Rydapt® (midostaurin)
(Oral)

Document Number: IC-0303

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Date of Origin: 5/30/2017
Dates Reviewed: 5/2017, 4/2018

I. Length of Authorization

- Acute myeloid leukemia: coverage will be provided for six months and may not be renewed.
- Systemic Mastocytosis: coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Rydapt 25 mg capsules (carton of 56): 2 capsules per day (1 carton per 28 days)
- Rydapt 25 mg capsules (carton of 112): 8 capsules per day (1 carton per 14 days)

B. Max Units (per dose and over time) [Medical Benefit]:

- AML: 100 mg per day Days 8-21 of a 28-day cycle
- Systemic Mastocytosis: 200 mg per day

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**

Acute Myeloid Leukemia (AML) †

- Patient must be diagnosed with AML (excluding acute promyelocytic leukemia); **AND**
- Patient's disease is FMS-like tyrosine kinase-3 (FLT3) mutation-positive (FLT3+), both ITD and TKD mutations, as detected by an FDA-approved test (e.g., LeukoStrat CDx FLT3 Mutation Assay); **AND**
  - Used in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation therapy; **OR**
  - Used in combination with cytarabine and daunorubicin after induction with cytarabine for patients with residual disease ‡; **OR**
  - Used post-remission in combination with cytarabine ‡; **OR**

- Used for relapsed/refractory disease as a component of repeating the initial induction regimen if there has been a late relapse (≥12 months)

Systemic Mastocytosis †

- Patient has a diagnosis of one of the following:
  - Aggressive systemic mastocytosis (ASM)
  - Systemic mastocytosis with associated hematologic neoplasm (SM-AHN)
  - Mast cell leukemia (MCL)

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria

Authorizations for systemic mastocytosis may be renewed based on the following criteria:

- Patient continues to meet the criteria in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: pulmonary toxicity (interstitial lung disease or pneumonitis), etc.; **AND**
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration

Indication	Dose
AML	50 mg orally twice daily Days 8 to 21 of each cycle of induction with cytarabine and daunorubicin and on Days 8 to 21 of each cycle of consolidation with high-dose cytarabine. (28-day cycles)*
Systemic Mastocytosis (ASM, SM-AHN, MCL)	100 mg orally twice daily

*Induction consists of 2 cycles with consolidation consisting of 4 cycles

VI. Billing Code/Availability Information

Jcode:

- J8999: Prescription drug, oral, chemotherapeutic, nos
- C9399: Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)

NDC:

- Rydapt 25 mg capsules: 00078-0698-xx

VII. References

1. Rydapt [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation, April 2017. Accessed March 2018.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) midostaurin. National Comprehensive Cancer Network, 2018. The NCCN

Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.

3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 2.2018. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.
4. Gotlib J, Kluin-Nelemans HC, George TI, et al. Efficacy and Safety of Midostaurin in Advanced Systemic Mastocytosis. N Engl J Med. 2016 Jun 30;374(26):2530-41.
5. Stone RM, Mandrekar S, Sanford BL, et al. The Multi-Kinase Inhibitor Midostaurin (M) Prolongs Survival Compared with Placebo (P) in Combination with Daunorubicin (D)/Cytarabine (C) Induction (ind), High-Dose C Consolidation (consol), and As Maintenance (maint) Therapy in Newly Diagnosed Acute Myeloid Leukemia (AML) Patients (pts) Age 18-60 with FLT3 Mutations (muts): An International Prospective Randomized (rand) P-Controlled Double-Blind Trial (CALGB 10603/RATIFY [Alliance]). Blood 2015 126:6

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C92.00	Acute myeloblastic leukemia not having achieved remission
C92.01	Acute myeloblastic leukemia in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.51	Acute myelomonocytic leukemia in remission
C92.52	Acute myelomonocytic leukemia, in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia in remission

ICD-10	ICD-10 Description
C93.02	Acute monoblastic/monocytic leukemia, in relapse
C94.00	Acute erythroid leukemia not having achieved remission
C94.01	Acute erythroid leukemia in remission
C94.02	Acute erythroid leukemia, in relapse
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.21	Acute megakaryoblastic leukemia in remission
C94.22	Acute megakaryoblastic leukemia, in relapse
C94.30	Mast cell leukemia not having achieved remission
C94.31	Mast cell leukemia in remission
C94.32	Mast cell leukemia in relapse
C96.2	Malignant mast cell tumor
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.29	Other malignant mast cell neoplasm
D47.02	Systemic mastocytosis

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC