

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

Reference Number: CP.PHAR.292

Effective Date: 12.01.16

Last Review Date: 08.21

Line of Business: HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Olanzapine (Zyprexa Relprevv<sup>®</sup>) 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<sup>®</sup> 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. Prescribed by or in consultation with a psychiatrist;
3. Age  $\geq$  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 405 mg every 4 weeks or 300 mg every 2 weeks.

**Approval duration: 6 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): HIM.PA.154 for health insurance marketplace 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 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 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): HIM.PA.154 for health insurance marketplace 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 – HIM.PA.154 for health insurance marketplace, 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

*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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
olanzapine (Zyprexa <sup>®</sup> )	Schizophrenia 5 to 10 mg PO QD	20 mg/day

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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 <sup>®</sup> )	Aripiprazole (Abilify <sup>®</sup> )*
Fluphenazine (Prolixin <sup>®</sup> )	Asenapine maleate (Saphris <sup>®</sup> )
Haloperidol (Haldol <sup>®</sup> )	Brexpiprazole (Rexulti <sup>®</sup> )
Loxapine (Loxitane <sup>®</sup> )	Cariprazine (Vraylar <sup>®</sup> )
Perphenazine (Trilafon <sup>®</sup> )	Clozapine (Clozaril <sup>®</sup> )
Pimozide (Orap <sup>®</sup> )	Iloperidone (Fanapt <sup>®</sup> )
Thioridazine (Mellaril <sup>®</sup> )	Lumateperone (Caplyta <sup>®</sup> )
Thiothixene (Navane <sup>®</sup> )	Lurasidone (Latuda <sup>®</sup> )
Trifluoperazine (Stelazine <sup>®</sup> )	Olanzapine (Zyprexa <sup>®</sup> )*
	Olanzapine/Fluoxetine (Symbyax <sup>®</sup> )
	Paliperidone (Invega <sup>®</sup> )*
	Quetiapine (Seroquel <sup>®</sup> )
	Risperidone (Risperdal <sup>®</sup> )*
	Ziprasidone (Geodon <sup>®</sup> )

†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

**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.

**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
Converted to new template. Added age restriction per PI/safety approach. Removed “Therapeutic plan includes initial concomitant use of oral antipsychotic therapy as appropriate” since requirement is subjective and specialist is involved in care. Removed requirements related to history of dementia-related psychosis and Alzheimer’s disease per safety approach Increased initial approval duration from 3 to 6 months. Re-auth: updated to allow continuation of therapy for schizophrenia; removed reasons to discontinue per safety approach. Added dementia-related psychosis and Alzheimer’s disease under section III.	08.17	11.17
3Q 2018 annual review: no significant changes; references reviewed and updated.	05.02.18	08.18
Initial and continued therapy criteria were revised to allow approval for members who initiate therapy during a recent inpatient visit, without the requirement to step through oral agents.	02.26.19	02.19
3Q 2019 annual review: no significant changes; added HIM-Medical Benefit line of business; added boxed warning; references reviewed and updated.	05.31.19	08.19
3Q 2020 annual review: no significant changes; revised HIM-Medical Benefit to HIM line of business; references reviewed and updated.	05.12.20	08.20
3Q 2021 annual review: no significant changes; added HCPCS codes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.22.21	08.21

**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.

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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.

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