Clinical Policy: Midostaurin (Rydapt)

Reference Number: CP.PHAR.344
Effective Date: 06.01.17
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

Midostaurin (Rydapt®) is a kinase inhibitor.

FDA Approved Indication(s)

Rydapt is indicated for the treatment of adult patients with:

- Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation
  Limitation(s) of use: Rydapt is not indicated as a single-agent induction therapy for the treatment of patients with AML.
- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL)

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 Rydapt is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Positive for the FLT3 mutation;
5. If induction therapy, prescribed in combination with cytarabine and daunorubicin;
6. If consolidation or post-induction therapy, prescribed in combination with cytarabine;
7. For brand Rydapt requests, member must use generic midostaurin, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

B. Advanced Systemic Mastocytosis (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. ASM;
   b. SM-AHN;
   c. MCL;
2. Prescribed by or in consultation with an oncologist, allergist, or immunologist;
3. Age ≥ 18 years;
4. For brand Rydapt requests, member must use generic midostaurin, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 200 mg (8 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Off-Label Indications (must meet all)**:**
1. Diagnosis of myeloid/lymphoid neoplasm with eosinophilia and FGFR1 or FLT3 rearrangements in blast or chronic phase;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand Rydapt requests, member must use generic midostaurin, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Rydapt for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;

3. For brand Rydapt requests, member must use generic midostaurin, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. AML: Dose does not exceed 100 mg (4 capsules) per day;
   b. ASM, SM-AHN, or MCL: Dose does not exceed 200 mg (8 capsules) per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
ASM: aggressive systemic mastocytosis
FDA: Food and Drug Administration
MCL: mast cell leukemia
SM-AHN: systemic mastocytosis with associated hematological neoplasm

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
AML induction therapy: cytarabine + daunorubicin	Cytarabine 100-200 mg/m^2 continuous IV infusion for 7 days with daunorubicin 60-90 mg/m^2 for 3 days	Varies
AML post-remission therapy (consolidation): cytarabine	3 g/m^2 IV over 3 hours every 12 hours on days 1, 3, and 5 for 3 to 4 cycles	Varies

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 midostaurin or any of the excipients.
- Boxed warning(s): None reported.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML	50 mg PO BID with food	100 mg/day
ASM, SM-AHN, MCL	100 mg PO BID with food	200 mg/day

VI. Product Availability

Capsules: 25 mg

VII. References

1. Rydapt Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2021. Available at: https://www.novartis.us/sites/www.novartis.us/files/rydapt.pdf. Accessed February 14, 2022.
2. Midostaurin. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://nccn.org/. Accessed February 14, 2022.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed February 14, 2022.
4. National Comprehensive Cancer Network. Systemic Mastocytosis Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed February 14, 2022.
5. National Comprehensive Cancer Network. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed February 14, 2022.
6. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed February 14, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes; policies combined for Commercial and Medicaid; references reviewed and updated.	03.06.18	05.18
2Q 2019 annual review: AML: hematologist added, FDA-approved test requirement removed; references reviewed and updated.	12.19.19	05.19
2Q 2020 annual review: no significant changes; HIM line of business added; references reviewed and updated.	02.13.20	05.20
2Q 2021 annual review: added generic redirection language to "must use" since oral oncology product; added off-label indication for myeloid/lymphoid neoplasm with eosinophilia and FGFR1 or FLT3 rearrangements in blast phase; updated reference for HIM off-label use	02.21.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
to HIM.PA.154 (replaces HIM.PHAR.21); added standard oncology generic redirection language; references reviewed and updated.		
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; WCG.CP.PHAR.344 to be retired and approval durations consolidated to 6 months initial and 12 months for continuation of therapy; per NCCN in AML added option for post-induction therapy prescribed in combination with cytarabine, for myeloid/lymphoid neoplasm added option for use in the chronic phase; references reviewed and updated.	02.14.22	05.22

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.