Clinical Policy: Olanzapine Long-Acting Injection (Weltruza, Zyprexa Relprevv)

Reference Number: CP.PHAR.292
Effective Date: 12.01.16
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

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

Description

Olanzapine (Weltruza™, Zyprexa Relprevv®) is a long-acting atypical antipsychotic.

FDA Approved Indication(s)

Weltruza and Zyprexa Relprevv are indicated for the treatment of schizophrenia.

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 Weltruza and Zyprexa Relprevv are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of schizophrenia;
2. Prescribed by or in consultation with a psychiatrist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. History of non-adherence to oral antipsychotic therapy (*see Appendix D for examples*) and has established tolerability to oral olanzapine;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
5. Dose does not exceed one of the following (a or b):
   a. Weltruza: 531 mg every month;
   b. Zyprexa Relprevv (i or ii):
      i. 405 mg every 4 weeks;
      ii. 300 mg every 2 weeks.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports one of the following (a or b):
   a. Member is currently receiving Weltruza or Zyprexa Relprevv for schizophrenia and has received this medication for at least 30 days;
   b. Therapy was initiated in an inpatient setting for schizophrenia during a recent (within 60 days) hospital admission;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Weltruza: 531 mg every month;
   b. Zyprexa Relprevv (i or ii):
      i. 405 mg every 4 weeks;
      ii. 300 mg every 2 weeks.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, 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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Dementia-related psychosis;

C. Alzheimer's disease.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
PDSS: post-injection delirium/sedation syndrome
REMS: Risk Evaluation and Mitigation Strategy

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
olanzapine (Zyprexa®)	Schizophrenia 5 to 10 mg PO QD	20 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 reported
- Boxed warning(s):
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
  - Patients are at risk for severe sedation (including coma) or delirium after each injection and must be observed for at least 3 hours in a certified healthcare setting with ready access to emergency response services (*Zyprexa Relprevv only*).

Appendix D: Examples of Oral Antipsychotics – Generic (Brand)

Typical/First Generation Antipsychotics†	Atypical/Second Generation Antipsychotics
Chlorpromazine (Thorazine®) Fluphenazine (Prolixin®) Haloperidol (Haldol®)	Aripiprazole (Abilify®)* Asenapine maleate (Saphris®) Brexpiprazole (Rexulti®)

Typical/First Generation Antipsychotics†	Atypical/Second Generation Antipsychotics
Loxapine (Loxitane®) Perphenazine (Trilafon®) Pimozide (Orap®) Thioridazine (Mellaril®) Thiothixene (Navane®) Trifluoperazine (Stelazine®)	Cariprazine (Vraylar®) Clozapine (Clozaril®) Iloperidone (Fanapt®) Lumateperone (Caplyta®) Lurasidone (Latuda®) Olanzapine (Zyprexa®)* Olanzapine/Fluoxetine (Symbyax®) Paliperidone (Invega®)* Quetiapine (Seroquel®) Risperidone (Risperdal®)* Ziprasidone (Geodon®)

†*Most typical/first generation antipsychotics are available only as generics in the U.S.*
**Long-acting injectable formulation available*

Appendix E: General Information

- Zyprexa Relprevv is available only through a restricted distribution program called Zyprexa Relprevv REMS and requires prescriber, healthcare facility, patient, and pharmacy enrollment. Adverse events with signs and symptoms consistent with olanzapine overdose, in particular, sedation (including coma) and/or delirium, have been reported following injections of Zyprexa Relprevv. The goal of the Zyprexa Relprevv REMS is to mitigate the risk of negative outcomes associated with Zyprexa Relprevv post-injection delirium/sedation syndrome (PDSS).
- Weltruza is administered SC into the abdomen only by a healthcare professional. Unlike Zyprexa Relprevv, Weltruza is not subject to a REMS program, and post-injection observation is not required. No cases of PDSS were reported in premarketing trials with Weltruza; however, the risk of PDSS with Weltruza is currently unknown, and PDSS should be considered in the differential diagnosis if signs or symptoms of olanzapine overdose occur.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Olanzapine (Zyprexa Relprevv)	IM: 150 mg/2 weeks, 300 mg/4 weeks, 210 mg/2 weeks, 405 mg/4 weeks, or 300 mg/2 weeks Zyprexa Relprevv should be administered by a healthcare professional.	405 mg every 4 weeks or 300 mg every 2 weeks
Olanzapine (Weltruza)	SC: 318 mg, 425 mg, or 531 mg once monthly For patients switching from oral olanzapine, administer on the next consecutive day. Neither a loading dose nor supplemental oral olanzapine is required.	531 mg every month

Drug Name	Dosing Regimen	Maximum Dose
	Weltruza should be administered by a healthcare professional.	

VI. Product Availability

Drug Name	Availability
Olanzapine (Zyprexa Relprevv)	Powder for suspension single-dose vials: 210 mg, 300 mg, 405 mg
Olanzapine (Weltruza)	Powder for extended-release injectable suspension in single-dose vials: 318 mg, 425 mg, 531 mg

VII. References

1. Zyprexa Relprevv Prescribing Information. Indianapolis, IN: Lilly USA, LLC; May 2026. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/022173s043lbl022173s040lbl.pdf. Accessed October 14, 2026.
2. Weltruza Prescribing Information. Parsippany, NJ: Teva Neuroscience, Inc.; October 2026. Available at: https://www.weltruza.com/globalassets/weltruza/prescribing-information.pdf. Accessed October 14, 2026.
3. ClinicalTrials.gov. A randomized, double-blind, placebo-controlled study with an open-label, long-term safety phase to evaluate the efficacy and safety of TV-44749 in adults with schizophrenia (SOLARIS). Available at: https://clinicaltrials.gov/study/NCT05693935. Accessed October 14, 2026.
4. Kim B, Lee SH, Yang YK, et al. Review Article: Long-acting injectable antipsychotics for first-episode schizophrenia: The pros and cons. Schizophr Res Treatment. August 14, 2012; 2012: 560836. doi:10.1155/2012/560836
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. Available at: https://www.clinicalkey.com/pharmacology/. Accessed May 22, 2026.
6. Keepers G, Fochtmann L, Anzia J, et al. American Psychiatric Association practice guideline for the treatment of patients with schizophrenia, third edition (2020). Available at: https://psychiatryonline.org/doi/10.1176/appi.books.9780890424841. Accessed May 22, 2026.
7. McDonagh MS, Dana T, Selph S, Devine EB, et al. Treatments for schizophrenia in adults: A systematic review. Comparative Effectiveness Review No. 198. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 17(18)-EHC031-EF. Rockville, MD: Agency for Healthcare Research and Quality; October 2017.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2358	Injection, olanzapine, long-acting, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications.	09.20.22	
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.11.23	08.23
3Q 2024 annual review: added Commercial line of business; no significant changes; references reviewed and updated.	05.09.24	08.24
3Q 2025 annual review: no significant changes; updated policy references to Commercial line of business; references reviewed and updated.	04.11.25	08.25
3Q 2026 annual review: no significant changes; added ICHRA line of business; revised initial approval duration from 6 months to 12 months for this chronic disease; references reviewed and updated.	04.13.26	08.26
RT4: added newly approved dosage form Weltruza to policy.	10.14.26	

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.

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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.

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