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

Reference Number: IL.PHAR.293
Effective Date: 12/16
Last Review Date: 1.18.24

Coding Implications
Revision Log

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

Description

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

FDA Approved Indication(s)

Risperdal and Rykindo are indicated:
• For the treatment of schizophrenia, Rykindo is specifically indicated in adults.
• For the maintenance treatment of bipolar I disorder as monotherapy or as adjunctive therapy to lithium or valproate, Rykindo is specifically indicated in adults.

Perseris and Uzedy are 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.

It is the policy of health plans affiliated with Centene Corporation® that Risperdal Consta, Perseris, Rykindo, Uzedy are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia/Bipolar Disorder (must meet all)**:**

1. Diagnosis of schizophrenia or bipolar disorder;
2. Age ≥ 18 years;
3. Request is for Perseris or Uzedy.
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 risperidone;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
5. The prescriber agrees to coordinate a follow up outpatient appointment for administration of the next recommended dose of the LAI atypical antipsychotic agents and provide documentation of the follow up appointment with request for prior approval;
6. Dose does not exceed any of the following (a, b, or c):
   c. Perseris: 120 mg every month;
   d. Risperdal Consta or Rykindo: 50 mg every 2 weeks;
   e. Uzedy (i or ii):
      i. 125 mg every month;

ii. 250 mg every 2 months.

Approval duration: 12 months

B. BBipolar Disorder (must meet all):

1. Diagnosis of bipolar disorder;
2. Request is for Risperdal Consta or Rykindo;
3. Member must have documented therapeutic failure or contraindications to Invega Sustenna, Invega Trinza, Abilify Maintena, or Aristada
4. Prescribed by or in consultation with a psychiatrist;
5. Age ≥ 18 years;
6. 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;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
7. The prescriber agrees to coordinate a follow up outpatient appointment for administration of the next recommended dose of the LAI atypical antipsychotic agents and provide documentation of the follow up appointment with request for prior approval;
8. Dose does not exceed 50 mg every 2 weeks.

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 (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for the relevant line of business: 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.PMN.53 for Medicaid.

II. Continued Therapy

A. Schizophrenia or Bipolar Disorder (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 Perseris, Risperdal Consta, Rykindo, or Uzedy for schizophrenia or bipolar disorder 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 any of the following (a, b, or c):
   a. Perseris: 120 mg every month;
   b. Risperdal Consta or Rykindo: 50 mg every 2 weeks;
   c. Uzedy (i or ii):
      i. 125 mg every month;
      ii. 250 mg every 2 months.

Approval duration: 12 months

B. 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 PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for the relevant line of business: 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.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.PHAR.21 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
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	Schizophrenia: 16 mg/day Bipolar disorder: 6 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Bipolar Disorder Adults: initially, 2-3 mg PO QD Effective dose range: 1 to 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, paliperidone, or to any excipients
  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, Rykindo)	Bipolar disorder, Schizophrenia	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/2 weeks
Risperidone (Perseris)	Schizophrenia	90 mg or 120 mg SC once monthly	120 mg/month
Risperidone (Uzedy)	Schizophrenia	Uzedy SC once monthly (50 mg, 75 mg, 100 mg, or 125	125 mg/month or 250 mg/2 months

Drug Name	Indication	Dosing Regimen	Maximum Dose
		mg) or once every 2 months (100 mg, 150 mg, 200 mg, or 250 mg) starting the day after the last dose of oral therapy. See Prescribing Information for dosage recommendations for switching from oral risperidone to Uzedy. Neither a loading dose or supplemental oral risperidone doses are recommended while switching. Patients can switch between doses of Uzedy once monthly and once every 2 months by administering the first dose of the new dosing regimen on the next scheduled date of administration in the original dosing regimen	

VI.

VII. 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
Risperidone (Rykindo)	Extended-release injectable suspension: 12.5 mg, 25 mg, 37.5 mg, and 50 mg
Risperidone (Uzedy)	Extended-release injectable suspension (single-dose prefilled syringes): 50 mg/0.14 mL, 75 mg/0.21 mL, 100 mg/0.28 mL, 125 mg/0.35 mL, 150 mg/0.42 mL, 200 mg/0.56 mL, and 250 mg/0.7 mL

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
J2794	Injection, risperidone (risperdal consta), 0.5 mg
J2798	Injection, risperidone, (perseris), 0.5 mg

VIII. 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. Rykindo Prescribing Information. Yantai, Shandong Province, China: Shandong Luye Pharmaceutical Co.,Ltd.; January 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/212849s000lbl.pdf. Accessed February 14, 2023.
4. Uzedy Prescribing Information. Parisppany, NJ: Teva Neuroscience, Inc.; May 2023. Available at: https://www.uzedy.com/. Accessed May 9, 2023.
5. 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
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 22, 2021.

Reviews, Revisions, and Approvals	Date	Approval Date
Removed requirement on prescriber specialty, removed requirement for nonadherence and established tolerability to oral risperidone. Extended initial approval to 12 months and removed criteria for continued approval.	11/17	11/17
Policy split from CP.PHARM.122.LAI Antipsychotics and converted to new template. Age removed and max dose added. Hypersensitivity contraindication added per PI. Appendix B: Oral Antipsychotics – reviewed, edited and updated per UptoDate and FDA websites (5-7). Specialist review by psychiatrist.	11/16	12/16
Added language to support migration to HFS PDL.	12.10.19	
2Q2021 Annual Review: Added criteria tolerability to risperidone and non-adherence to oral, or received the medication in an inpatient setting; removed criteria no history of dementia related psychosis and does not have Alzheimer disease; Removed criteria hypersensitivity; added age ≥ 18; added criteria for continued request; references reviewed and updated	6.17.21	
3Q 2021 annual review: no significant changes; added HCPCS codes; references reviewed and updated.	9.8.21	
2Q 2023 Annual review and RT4: added newly approved dosage form Rykindo to policy, template changes applied, references reviewed and updated.	3.30.23	
1Q 2024 annual review: Added Uzedy to criteria. Updated Initial approval, dosage and administration, and dosage forms sections. References reviewed and updated	1.18.24	

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.