Clinical Policy: Olanzapine Orally Disintegrating Tablet (Zyprexa Zydis)

Reference Number: CP.PMN.29
Effective Date: 09.01.15
Last Review Date: 08.23
Line of Business: Medicaid

Revision Log

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

Description

Olanzapine orally disintegrating tablet (Zyprexa Zydis®) is an atypical antipsychotic.

FDA Approved Indication(s)

Zyprexa Zydis is indicated for the treatment of:

- Schizophrenia in adults and adolescents (ages 13-17)
- Acute manic or mixed episodes associated with bipolar I disorder and maintenance of bipolar I disorder in adults and adolescents (ages 13-17)
- Manic or mixed episodes associated with bipolar I disorder in adults as an adjunct to valproate or lithium
- Depressive episodes associated with bipolar I disorder in adults and children/adolescents (ages 10-17) in combination with fluoxetine
- Treatment-resistant depression in adults in combination with fluoxetine

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 Zyprexa Zydis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of schizophrenia;
2. Age ≥ 13 years;
3. Member meets one of the following (a or b):
   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. Failure of a ≥ 4-week trial of risperidone orally disintegrating tablet or oral solution at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Member meets one of the following (a or b):
   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. Member must use regular (non-orally disintegrating) olanzapine tablets, unless contraindicated or clinically significant adverse effects are experienced;
5. 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. Bipolar Disorder (must meet all)**:**
1. Diagnosis of bipolar disorder;
2. Age ≥ 10 years;
3. Member must use regular (non-orally disintegrating) olanzapine tablets, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 20 mg (1 tablet) per day.

Approval duration: 12 months

C. Treatment-Resistant Depression (must meet all)**:**
1. Diagnosis of treatment-resistant depression;
2. Age ≥ 18 years;
3. Member must use regular (non-orally disintegrating) olanzapine tablets, unless contraindicated or clinically significant adverse effects are experienced;
4. Zyprexa Zydis is prescribed concurrently with fluoxetine;
5. Dose does not exceed both of the following (a and b):
   a. 15 mg per day;
   b. 1 tablet per day.

Approval duration: 12 months

D. 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 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 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. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit;
   b. Documentation supports that member is currently receiving Zyprexa Zydis for bipolar disorder or schizophrenia and has received this medication for at least 30 days;
   c. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);
2. Member is responding positively to therapy;

3. If request is for a dose increase, new dose does not exceed any of the following (a or b):
   a. Schizophrenia, bipolar disorder (i and ii):
      i. 20 mg per day;
      ii. 1 tablet per day;
   b. Treatment-resistant depression (i and ii):
      i. 15 mg per day;
      ii. 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 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 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 for Medicaid or evidence of coverage documents;

B. Dementia-related psychosis.

IV. Appendices/General Information

Appendix A: Abbreviation Key

FDA: Food and Drug Administration
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
risperidone orally disintegrating tablet (Risperdal®)	2 mg to 16 mg PO QD or BID	Adults: 16 mg/day Adolescents: 6 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):
  - None with Zyprexa monotherapy
  - When using Zyprexa and fluoxetine in combination, refer to the contraindications section of the package insert for Symbyax®: concomitant use with monoamine oxidase inhibitors (MAOIs), pimodzide, or thioridazine.
  - When using Zyprexa in combination with lithium or valproate, refer to the contraindications section of the package inserts for those products
- Boxed warning(s):
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Zyprexa is not approved for the treatment of patients with dementia-related psychosis.
  - When using Zyprexa and fluoxetine in combination, also refer to the boxed warning section of the package insert for Symbyax: increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. The combination of Zyprexa and fluoxetine is not approved for use in children less than 10 years of age. Monitor for worsening and emergence of suicidal thoughts and behaviors.

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

State	Step Therapy Prohibited?	Notes
NV	No	**Applies to Medicaid requests only** Schizophrenia: Failure of ONE of the following, unless all are contraindicated or clinically significant adverse effects are experienced: risperidone ODT, risperidone oral solution, regular (non-orally disintegrating) clozapine tablets.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	*Adults* Initial: 5-10 mg PO once daily Target: 10 mg/day within several days *Adolescents* Initial: 2.5-5 mg PO once daily Target: 10 mg/day	20 mg/day
Bipolar I disorder	Manic or mixed episodes *Adults* Monotherapy: 10-15 mg PO once daily Adjunct: 10 mg PO once daily *Adolescents* Initial: 2.5-5 mg PO once daily Target: 10 mg/day Depressive episodes *Adults*	Manic or mixed episodes 20 mg/day Depressive episodes *Adults*: 15 mg/day*

Indication	Dosing Regimen	Maximum Dose
	5 mg Zyprexa Zydis with 20 mg fluoxetine PO once daily *Children and adolescents* 2.5 mg Zyprexa Zydis with 20 mg fluoxetine PO once daily	*Children and adolescents*: 10 mg/day*
Treatment-resistant depression	*Adults* 5 mg Zyprexa Zydis with 20 mg fluoxetine PO once daily	15 mg/day*

**Actual maximum dose is 18 mg/day for adults and 12 mg/day for children and adolescents; dose provided in table reflects maximum dose of Zyprexa Zydis per available dosage forms*

VI. Product Availability

Orally disintegrating tablets: 5 mg, 10 mg, 15 mg, 20 mg

VII. References

1. Zyprexa Zydis Prescribing Information. Indianapolis, IN: Lilly USA, LLC; November 2022. Available at: www.dailymed.nlm.nih.gov. Accessed April 21, 2023.
2. Symbyax Prescribing Information. Indianapolis, INL Lilly USA, LLC: September 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021520s054lbl.pdf. Accessed May 8, 2023.
3. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. Practice guideline for the treatment of patients with bipolar disorder, second edition. Arlington, VA: American Psychiatric Association; April 2002. Available online at http://www.psychiatryonline.org/guidelines. Accessed May 8, 2023
4. Washburn JJ, West AE, and Heil JA. Treatment of pediatric bipolar disorder: a review. Minerva Psichiatr. 2011 March;52(1):21-35.
5. Patino LR, Bruns KM, Witt NM, et al. Management of bipolar disorder in children and adolescents. Focus 2015;13(1): 25-36.
6. 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 http://www.psychiatryonline.org/guidelines. Accessed May 8, 2023.
7. Qaseeem A, Owens DK, Etxeandia-Ikobaltzeta I, et al. Nonpharmacological and pharmacologic treatments of adults in the acute phase of major depressive disorder: A living clinical guideline from the American College of Physicians. Annals of Internal Medicine. February 2023; 172(2):239-253.
8. 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
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.30.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; converted "Medical justification" to "Member must use" language; re-named the Major Depressive Disorder subsection title and required diagnosis to Treatment-Resistant Depression, and added a requirement that Zyprexa Zydis be used in combination with fluoxetine for treatment-resistant depression, to align with the language of the existing FDA-approved indication; references reviewed and updated.	11.13.21	02.22
Template changes applied to other diagnoses/indications.	09.20.22	
1Q 2023 annual review: no significant changes; changed age limit for treatment resistant depression to ≥ 18 years old per PI; template changes applied to continued therapy section; references reviewed and updated.	10.27.22	02.23
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.20.23	08.23
For schizophrenia, added redirection bypass for members in a State with limitations on step therapy in certain mental health settings along with Appendix D, which includes Nevada with requirements for single drug redirection for Medicaid requests.	08.31.23	

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.