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

Reference Number: IL.PHAR.292
Effective Date: 12/16
Last Review Date: 9.8.21

Coding Implications
Revision Log

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

Description
Olanzapine (Zyprexa Relprevv®) is a long-acting atypical antipsychotic.

FDA Approved Indication(s)
Zyprexa Relprevv is 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 Zyprexa Relprevv is **medically necessary** when the following criteria are met:

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It is the policy of health plans affiliated with Centene Corporation® that Zyprexa Relprevv is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia (must meet all):

1. Diagnosis of schizophrenia;
2. Age ≥ 18 years;
3. 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;
4. Member must have documented therapeutic failure or contraindications to Invega Sustenna, Invega Trinza, Aristada, or Abilify Maintena
5. Prescribed dose of Zyprexa Relprevv does not exceed 405 mg every 4 weeks or 300 mg every 2 weeks administered by intramuscular injection;

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.53 - No Coverage Criteria/Off-Label Use Policy**.**

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports the following:
   a. Member is currently receiving Zyprexa Relprevv for schizophrenia 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 405 mg every 4 weeks or 300 mg every 2 weeks.

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 6 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): 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.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

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): 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 registered facility with ready access to emergency response services.

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

Typical/First Generation Antipsychotics†	Atypical/Second Generation Antipsychotics
Chlorpromazine (Thorazine®) Fluphenazine (Prolixin®) Haloperidol (Haldol®) Loxapine (Loxitane®) Perphenazine (Trilafon®) Pimozide (Orap®) Thioridazine (Mellaril®) Thiothixene (Navane®) Trifluoperazine (Stelazine®)	Aripiprazole (Abilify®)* Asenapine maleate (Saphris®) Brexpiprazole (Rexulti®) 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 Patient Care Program 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 Patient Care Program is to mitigate the risk of negative outcomes associated with Zyprexa Relprevv post-injection delirium/sedation syndrome.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	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

VI. Product Availability
Powder for suspension: 210 mg, 300 mg, and 405 mg

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

VII. References

1. Zyprexa Relprevv Prescribing Information. Indianapolis, IN: Lilly USA, LLC; October 2019. Available at https://www.zyprexarelprevvprogram.com/public/Default.aspx. Accessed March 22, 2021.
2. 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
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 22, 2021.

Reviews, Revisions, and Approvals	Date	Approval Date
Removed requirement on prescriber specialty, removed requirement for nonadherence to oral antipsychotic therapy and established tolerability with oral olanzapine. Removed requirement for initial concomitant use of oral antipsychotic therapy. Extended initial approval to 12 months and removed criteria for continued approval.	11/17	11/17
Policy split from CP.PHAR.122.LAI Antipsychotics and converted to new template. Removed REMS program and age. Max dose added. Alzheimer's disease added as an exclusion to the criteria. Appendix B: Oral Antipsychotics – reviewed, edited. Specialist review by psychiatrist.	11/16	12/16
Added language to support migration to HFS PDL.	12.10.19	1.7.20
2Q2021 Annual review: added failure or contraindication of Aristada; Added tolerability to olanzapine and non-adherence to oral, or received Zyprexa Relprevv in an inpatient setting; Removed criteria no history of dementia and does not have Alzheimer disease; added age ≥ 18; added criteria for continued request; references reviewed and updated	6.17.21	
3Q 2021 annual review: no significant changes; added HCPCS codes; references reviewed and updated.	9.8.21	

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.