Clinical Policy: Iloperidone (Fanapt) and Milsaperidone (Bysanti)

Reference Number: CP.PMN.32
Effective Date: 09.01.15
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Iloperidone (Fanapt®) and milsaperidone (Bysanti™) are atypical antipsychotics.

FDA Approved Indication(s)

Fanapt and Bysanti are indicated for the:

- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder 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 Fanapt and Bysanti are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia (must meet all)**:**

1. Diagnosis of schizophrenia;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of two preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated;
4. Requested agent is not prescribed concurrently with Fanapt or Bysanti;
5. Dose does not exceed both of the following (a and b):
   a. 24 mg per day;
   b. 2 tablets per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Bipolar Disorder (must meet all)**:**

1. Diagnosis of bipolar disorder;

2. Age ≥ 18 years;
3. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of two preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated;
4. Requested agent is not prescribed concurrently with Fanapt or Bysanti;
5. Dose does not exceed both of the following (a and b):
   a. 24 mg per day;
   b. 2 tablets per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

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/ICHRA) 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/ICHRA/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or documentation supports that member is currently receiving Fanapt or Bysanti for schizophrenia or bipolar disorder and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Requested agent is not prescribed concurrently with Fanapt or Bysanti;
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 24 mg per day;
   b. 2 tablets per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

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 formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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/ICHRA, 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
aripiprazole (Abilify®)	**Bipolar Disorder and Schizophrenia** Adults: 10 to 15 mg PO QD	30 mg/day
olanzapine (Zyprexa®)	**Schizophrenia** Initial: 5 to 10 mg PO QD; target: 10 mg PO QD	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Bipolar Disorder Monotherapy: 10 to 15 mg PO QD; adjunct to lithium or valproate: 10 mg PO QD	
quetiapine (Seroquel®)	**Schizophrenia** Initial: 25 mg PO BID; target: 400 to 800 mg/day **Bipolar Disorder** Initial: 50 mg PO BID; target: 400 to 800 mg/day	800 mg/day
risperidone (Risperdal®)	**Schizophrenia** Initial: 1 mg PO BID or 2 mg PO QD; target: 4 to 8 mg PO QD **Bipolar Disorder** 2 to 3 mg PO QD	Schizophrenia: 16 mg/day Bipolar Disorder: 6 mg/day
ziprasidone (Geodon®)	**Schizophrenia** 20 mg PO BID **Bipolar Disorder** Initial: 40 mg PO BID; target: 40 to 80 mg PO BID	160 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 Fanapt or milsaperidone or to any components in the formulation
- Boxed warning(s): elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Fanapt and Bysanti are not approved for use in patients with dementia-related psychosis.

Appendix D: States with Limitations against Redirections in Certain Mental Health Settings

State	Step Therapy Prohibited?	Notes
AR	Yes	For the treatment of psychosis and serious mental illness through antipsychotic prescription drugs, no step therapies allowed.
NV	No	**Applies to Medicaid requests only** Failure of ONE preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine) at up to maximally indicated doses, used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated.
TX	No	Failure of ONE preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine) at up to maximally indicated doses, used for ≥ 4 weeks, unless

State	Step Therapy Prohibited?	Notes
		clinically significant adverse effects are experienced or all are contraindicated.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Iloperidone (Fanapt), milsaperidone (Bysanti)	Schizophrenia	Initial: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, and 12 mg PO BID on consecutive days from Day 1 to Day 7 Maintenance: 6 to 12 mg PO BID	24 mg/day
Iloperidone (Fanapt), milsaperidone (Bysanti)	Bipolar disorder	Initial: 1 mg, 3 mg, 6 mg, 9 mg, and 12 mg PO BID on consecutive days from Day 1 to Day 5 Maintenance: 12 mg PO BID	24 mg/day

VI. Product Availability

Drug Name	Availability
Iloperidone (Fanapt)	Tablets: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg
Milsaperidone (Bysanti)	Tablets: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg

VII. References

1. Fanapt Prescribing Information. Washington, D.C: Vanda Pharmaceuticals Inc.; April 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/022192s024lbl.pdf. Accessed April 14, 2026.
2. Bysanti Prescribing Information. Washington, D.C: Vanda Pharmaceuticals Inc.; February 2026. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/220358Orig1s000lbl.pdf. Accessed April 14, 2026.
3. American Psychiatric Association: Guideline Watch (September 2009): Practice Guideline for the Treatment of Patients with Schizophrenia, 2009. http://psychiatryonline.org/guidelines. Accessed May 29, 2026.
4. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.
5. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. Practice guideline for the treatment of patients with bipolar disorder, second edition. Arlington, VA: American Psychiatric Association; April 2002. Available online at: http://www.psychiatryonline.org/guidelines. Accessed May 29, 2026.
6. Management of bipolar disorder work group. Clinical practice guideline for management of bipolar disorder Version 2.0 - 2023. Veterans Affairs/Department of Defense. Available at: https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf. Accessed May 29, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications and continued therapy section.	09.20.22	
1Q 2023 annual review: no significant changes; added dementia-related psychosis to section III; references reviewed and updated.	11.02.22	02.23
3Q 2023 annual review: no significant changes; added redirection bypass for members in a State with limitations on step therapy in certain mental health settings along with Appendix D, which includes Texas with requirements for single drug redirection for HIM requests; references reviewed and updated.	04.21.23	08.23
Added Nevada to Appendix D with requirements for single drug redirection for Medicaid requests.	08.31.23	
RT4: criteria added for newly approved indication of bipolar disorder; corrected maintenance dosing for schizophrenia in Section V Dosing and Administration per PI.	04.10.24	
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.09.24	08.24
Added Arkansas to Appendix D with requirement for no step therapies allowed for HIM requests.	09.25.24	
3Q 2025 annual review: added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	04.23.25	08.25
Removed "applies to HIM request only" from Appendix D for Arkansas per AR HB 1276. RT4: added Bysanti to policy and requirement against concurrent use of Fanapt and Bysanti (duplicate therapy).	03.11.26	
3Q 2026 annual review: added ICHRA line of business; removed all line of business-specific distinctions from Appendix D; references reviewed and updated.	04.14.26	08.26
Added Medicaid-specific distinction to NV in Appendix D per VPRP request and Compliance.	10.28.26	

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.

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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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