Clinical Policy: Vortioxetine (Trintellix)

Reference Number: CP.PMN.65
Effective Date: 05.01.15
Last Review Date: 08.21
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. Depression (must meet all)**:**

1. Diagnosis of major depressive disorder;
2. Age ≥ 18 years;
3. 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;
4. Dose does not exceed 20 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Depression (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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
SSRI: selective serotonin reuptake inhibitor
SNRI: serotonin norepinephrine 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 to 450 mg PO QAM	450 mg/day
mirtazapine (Remeron®)	15 to 45 mg PO QHS	45 mg/day
SSRIs		
citalopram (Celexa®)	20 mg PO QD; may increase to 40 mg PO QD after one week	40 mg/day (≤ 60 years) 20 mg/day (> 60 years)
escitalopram (Lexapro®)	10 mg PO QD; may increase to 20 mg PO QD after 1 week	20 mg/day
fluoxetine (Prozac®, Prozac Weekly®)	Prozac: 20 mg PO QD; may increase by 10-20 mg after several weeks Prozac Weekly: 90 mg PO q week beginning 7 days after the last daily dose	Prozac: 80 mg/day Prozac Weekly: 90 mg/week
paroxetine (Paxil®, Paxil CR®, Pexeva®)	Paxil, Pexeva: 20 mg PO QD; may increase by 10 mg every week as needed	Paxil, Pexeva: 50 mg/day Paxil CR: 62.5 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Paxil CR: 25 mg PO QD; may increase by 12.5 mg every week as needed	
sertraline (Zoloft®)	50 mg PO QD; may increase every week as needed	200 mg/day
SNRI		
duloxetine (Cymbalta®)	20 mg PO BID or 30 mg PO BID or 60 mg PO QD	120 mg/day
venlafaxine (Effexor®, Effexor XR®)	Effexor: 75 mg/day PO in 2-3 divided doses; may increase by 75 mg every 4 days as needed Effexor XR: 75 mg PO QD; may increase by 75 mg every 4 days as needed	Effexor: 225 mg/day (outpatient) or 375 mg/day (inpatient) Effexor XR: 225 mg/day
desvenlafaxine (Pristiq®, Khedezla®)	50 mg PO QD	400 mg/day
Fetzima® (levomilnacipran)	20 mg PO QD for 2 days, then 40 mg PO QD; may increase by 40 mg every 2 days	120 mg/day

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 cortioxetine 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.

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

Immediate release tablet: 5 mg, 10 mg, 20 mg

VII. References

1. Trintellix Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; January 2021. Available at http://www.trintellix.com. Accessed May 3, 2021.

2. Monograph for Trintellix. Clinical Pharmacology. http://www.clinicalpharmacology-ip.com. Accessed May 3, 2021.
3. American Psychiatric Association: Practice guideline for the treatment of patients with major depressive disorder, third edition, 2010. Available at http://psychiatryonline.org/guidelines.aspx. Accessed May 3, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Removed age requirement, age is not an absolute contraindication. Added max dose and updated references	03.17	08.17
3Q 2018 annual review: combined HIM (HIM.PA.136) and Medicaid; no significant changes added age to Medicaid; references reviewed and updated.	04.11.18	08.18
3Q 2019 annual review: no significant changes; added contraindications and boxed warnings; references reviewed and updated.	06.03.19	08.19
3Q 2020 annual review: no significant changes; added contraindications and boxed warnings; references reviewed and updated.	05.06.20	08.20
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

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.

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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.