INDICATION

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

Healthcare Provider Frequently Asked Questions

Information Regarding the Expiration of the FDA-Granted Market Exclusivity for TRINTELLIX® (vortioxetine)

The following is intended to inform healthcare providers, who may treat appropriate adult patients with TRINTELLIX, about the expiration of the FDA-granted market exclusivity for the product, and associated Takeda support programs.

1. What is Loss of Exclusivity (LOE)?
LOE is part of the medication lifecycle, and generic versions of a medication can become available when a medicine's patent exclusivity and/or FDA-granted regulatory exclusivity period ends. Patent terms and periods of regulatory exclusivity for all pharmaceutical medicines end after a period of time. These periods were established and are intended to promote a balance between medical innovation and the development of generic versions of brand-name therapies.

The entry of generic vortioxetine medicines is expected to provide multiple lower-cost vortioxetine treatment options for adults living with MDD.

2. When will the generic versions of TRINTELLIX enter the market?
Once the TRINTELLIX exclusivity period ends on December 17, 2026, generic versions of TRINTELLIX may become available shortly thereafter.

Takeda does not plan to manufacture a generic version of TRINTELLIX. Please refer to the FDA website for more information regarding availability of generic versions of brand-name medicines.

3. What does LOE mean for patients taking TRINTELLIX? Will patients' insurance still cover prescriptions for TRINTELLIX?
Insurance companies may continue to cover brand-name TRINTELLIX after generic vortioxetine options become available, but coverage will likely vary by insurance carrier or type. Formulary tiers or requirements, coverage levels, and costs will be specific to the patient's healthcare insurer. Patients should check with their healthcare insurer to confirm prescription coverage for TRINTELLIX.

If you determine that branded TRINTELLIX is appropriate for your adult patients, you should specify "dispense as written" (or similar language) on the brand-name prescription, in accordance with local and state requirements and regulations. Government requirements and regulations can vary by state and territory, and healthcare providers should consult their state or territory's Board of Pharmacy to verify prescribing requirements.

4. Will Takeda continue to offer the Savings Card program for TRINTELLIX?
The TRINTELLIX Savings Card program will end on **December 31, 2026**. This will be the final day eligible patients may enroll and/or redeem the Savings Card at the pharmacy.

Eligible, commercially insured patients with questions about the Savings Card program should visit **us.trintellix.com** or call **1-866-279-0287**.

5. Why is Takeda discontinuing the TRINTELLIX Savings Card program when market exclusivity ends?
At the time of TRINTELLIX LOE, several generic versions of vortioxetine are anticipated to receive FDA approval. These generic entries may create additional prescription options with lower retail pharmacy costs for appropriate adult patients with MDD. Some states, such as California and Massachusetts, generally do not allow manufacturer copay assistance programs to continue following the entry of a generic version of the brand-name medicine.

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, and click for Full Prescribing Information.

6. Will Takeda continue to offer TRINTELLIX product samples?
As part of our continued support for TRINTELLIX prescribers, healthcare providers can order product samples through MySampleCloset at **takeda.mysamplecloset.com/login** until **December 17, 2026.**

7. What is happening with the Takeda Help At Hand program for TRINTELLIX?
The Takeda Help At Hand program will accept new enrollees for TRINTELLIX until **March 31, 2027,** and the program will end on **December 31, 2028.** Takeda will continue/continued the Help At Hand program for TRINTELLIX one full calendar year beyond LOE to allow time for patients to work with their healthcare providers to determine an appropriate course of care for their individual needs, while maintaining access to TRINTELLIX during that time.

Enrolled Help At Hand healthcare providers will be/were notified in February 2027 of the application end date and the program end date for TRINTELLIX.

Patients and healthcare providers with questions about the Help At Hand program should visit **www.helpathandpap.com** or call **1-800-830-9159.**

8. Will Takeda be proactively communicating with healthcare professionals and patients about relevant assistance programs and important dates?
Yes. Takeda is proactively communicating/has proactively communicated with healthcare providers, patients, and patient advocacy organizations about the LOE for brand-name TRINTELLIX, including potential implications for insurance coverage and access. Our communications include/included notifications about the end date of the TRINTELLIX Savings Card program and the direct-to-patient self-pay program, as well as the end date for the Takeda Help At Hand program for TRINTELLIX.

9. Who can patients contact if they have questions about TRINTELLIX patient support programs?
Patients can/could visit **us.trintellix.com** for information about the TRINTELLIX Savings Card program and the direct-to-patient self-pay program. For the Takeda Help At Hand program, TRINTELLIX patients should visit **www.helpathandpap.com** for program eligibility and timelines.

10. What if patients cannot afford generic options?
Patients who cannot afford generics should work with their prescribing healthcare provider, pharmacist, and insurer to determine the most affordable course of care that meets their needs. The Takeda Help At Hand program will accept/accepted applications for TRINTELLIX until March 31, 2027, and the program will end/ended on December 31, 2027 for TRINTELLIX. For more information about the program and eligibility requirements, please visit **www.helpathandpap.com**. For information about Takeda's other patient support programs for TRINTELLIX, patients should visit **www.trintellix.com**.

11. Will Takeda stop manufacturing TRINTELLIX?
No. We currently do not have any plans to stop manufacturing brand-name TRINTELLIX. We remain committed to making TRINTELLIX commercially available for adults living with MDD.

12. Are there any changes to brand-name TRINTELLIX following loss of exclusivity?
No. Brand-name TRINTELLIX will remain/remains the same. The LOE does not change how TRINTELLIX is made, its efficacy and safety profile, or how it should be taken.

Patients should always follow their healthcare provider's guidance when taking TRINTELLIX or considering treatment changes.

If you have any other questions, please call 1-877-TAKEDA-7 (1-877-825-3327).

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 (vortioxetine) 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.

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

IMPORTANT SAFETY INFORMATION (cont'd)

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.
- **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.
- **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.
- **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 (vortioxetine) and strong CYP2D6 inhibitors or strong CYP inducers may require a dose adjustment of TRINTELLIX.

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IMPORTANT SAFETY INFORMATION (cont'd)

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 throughout, including Boxed WARNING regarding Suicidal Thoughts and Behaviors, and click for Full Prescribing Information.

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