

Clinical Policy: Olanzapine LA Injection (Zyprexa Relprevv)

Reference Number: CP.PHAR.292

Effective Date: 12.01.16

Last Review Date: 08.19

Line of Business: Medicaid, HIM-Medical Benefit

[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:

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 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): 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): CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 and HIM-Medical Benefit 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 [®]) 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

VII. References

1. Zyprexa Relprevv Prescribing Information. Indianapolis, IN: Lilly USA, LLC; July 2018. Available at <https://www.zyprexarelprevvprogram.com/public/Default.aspx>. Accessed May 31, 2019.

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.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed May 31, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
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

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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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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