Clinical Policy: Vortioxetine (Trintellix)

Reference Number: CP.PMN.65
Effective Date: 05.01.15
Last Review Date: 08.24
Line of Business: HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Vortioxetine (Trintellix®) is an antidepressant.

FDA Approved Indication(s)

Trintellix is indicated for the treatment of major depressive disorder.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Trintellix is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Major Depressive Disorder (must meet all)**:**

1. Diagnosis of major depressive disorder;
2. Age ≥ 18 years;
3. Member meets one of the following (a, b, or c):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Request is for Fidelis Ambetter (New York Exchange): Failure of ONE of the following, tried for ≥ 4 weeks at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), bupropion, mirtazapine, vilazodone (generic Viibryd®);
   c. Failure of TWO of the following, each tried for ≥ 4 weeks at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: SSRI, SNRI, bupropion, mirtazapine, vilazodone (generic Viibryd®);
4. Dose does not exceed both of the following (a and b):
   a. 20 mg per day;
   b. 1 tablet per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Major Depressive Disorder (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Trintellix for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 20 mg per day;
   b. 1 tablet per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor
SNRI: serotonin norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bupropion (Wellbutrin® XL)	150-450 mg PO QAM	450 mg/day
bupropion (Wellbutrin SR)	150 mg PO QAM or 150-200 mg PO BID	400 mg/day
mirtazapine (Remeron®)	15-45 mg PO QHS	45 mg/day
vilazodone (Viibryd®)	10 mg PO QD for 7 days, followed by 20 mg PO QD	40 mg/day
SSRIs		
citalopram (Celexa®)	20 mg PO QD	40 mg/day (≤ 60 years) 20 mg/day (> 60 years)
escitalopram (Lexapro®)	10-20 mg PO QD	20 mg/day
fluvoxamine*	50-300 mg PO QD	300 mg/day
fluoxetine (Prozac®)	20 mg PO QD	80 mg/day
paroxetine (Paxil®)	20 mg PO QD	50 mg/day
paroxetine controlled release (Paxil CR®)	25 mg PO QD	62.5 mg/day
sertraline (Zoloft®)	50 mg PO QD	200 mg/day
SNRIs		
desvenlafaxine (Pristiq®)	50 mg PO QD	400 mg/day
duloxetine (Cymbalta®)	20 mg PO BID, 30 mg BID, or 60 mg PO QD	120 mg/day
venlafaxine (Effexor® XR)	75 mg PO BID to TID	225 mg/day
Fetzima® (levomilnacipran)	40-120 mg PO QD	120 mg/day

**Off-label*

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications

- Contraindication(s): Hypersensitivity to vortioxetine or any components of the vortioxetine formulation. The use of MAOIs intended to treat psychiatric disorders within 21 days of stopping treatment with vortioxetine due to increased risk of serotonin syndrome. Use of Trintellix within 14 days of stopping an MAOI. Do not start vortioxetine in a patient who is being treated with linezolid or intravenous methylene blue.
- Boxed warning(s): increased risk of suicidal thinking and behavior in pediatric and young adult patients taking antidepressants. Closely monitor for worsening and emergence of suicidal thoughts and behaviors. Vortioxetine is not approved for use in pediatric patients.

Appendix D: States with Limitations against Redirections in Certain Mental Health Settings

State	Step Therapy Prohibited?	Notes
TX	No	**Applies to HIM requests only** Failure of ONE of the following, used for ≥ 4 weeks at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: SSRI, SNRI, bupropion, mirtazapine, vilazodone (generic Viibryd®)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Major depressive disorder	10 mg orally daily then increased to 20 mg/day as tolerated	20 mg/day

VI. Product Availability

Tablet: 5 mg, 10 mg, 20 mg

VII. References

1. Trintellix Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; August 2023. Available at: http://www.trintellix.com. Accessed May 9, 2024.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. Updated periodically. Accessed May 9, 2024.
3. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. Arlington, VA: American Psychiatric Association; May 2010. Available online at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed May 9, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2020 annual review: no significant changes; added contraindications and boxed warnings; references reviewed and updated.	05.06.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: shortened the trial durations of alternative agents from 8 weeks to 4 weeks; added bupropion and mirtazapine as additional options for trial; combined trial requirements by providing an option to try any two among SSRI, SNRI, bupropion, and mirtazapine; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	05.27.21	08.21
3Q 2022 annual review: no significant changes; reformatted and updated table in Appendix B; references reviewed and updated.	03.22.22	08.22
Per August SDC and prior clinical guidance, added vilazodone (generic Viibryd) to list of redirect options. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22
3Q 2023 annual review: no significant changes; added redirection bypass for members in a State with limitations on step therapy in certain mental health settings along with Appendix D, which includes Texas with requirements for single drug redirection for HIM requests; references reviewed and updated.	04.18.23	08.23
Per SDC, revised to allow single step redirection for Fidelis Ambetter (New York Exchange).	01.18.24	
3Q 2024 annual review: revised continued therapy to allow continuity of care for antidepressants; in Appendix B, added Wellbutrin SR to therapeutic alternatives and clarified that fluvoxamine used in depression is off-label; references reviewed and updated.	05.29.24	08.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.