Clinical Policy: Polyserotonergic Antidepressants- Vortioxetine (Trintellix) or Vilazodone (Viibryd)

Reference Number: AZ.CP.PMN.20
Effective Date: 06.17
Last Review Date: 07.21
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st) Revision Log

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

Description
Vortioxetine (Trintellix®) and Vilazodone (Viibryd®) are antidepressants that enhance serotoninergic activity via multiple mechanisms

FDA approved indications
Trintellix and Viibryd are 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 Arizona Complete Health-Complete Care Plan and Care1st that Trintellix and Viibryd are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of major depressive disorder (MDD);
2. For Trintellix- age ≥ 18 years and for Viibryd- age ≥ 12 years;
3. Failure of a ≥ 4 week trial of one SSRI at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a ≥ 4 week trial of one SNRI at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of one SSRI or SNRI used adjunctively with one of the following: bupropion, mirtazapine, or tricyclic antidepressant (TCA) unless contraindicated
6. Dose of Trintellix does not exceed 20 mg/day (1 tablet/day) or dose of Viibryd does not exceed 40 mg/day (1 tablet/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): AZ.CP.PMN.53 for Arizona 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. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose of Trintellix does not exceed 20 mg/day (1 tablet/day) or dose of Viibryd does not exceed 40 mg/day (1 tablet/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): AZ.CP.PMN.53 for Arizona 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 – AZ.CP.PMN.53 for Arizona Medicaid.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 CR: 25 mg PO QD; may increase by 12.5 mg every week as needed	Paxil, Pexeva: 50 mg/day Paxil CR: 62.5 mg/day
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/Boxed Warnings

- 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.
- Contraindication(s): Concomitant use of monoamine oxidase inhibitors (MAOIs), or use within 14 days of stopping MAOIs because of an increased risk of serotonin syndrome.

- Boxed warning(s): increased risk of suicidal thoughts and behavior in children, adolescents, and young adults under age 24. Closely monitor for worsening and mergence of suicidal thoughts and behaviors. Vortioxetine has not been evaluated for use in pediatric patients.

Appendix D: General Information

- Vortioxetine and Vilazodone are pharmacologically distinct from other antidepressants.
- Vortioxetine inhibits serotonin reuptake, antagonizes serotonin 5-HT3 receptors, and is an agonist for 5-HT1A receptors. The clinical benefit of this mechanism of action is unknown.
- Vilazodone is a selective serotonin reuptake inhibitor and 5-hydroxytryptamine partial agonist.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Voritioxetine (Trintellix)	Major depressive disorder	10 mg daily then increased to 20 mg/day as tolerated	20 mg/day
Vilazodone (Viibryd)	Major depressive disorder	10 mg/day for 7 days, then 20 mg/day with food for 7 days. The dose may be increased up to 40 mg once daily with food after minimum of 7 days between dosage increases. Target dose is 20-40 mg/day with food.	40 mg/day

VI. Product Availability

Drug Name	Availability
Voritioxetine (Trintellix)	Tablets: 5 mg, 10 mg, and 20 mg
Vilazodone (Viibryd)	Tablets: 10 mg, 20 mg, and 40 mg Starter Kit: 10mg-20mg

VII. References

1. Trintellix Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; January 2021. Available at http://www.trintellix.com. Accessed July 15, 2021.
2. Viibryd Prescribing Information. Madison, NJ: Allergan USA, INC.; Revised 1/2020. Available at https://www.allergan.com/assets/pdf/viibryd_pi. Accessed July 15, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL Elsevier: Gold Standard, Inc.; 2020. Available http://www.clinicalpharmacology-ip.com/ Accessed July 15, 2021.
4. Stahl, Stephen. Stahl's Essential Psychopharmacology Prescriber's Guide Fifth Edition Cambridge University Press Published 2014

5. 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 July 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Reformat into new template; References updated	03.18	04.18
Reviewed and updated for AZ.	09.18	07.18
Renamed policy Polyserotonergic Antidepressants and added vilazodone (Viibryd) information. Updated logo.	07.19	07.19
Annual review: references reviewed and updated. Added contraindications and boxed warnings.	07.20	07.20
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21
Annual review. Changed trial s of SSRI and SNRI from ≥ 8 weeks to ≥ 4 weeks. Boxed warnings updated. References reviewed and updated.	07.15.21	07.21

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.

CLINICAL POLICY
Polyserotonergenic Antidepressants

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.

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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.