angioedema, and urticaria have been reported in patients treated with TRINTELLIX.
- **Monoamine Oxidase Inhibitors (MAOIs):** Do not use MAOIs intended to treat psychiatric disorders with TRINTELLIX or within 21 days of stopping treatment with TRINTELLIX, due to an increased risk of serotonin syndrome. Do not use TRINTELLIX within 14 days of stopping an MAOI intended to treat psychiatric disorders.
- **Linezolid and Methylene Blue:** Do not start TRINTELLIX in a patient being treated with MAOIs such as linezolid or intravenous methylene blue, due to an increased risk of serotonin syndrome.

WARNINGS AND PRECAUTIONS

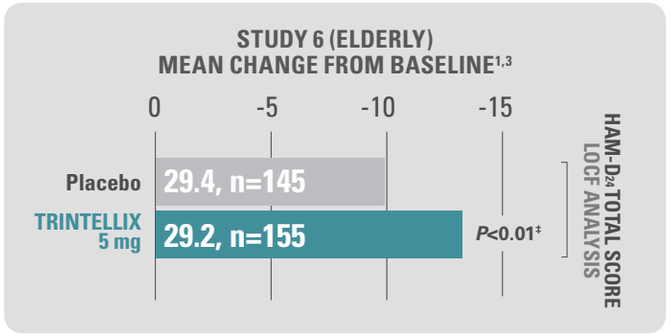
- **Suicidal Thoughts and Behaviors in Adolescents and Young Adults:** Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing TRINTELLIX, in patients whose depression is persistently worse, or who are experiencing emergence of suicidal thoughts and behaviors. In pooled analyses of placebo-controlled trials of antidepressants, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients ages 24 and younger was greater than in placebo-treated patients.

It was estimated that ≥70% of patients aged 65 and up underreported major depressive episodes[2*]

TRINTELLIX IMPROVED OVERALL MDD SYMPTOMS IN ELDERLY PATIENTS[1]

One short-term study[1,3]:

- Was a randomized, double-blind, placebo-controlled, fixed-dose study of TRINTELLIX 5 mg once daily
- Lasted 8 weeks and included patients aged 64-88[†]
- Showed significant improvement in HAM-D_{24} total score vs placebo



Hyponatremia has occurred as a result of treatment with serotonergic drugs, including TRINTELLIX. Elderly patients may be at greater risk of developing hyponatremia with a serotonergic antidepressant.[1]

Please see Warning and Precaution for Hyponatremia listed in the Important Safety Information on the last page.

*Data from a simulation model based on the 2005-2017 National Surveys on Drug Use and Health data.[2]

[†]Patients meeting diagnostic criteria for recurrent MDD with at least 1 previous major depressive episode before age 60 without any comorbid cognitive impairment.[1]

[‡]Doses significantly superior to placebo after adjusting for multiplicity.[1]

LOCF, last observation carried forward.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Serotonin Syndrome:** Serotonergic antidepressants, including TRINTELLIX, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, meperidine, methadone, buspirone, amphetamines, and St. John's Wort) and with drugs that impair metabolism of serotonin, i.e., MAOIs. Serotonin syndrome signs and symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Monitor all patients taking TRINTELLIX for the emergence of serotonin syndrome. Discontinue treatment with TRINTELLIX and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of TRINTELLIX with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

Please see additional Important Safety Information, including Boxed WARNING regarding Suicidal Thoughts and Behaviors, throughout this brochure, and click for Full Prescribing Information.

Trintellix
vortioxetine
5mg•10mg•20mg tablets

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Increased Risk of Bleeding:** The use of drugs that interfere with serotonin reuptake inhibition, including TRINTELLIX, may increase the risk of bleeding events, including but not limited to gastrointestinal. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, and other anticoagulants may add to this risk. Inform patients about the increased risk of bleeding when TRINTELLIX is coadministered with NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. Exposure to SSRIs or SNRIs, particularly in the month before delivery, has been associated with a less than 2-fold increase in the risk of postpartum hemorrhage.
- **Activation of Mania/Hypomania:** In patients with bipolar disorder, treating a depressive episode with TRINTELLIX or another antidepressant may precipitate a mixed/manic episode. Prior to initiating treatment with TRINTELLIX, screen patients for any personal or family history of bipolar disorder, mania, or hypomania.
- **Discontinuation Syndrome:** Adverse reactions have been reported upon abrupt discontinuation of treatment with TRINTELLIX at doses of 15 mg/day and 20 mg/day. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible.
- **Angle-Closure Glaucoma:** The pupillary dilation that occurs following use of many antidepressant drugs, including TRINTELLIX, may trigger an angle-closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.
- **Hyponatremia:** Hyponatremia has occurred as a result of treatment with serotonergic drugs, including TRINTELLIX, and in many cases appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Elderly patients and patients taking diuretics or who are otherwise volume-depleted can be at greater risk. Symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. More severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. Discontinue TRINTELLIX in patients with symptomatic hyponatremia and institute appropriate medical intervention.

WARNINGS AND PRECAUTIONS (cont'd)

- **Sexual Dysfunction:** Use of serotonergic antidepressants, including TRINTELLIX, may cause symptoms of sexual dysfunction. In male patients, serotonergic antidepressant use may result in ejaculatory delay or failure, decreased libido, and erectile dysfunction. In female patients, use may result in decreased libido and delayed or absent orgasm.

ADVERSE REACTIONS

The most commonly observed adverse reactions for TRINTELLIX in 6- to 8-week placebo-controlled studies (incidence ≥5% and at least twice the rate of placebo) were: nausea, constipation, and vomiting.

DRUG INTERACTIONS

Concomitant administration of TRINTELLIX and strong CYP2D6 inhibitors or strong CYP inducers may require a dose adjustment of TRINTELLIX.

PREGNANCY

Exposure to serotonergic antidepressants, including TRINTELLIX, in late pregnancy may increase the risk for neonatal complications requiring prolonged hospitalization, respiratory support, and tube feeding, and/or persistent pulmonary hypertension of the newborn (PPHN). Monitor neonates who were exposed to TRINTELLIX in the third trimester for PPHN and drug discontinuation syndrome. Use of TRINTELLIX in the month before delivery may be associated with an increased risk of postpartum hemorrhage.

Please see additional Important Safety Information, including Boxed WARNING regarding Suicidal Thoughts and Behaviors, throughout this brochure, and click for Full Prescribing Information.

References: 1. TRINTELLIX (vortioxetine) prescribing information. Takeda Pharmaceuticals. **2.** Tam J, Mezuk B, Zivin K, Meza R. *Am J Prev Med*. 2020;59(2):e39-e47. **3.** Katona C, Hansen T, Olsen CK. *Int Clin Psychopharmacol*. 2012;27(4):215-223.

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Takeda

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