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

Reference Number: CP.PHAR.291
Effective Date: 12.01.16
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

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

FDA Approved Indication(s)

Invega Hafyera is indicated for the treatment of schizophrenia in adults after they have been adequately treated with:

- A once-a-month paliperidone palmitate extended-release injectable suspension (e.g., Invega Sustenna) for at least four months or;
- An every-three-month paliperidone palmitate extended-release injectable suspension (e.g., Invega Trinza) for at least one three-month cycle.

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 Hafyera, 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. Member meets one of the following (a or b):
   a. The requested product was initiated in an inpatient setting during a recent (within 60 days) hospital admission;

b. History of non-adherence to oral antipsychotic therapy (*see Appendix D for examples*), and one of the following (i, ii, or iii):
   i. If Invega Trinza is requested, adequate treatment has been established with Invega Sustenna for at least the last 4 months;
   ii. If Invega Sustenna is requested, both of the following (a and b):
      a) Established tolerability with oral paliperidone or oral risperidone;
      b) No known hypersensitivity to paliperidone or risperidone;
   iii. If Invega Hafyera is requested, one of the following (a or b):
      a) Adequate treatment has been established with Invega Sustenna for at least the last 4 months;
      b) Adequate treatment has been established with Invega Trinza for at least one three-month cycle;

5. Dose does not exceed any of the following (a, b, or c):
   a. Invega Hafyera: 1,560 mg every 6 months;
   b. Invega Sustenna: 234 mg per month;
   c. 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 (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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*
   c. Therapy was initiated in an inpatient setting for a covered indication 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 any of the following (a, b, or c):
   a. Invega Hafyera: 1,560 mg every 6 months;
   b. Invega Sustenna: 234 mg per month;
   c. Invega Trinza: 819 mg every 3 months.

Approval duration: 12 months

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

1. If his 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, and CP.PMN.53 for Medicaid, 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 disorder** 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

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): known hypersensitivity to paliperidone, risperidone, or to any excipients.
- Boxed warning(s): increased risk of death 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®) 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*

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Paliperidone (Invega Hafyera)	Schizophrenia	Invega Hafyera is to be used only after Invega Sustenna has been established as adequate treatment for at least four months or after Invega Trinza has been established as adequate treatment for at least one three-month cycle. The recommended initial Invega Hafyera dose is based on the previous dose of either Invega Sustenna or Invega Trinza, and is initiated when the next Invega Sustenna or Invega Trinza dose would have been scheduled. *Last Invega Sustenna dose: Invega Hafyera dose to initiate** 156 mg: 1,092 mg 234 mg: 1,560 mg **There are no equivalent doses of Invega Hafyera for the 39 mg, 78 mg, or 117 mg doses of Invega Sustenna, which were not studied.* *Last Invega Trinza dose: Invega Hafyera dose to initiate*** 546 mg: 1,092 mg 819 mg: 1,560 mg ***There are no equivalent doses of Invega Hafyera for the 273 mg or 410 mg, or 117 mg doses of Invega Trinza, which were not studied.* Following the initial dose, Invega Hafyera should be administered IM every 6 months.	1,560 mg every 6 months
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

Drug Name	Indication	Dosing Regimen	Maximum Dose
	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: *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.	819 mg every 3 months

**Administered 5 weeks after the first injection*

VI. Product Availability

Drug Name	Availability
Paliperidone (Invega Hafyera)	Extended-release injectable suspension: 1,092 mg/3.5 mL, 1,560 mg/5 mL
Paliperidone (Invega Sustenna)	Extended-release injectable suspension: 39 mg/0.25 mL, 78 mg/0.5 mL, 117 mg/0.75 mL, 156 mg/1 mL, or 234 mg/1.5 mL
Paliperidone (Invega Trinza)	Extended-release injectable suspension: 273 mg/0.875 mL, 410 mg/1.315 mL, 546 mg/1.75 mL, or 819 mg/2.625 mL

VII. References

1. Invega Hafyera Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207946Orig1s010lbl.pdf. Accessed May 12, 2022.
2. Invega Sustenna Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022264Orig1s033lbl.pdf. Accessed May 12, 2022.
3. Invega Trinza Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207946Orig1s011lbl.pdf. Accessed May 12, 2022.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 12, 2022.

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
J2426	Injection, paliperidone palmitate extended release, 1 mg
J3490, C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
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; for Invega Sustenna, clarified language for established tolerability and no known hypersensitivity to paliperidone or risperidone; added HCPCS codes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.19.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: Added newly approved Invega Hafyera to the policy.	09.23.21	
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.20.22	

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members 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.