Clinical Policy: Clozapine Orally Disintegrating Tablet

Reference Number: CP.PMN.12
Effective Date: 09.01.15
Last Review Date: 02.22
Line of Business: Medicaid

RevisionLog

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

Description

Clozapine orally disintegrating tablet (ODT) is an atypical antipsychotic.

FDA Approved Indication(s)

Clozapine ODT is indicated for:

- Treatment-resistant schizophrenia
- Reducing suicidal behavior in patients with schizophrenia or schizoaffective 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 clozapine ODT is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia or Schizoaffective Disorder (must meet all)**:**

1. Diagnosis of schizophrenia or schizoaffective disorder;
2. Age ≥ 18 years;
3. Failure of a ≥ 4 week trial of risperidone ODT or oral solution at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Member must use regular (non-orally disintegrating) clozapine tablets, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 900 mg 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: 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: 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: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or documentation supports that member is currently receiving clozapine ODT for schizophrenia or schizoaffective disorder 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 900 mg 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: 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: 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: 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 policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
ODT: orally disintegrating tablet

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
risperidone ODT (Risperdal®)	2 mg to 16 mg PO QD to BID	16 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): Known serious hypersensitivity to clozapine or any other component of clozapine ODT
- Boxed warning(s):
  - Severe neutropenia: Clozapine can cause severe neutropenia, which can lead to serious and fatal infections. Patients initiating and continuing treatment with clozapine ODT must have a baseline blood absolute neutrophil count measured before treatment initiation and regular absolute neutrophil count monitoring during treatment.
  - Clozapine ODT is available only through a restricted program called the Clozapine REMS.
  - Orthostatic hypotension, bradycardia, and syncope: Risk is dose related. Starting dose is 12.5 mg. Titrate gradually and use divided dosages.
  - Seizure: Risk is dose-related. Titrate gradually and use divided doses. Use with caution in patients with history of seizure or risk factors for seizure.
  - Myocarditis and cardiomyopathy: Can be fatal. Discontinue and obtain cardiac evaluation if findings suggest these cardiac reactions.
  - Increased mortality in elderly patients with dementia-related psychosis: clozapine ODT is not approved for this condition.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia/ schizoaffective disorder	12.5 mg PO QD or BID. Titrate the total daily dosage in increments of 25 mg to 50 mg per day, to a target dose of 300 mg to 450 mg per day, in divided doses, by the end of 2 weeks.	900 mg/day

VI. Product Availability

Orally disintegrating tablets: 12.5 mg, 25 mg, 100 mg, 150 mg, 200 mg

VII. References

1. Clozapine Orally Disintegrating Tablet Prescribing Information. Horsham, PA: Teva Pharmaceuticals, Inc.; February 2017. Available at: www.dailymed.nlm.nih.gov. Accessed November 13, 2021.
2. Fazaclo Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; February 2020. Available at: http://pp.jazzpharma.com/pi/fazaclo.en.USPI.pdf. Accessed November 30, 2020.
3. Clozapine REMS Web site. https://www.clozapinerems.com/. Accessed November 13, 2021.
4. Lehman AF, Lieberman JA, Dixon LB et al. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry. 2004 Feb;161(2 Suppl):1-56.
5. American Psychiatric Association: Guideline Watch (September 2009): Practice Guideline for the Treatment of Patients with Schizophrenia, 2009. http://psychiatryonline.org/guidelines. Accessed November 30, 2019.

6. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: No significant changes; References reviewed and updated.	11.02.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.30.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.29.20	02.21
1Q 2022 annual review: no significant changes; replaced any references to the Fazaclo brand name product with the generic clozapine ODT name, since Fazaclo is no longer manufactured; changed "Medical justification" to "Member must use" language; references reviewed and updated.	11.13.21	02.22
Template changes applied to other diagnoses/indications.	09.20.22	

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.