

## Rydapt® (midostaurin) (Oral)

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### I. Length of Authorization

- Acute myeloid leukemia: coverage will be provided for six months and may not be renewed.
- Systemic Mastocytosis & MDS/MPN Overlap Neoplasms: coverage will be provided for six months and may be renewed.

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [NDC Unit]:

- 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) [HCPCS Unit]:

- AML: 100 mg per day Days 8-21 of a 28-day cycle
- Systemic Mastocytosis & MDS/MPN Overlap Neoplasms: 200 mg per day

### III. Initial Approval Criteria <sup>1-6</sup>

Coverage is provided in the following conditions:

#### Universal Criteria

- Patient is at least 18 years old; **AND**
- Not used in combination with other FMS-like tyrosine kinase (FLT)-inhibitors (e.g., gilteritinib, sorafenib, etc.); **AND**

#### Acute Myeloid Leukemia (AML) † <sup>1,2,3,5,6</sup>

- 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 confirmed by an FDA-cleared or CLIA-compliant test\*; **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 †<sup>1,2,4</sup>**

- Used as single agent therapy; **AND**
- Patient has a diagnosis of one of the following:
  - Aggressive systemic mastocytosis (ASM); **OR**
  - Systemic mastocytosis with associated hematologic neoplasm (SM-AHN); **OR**
  - Mast cell leukemia (MCL)

#### **Myelodysplastic/Myeloproliferative (MDS/MPN) Overlap Neoplasms ‡<sup>2,4</sup>**

- Used as single agent therapy; **AND**
- Used for the treatment of chronic myelomonocytic leukemia (i.e., CMML-0, CMML-1, CMML-2); **AND**
- Patients has CMML-associated systemic mastocytosis (SM-AHN) and KIT816V mutation

*\*<http://www.fda.gov/CompanionDiagnostics>*

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

## **IV. Renewal Criteria<sup>1</sup>**

Coverage may be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified 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**

#### **Systemic Mastocytosis & MDS/MPN Overlap Neoplasms**

- Disease response with treatment as defined by stabilization of disease or decrease in the size of tumor or tumor spread.

#### **Acute Myeloid Leukemia (AML)**

- Coverage may NOT be renewed

## **V. Dosage/Administration**

Indication	Dose
AML	50 mg orally twice daily on 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) & MDS/MPN Overlap Neoplasms	100 mg orally twice daily. Continue treatment until disease progression or unacceptable toxicity occurs.
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\*Induction consists of 2 cycles with consolidation consisting of 4 cycles

## VI. Billing Code/Availability Information

HCPCS code:

- J8999: Prescription drug, oral, chemotherapeutic, nos

NDC:

- Rydapt 25 mg capsules: 00078-0698-xx

## VII. References

1. Rydapt [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation, July 2019. Accessed January 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) midostaurin. National Comprehensive Cancer Network, 2020. 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 January 2020.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2020. National Comprehensive Cancer Network, 2020. 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 January 2020.
4. Gotlib J, Kluijn-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 (mut): An International Prospective Randomized (rand) P-Controlled Double-Blind Trial (CALGB 10603/RATIFY [Alliance]). *Blood* 2015 126:6
6. Stone RM, Mandrekar SJ, Sanford BL, et al. Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation. *N Engl J Med.* 2017;377(5):454. Epub 2017 Jun 23.

## 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
C93.02	Acute monoblastic/monocytic leukemia, in relapse
C93.10	Chronic myelomonocytic leukemia not having achieved remission
C93.12	Chronic myelomonocytic 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
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
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
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