

Rydapt® (midostaurin) (Oral)

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I. Length of Authorization

- Acute Myeloid Leukemia & Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes: Coverage will be provided for 6 months and may not be renewed.
 - Patients with residual disease requiring re-induction may repeat two cycles of induction therapy for a total of 8 cycles of therapy (4 cycles of induction and 4 cycles of consolidation).
- Systemic Mastocytosis & MDS/MPN Overlap Neoplasms: Coverage will be provided for 6 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 & Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes: 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 ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Will not be used in combination with other FMS-like tyrosine kinase (FLT)-inhibitors (e.g., gilteritinib, sorafenib, etc.); **AND**
- Patient will avoid concomitant therapy with all of the following:

- Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
- Coadministration with strong CYP3A inhibitors (e.g., ketoconazole, grapefruit juice, clarithromycin, diltiazem, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Acute Myeloid Leukemia (AML) † Φ 1-3,5,6

- Patient must be diagnosed with AML (excluding acute promyelocytic leukemia); **AND**
- Patient's disease is FLT3 mutation-positive (*includes ITD or TKD positive mutations*), as confirmed by an FDA-approved or CLIA-compliant test \diamond ; **AND**
 - Used in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation therapy †; **OR**
 - Used in combination with cytarabine and daunorubicin as re-induction therapy after induction with cytarabine for patients with residual disease †; **OR**
 - Used as post-induction therapy in combination with cytarabine for patients ≥ 60 years of age with complete response to previous intensive therapy who are able to receive conventional consolidation therapy †; **OR**
 - Used for relapsed/refractory disease as a component of repeating the initial induction regimen if there has been a late relapse (≥ 12 months) †; **AND**
 - Therapy was not administered continuously and was not discontinued due to the development of clinical resistance

Systemic Mastocytosis † Φ 1,2,4

- 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 Overlap Neoplasms (MDS/MPN) † 2,4

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

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes † 2,7

- Used for myeloid or lymphoid neoplasms with eosinophilia; **AND**
 - Patient has FGFR1 or FLT3 rearrangements in chronic phase; **AND**

- Used as a single agent; **OR**
- Patient has FGFR1 or FLT3 rearrangements in blast phase (*Note: May be used in mixed lineage neoplasms as well*); **AND**
 - Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic transplant in transplant eligible patients

❖ *If confirmed using an immunotherapy assay* - <http://www.fda.gov/companiondiagnostics>

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

IV. Renewal Criteria ¹

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: 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)/Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes

- Coverage may NOT be renewed (*Note: Patients with residual AML disease requiring re-induction may repeat two cycles of induction for a total of 8 cycles of therapy*).

V. Dosage/Administration ^{1,4}

Indication	Dose
AML & Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes	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. <i>* Induction consists of two 28-day cycles followed by consolidation consisting of four 28-day cycles for a total of 6 cycles of therapy.</i> <i>*Patients requiring re-induction for residual disease may repeat two cycles of induction.</i>
Systemic Mastocytosis (ASM, SM-AHN, MCL); MDS/MPN Overlap Neoplasms	100 mg orally twice daily. Continue treatment until disease progression or unacceptable toxicity occurs.

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, November 2021. Accessed March 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) midostaurin. National Comprehensive Cancer Network, 2022. 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 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 1.2022. National Comprehensive Cancer Network, 2022. 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 2022.
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
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.
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes. Version 4.2021. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are

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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
C94.30	Mast cell leukemia not having achieved remission
C94.31	Mast cell leukemia in remission
C94.32	Mast cell leukemia in relapse
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission
C94.81	Other specified leukemias in remission
C94.82	Other specified leukemias in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type in remission
C95.12	Chronic leukemia of unspecified cell type in relapse
C96.20	Malignant mast cell neoplasm, unspecified

ICD-10	ICD-10 Description
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
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), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/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/LCA): 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