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

Reference Number: IL.ERX.SPA.178
Effective Date: 06.01.21
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Line of Business: Illinois Medicaid

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 4 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 (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. 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 with oral risperidone 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: 12 months

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 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 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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
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): 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.	1,560 mg every 6 months

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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.	
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: If the last dose of Invega Sustenna is: → Initiate Invega Trinza at the following dose: 78 mg → 273 mg 117 mg → 410 mg 156 mg → 546 mg 234 mg → 819 mg	819 mg every 3 months

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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 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.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA+HAFYERA-pi.pdf. Accessed September 23, 2021.
2. Invega Sustenna Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; February 2019. Available at https://www.invegasustennahcp.com/. Accessed March 19, 2021.
3. Invega Trinza Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; February 2021. Available at https://www.invegatrinzahcp.com/. Accessed March 19, 2021.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 19, 2021.
5. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.23.21	05.21
3Q 2021 annual review: added initial and continued criteria for either history of non-adherence to PO antipsychotic therapy or therapy initiated recently in an inpatient setting; hypersensitivity contraindication added for risperidone and paliperidone; references reviewed and updated.	07.16.21	08.21
RT4: Added newly approved Invega Hafyera to the policy.	09.23.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.