Clinical Policy Title:	midostaurin
Policy Number:	RxA.271
Drug(s) Applied:	Rydapt®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Midostaurin (Rydapt®) is a kinase inhibitor.
It 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).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
midostaurin (Rydapt®)	AML	50 mg PO twice daily with food	100 mg/day
	ASM, SM-AHN, MCL	100 mg PO twice daily with food	200 mg/day

Dosage Forms

- Capsules: 25 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Member has FLT3 mutation-positive diagnosis, as detected by an FDA-approved test;
5. If request is for induction therapy, prescribed in combination with standard cytarabine and daunorubicin;
6. If request is for consolidation therapy, prescribed in combination with cytarabine;
7. Request meets one of the following (a or b): *
   a. Dose does not exceed 100 mg 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
Commercial: 6 months
Medicaid: 6 months

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. Request meets one of the following (a or b): *
   a. Dose does not exceed 200 mg 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving midostaurin that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. 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 per day;
   b. ASM, SM-AHN, or MCL: Dose does not exceed 200 mg 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
FLT 3: fms-like tyrosine kinase 3

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	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.

APPENDIX D: General Information

None.

References

1. Rydapt® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/207997s006lbl.pdf. Accessed April 01, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed April 01, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Updated March 2, 2021. Accessed April 01, 2021.
4. National Comprehensive Cancer Network. Systemic Mastocytosis Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Updated May 21, 2020. Accessed April 01, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020

Policy was reviewed: 1. Policy title table was updated. 2. Rephrased initial therapy criteria I.A.4. and included “as detected by FDA approved test”Removed initial therapy criteria I.A.7.b. and I.B.4.b. 3. Continued therapy criteria II.A.1. rephrased to “Member is currently receiving midostaurin that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy”. 4. Length of duration for initial and continued therapy was updated. 5. Updated Appendix A to include “FLT3”. 6. References were updated.	07/10/2020	09/14/2020
Policy was reviewed: 1. Dosing regimen updated to include route of administration. 2. Clinical policy section standard verbiage was updated to include “The provision of prescriber samples…”. 3. Continued therapy II.A.1 criteria was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance...”. 4. Appendix B for therapeutic alternatives standard verbiage was updated to “Below are suggested therapeutic alternatives based on clinical guidance...”. 5. References were updated.	04/01/2021	06/10/2021