Clinical Policy: Paliperidone Long-Acting Injections (Invega Sustenna, Invega Trinza)

Reference Number: CP.PHAR.291
Effective Date: 12.01.16
Last Review Date: 08.19 Revision Log
Line of Business: Medicaid, Commercial, HIM-Medical Benefit

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

Description
Paliperidone (Invega Sustenna®, Invega Trinza®) is an atypical antipsychotic.

FDA Approved Indication(s)
Invega Sustenna is indicated:
- For the treatment of schizophrenia in adults
- For the treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants

Invega Trinza is indicated for the treatment of schizophrenia in patients after they have been adequately treated with Invega Sustenna (1-month paliperidone palmitate extended-release injectable suspension) for at least four months.

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 Invega Sustenna and Invega Trinza 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. One of the following (a, b, or c):
   a. If Invega Sustenna is requested, meets (i or ii):
      i. Established tolerability with long-acting risperidone injection (Risperdal Consta®);
      ii. Established tolerability with oral paliperidone or risperidone (preferred agent) AND has a history of non-adherence to oral antipsychotic therapy (*see Appendix D for examples*);
   b. If Invega Trinza is requested, adequate treatment has been established with Invega Sustenna for ≥ 4 months;
   c. Invega Sustenna or Invega Trinza therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;

5. Dose does not exceed (a or b):
   a. Invega Sustenna: 234 mg per month;
   b. Invega Trinza: 819 mg every 3 months.

Approval duration: 6 months

B. Schizoaffective Disorder (must meet all)**:**
1. Diagnosis of schizoaffective disorder;
2. Request is for Invega Sustenna;
3. Prescribed by or in consultation with a psychiatrist;
4. Age ≥ 18 years;
5. 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 risperidone (*preferred agent*) or paliperidone;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
6. Dose does not exceed 234 mg per month.

Approval duration: 6 months

C. 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.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

A. All Indications in Section I (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 the requested agent for a covered indication and has received this medication for at least 30 days;
   b. Therapy was initiated in an inpatient setting for a covered indications 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 the following (a or b):
   a. Invega Sustenna: 234 mg per month;
   b. Invega Trinza: 819 mg every 3 months.

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.CPA.09 for commercial and 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.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit or evidence of coverage documents;

B. Dementia-related psychosis.

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
paliperidone (Invega®)	Schizophrenia and schizoaffective Adults: initially, 6 mg PO QD Recommended dose: 3-12 mg/day	12 mg/day
risperidone (Risperdal®)	Schizophrenia Adults: initially, 2 mg/day PO (as a single dose) or 1 mg PO BID; adjust as tolerated to the recommended target dose of 4 to 8 mg/day Effective dose range: 4 to 16 mg/day	16 mg/day
Risperdal Consta (risperidone)	Schizophrenia Adults: 25 mg IM (deep gluteal or deltoid injection) once every 2 weeks; some adult patients not responding to the 25 mg dose may benefit from 37.5 mg or 50 mg IM once every 2 weeks	50 mg every 2 weeks
Invega Sustenna (paliperidone)	See Section V Dosage and Administration	See Section V Dosage and Administration

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): Risk of death is increased in elderly patients with dementia-related psychosis treated with antipsychotic drugs.

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*

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Paliperidone (Invega Sustenna)	Schizophrenia	Initial: 234 mg IM on day 1 and 156 mg one week later (day 8), both administered in the deltoid muscle Maintenance*: 39-234 mg IM monthly in either the deltoid or gluteal muscle	234 mg/month
	Schizoaffective disorder	Initial: 234 mg IM on day 1 and 156 mg one week later (day 8), both administered in the deltoid muscle Maintenance*: 78-234 mg IM monthly in either the deltoid or gluteal muscle	234 mg/month
Paliperidone (Invega Trinza)	Schizophrenia	Invega Trinza is to be used only after Invega Sustenna® (1-month paliperidone palmitate extended-release injectable suspension) has been established as adequate treatment for at least four months. Initiate Invega Trinza when the next 1-month paliperidone palmitate dose is scheduled with an Invega Trinza dose based on the previous 1-month injection dose, using the equivalent 3.5-fold higher dose as shown:	819 mg every 3 months

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Last Invega Sustenna dose: Invega Trinza dose to initiate 78 mg: 273 mg 117 mg: 410 mg 156 mg: 546 mg 234 mg: 819 mg Following the initial Invega dose, Invega Trinza should be administered IM every 3 months. Invega Trinza may be administered up to 7 days before or after the monthly time point of the next scheduled paliperidone palmitate 1-month dose.	

**Administered 5 weeks after the first injection*

VI. Product Availability

Drug Name	Availability
Paliperidone (Invega Sustenna)	Extended-release injectable suspension: 39 mg, 78 mg, 117 mg, 156 mg, or 234 mg
Paliperidone (Invega Trinza)	Extended-release injectable suspension: 273 mg, 410 mg, 546 mg, or 819 mg

VII. References

1. Invega Sustenna Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; July 2018. Available at https://www.invegasustennahcp.com/. Accessed May 2019.
2. Invega Trinza Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; July 2018. Available at https://www.invegatrinzahcp.com/. Accessed May 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 2019

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.122.LAI Antipsychotics and converted to new template. Age removed and max dose added. Added Risperdal Consta to Invega Sustenna tolerability statement per PI. Hypersensitivity contraindication added. Appendix B: Oral Antipsychotics – reviewed, edited and updated per UpToDate and FDA websites (6-8). Specialist review by psychiatrist.	11.16	12.16
Converted to new template. Added age restriction per PI. Removed requirements related to hypersensitivity to either paliperidone or risperidone and history of dementia-related psychosis per safety approach. Removed "therapeutic plan includes initial concomitant	07.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
use of oral antipsychotic therapy as appropriate" since requirement is subjective and specialist is involved in care. Increased initial approval duration from 3 to 6 months. Re-auth: combined criteria sets and updated to allow continuation of therapy for schizophrenia and schizoaffective disorder. Added dementia-related psychosis under section III.		
3Q 2018 annual review: no significant changes; references reviewed and updated.	05.01.18	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: added commercial and HIM-Medical Benefit lines of businesses; added contraindications; references reviewed and updated.	05.24.19	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.

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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