Clinical Policy: Risperidone Long-Acting Injection (Perseris, Risperdal Consta)

Reference Number: IL.ERX.SPA.179
Effective Date: 06.01.21
Last Review Date: 08.21
Line of Business: Illinois Medicaid

Revision Log

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

Description
Risperidone (Perseris™, Risperdal Consta®) is an atypical antipsychotic.

FDA Approved Indication(s)
Risperdal Consta is indicated:
- For the treatment of schizophrenia
- For the maintenance treatment of bipolar I disorder as monotherapy or as adjunctive therapy to lithium or valproate

Perseris is indicated for the treatment of schizophrenia in adults.

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 Perseris and Risperdal Consta are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia or Bipolar Disorder (must meet all)**:**
1. Diagnosis of schizophrenia or bipolar disorder;
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 both of the following (i and ii):
      i. Failure of one of the following unless clinically significant adverse effects are experienced or all are contraindicated: Invega Sustenna®, Invega Trinza®, Abilify Maintena®, Aristada®;
      ii. Established tolerability with oral risperidone;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
5. Request meets one of the following (a or b):
   a. For Perseris requests, dose does not exceed 120 mg every four weeks;
   b. For Risperdal Consta requests, dose does not exceed 50 mg every two weeks.

Approval duration: 12 months

B. 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. Schizophrenia or Bipolar Disorder (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 medication 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, request meets one of the following (a or b):
   a. For Perseris requests, new dose does not exceed 120 mg every four weeks;
   b. For Risperdal Consta requests, new dose does not exceed 50 mg every two weeks.

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.

<table>
<tr><th>Drug Name</th><th>Dosing Regimen</th><th>Dose Limit/ Maximum Dose</th></tr>
<tr><td>Invega Sustenna® (paliperidone)</td><td><u>Schizophrenia</u>
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</td><td>234 mg/month</td></tr>
<tr><td>Invega Trinza® (paliperidone)</td><td><u>Schizophrenia</u>
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:
<table>
<tr><th>If the last dose of Invega Sustenna is:</th><th>Initiate Invega Trinza at the following dose:</th></tr>
<tr><td>78 mg</td><td>273 mg</td></tr>
<tr><td>117 mg</td><td>410 mg</td></tr>
<tr><td>156 mg</td><td>546 mg</td></tr>
<tr><td>234 mg</td><td>819 mg</td></tr>
</table></td><td>819 mg/3 months</td></tr>
</table>

Drug Name	Dosing Regimen	Dose Limit/ 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.	
Aristada® (aripiprazole lauroxil)	Schizophrenia *Initiation Method 1*: Administer one IM injection of Aristada Initio 675 mg (deltoid or gluteal muscle) and one dose of oral aripiprazole 30mg in conjunction with the first Aristada injection. • First Aristada injection may be started on same day or up to 10 days after administration of Aristada Initio • Avoid injection of both Aristada and Aristada Initio into the same deltoid or gluteal muscle. *Initiation Method 2:* Used in combination with oral aripiprazole for the first 21 consecutive days. Depending on individual patient's needs, treatment can be initiated at a dose of 441 mg, 662 mg, or 882 mg IM administered monthly; 882 mg administered every 6 weeks; or 1,064 mg administered every 2 months. Dose adjustments are required for 1) known CYP2D6 poor metabolizers and 2) for patients taking CYP3A4 inhibitors, CYP2D6 inhibitors, or CYP3A4 inducers for more than 2 weeks.	882 mg/month
Abilify Maintena® (aripiprazole monohydrate)	Schizophrenia and Bipolar I disorder The recommended starting and maintenance dose is 400 mg IM monthly (no sooner than 26 days after the previous injection). Dose can be reduced to 300 mg in patients with adverse reactions. • Used in combination with oral aripiprazole for the first 14 consecutive days. • Known CYP2D6 poor metabolizers: Recommended starting and maintenance dose is 300 mg IM monthly as a single injection.	400 mg/month
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 Bipolar Disorder Adults: initially, 2-3 mg PO QD Effective dose range: 1 to 6 mg/day	Schizophrenia: 16 mg/day Bipolar disorder: 6 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): hypersensitivity to risperidone or paliperidone

- Boxed warning(s): increased mortality in elderly patients with dementia-related psychosis

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
Risperidone (Risperdal Consta)	Bipolar disorder, Schizophrenia	The recommended dose is 25 mg IM every 2 weeks. Some patients not responding to 25 mg may benefit from a higher dose of 37.5 mg or 50 mg.	50 mg every 2 weeks
Risperidone (Perseris)	Schizophrenia	90 mg or 120 mg SC once monthly	120 mg every 4 weeks

VI. Product Availability

Drug Name	Availability
Risperidone (Risperdal Consta)	Vial kits: 12.5 mg, 25 mg, 37.5 mg, and 50 mg
Risperidone (Perseris)	Extended-release injectable suspension: 90 mg, 120 mg

VII. References

1. Risperdal Consta Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; February 2021. Available at http://www.janssencns.com/risperdal. Accessed March 22, 2021.
2. Perseris Prescribing Information. North Chesterfield, VA: Indivior, Inc.; December 2019. Available at: www.perseris.com. Accessed March 22, 2021.
3. 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
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 22, 2021.

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	07.16.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
an inpatient setting; updated therapeutic alternatives section; references reviewed and updated.		

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.