Rydapt® (midostaurin)
(Oral)

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I. Length of Authorization [1,7]

- 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: 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): 4 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: 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 [1]

- Will not be used in combination with other FMS-like tyrosine kinase (FLT)-inhibitors (e.g., gilteritinib, sorafenib, quizartinib, 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 has FLT3 mutation-positive (FLT3+) *(including ITD or TKD positive mutations)* disease, as confirmed by an FDA-approved or CLIA-compliant, test❖; **AND**
  - Used in combination with standard cytarabine AND daunorubicin or idarubicin induction therapy and cytarabine consolidation therapy † ‡; **OR**
  - Used as re-induction therapy in combination with standard dose cytarabine AND daunorubicin or idarubicin after cytarabine-based induction therapy in patients with residual disease ‡; **OR**
  - Used in combination with cytarabine as consolidation therapy ‡; **OR**
  - Used for relapsed/refractory disease as a component of repeating the initial successful induction regimen if ≥ 12 months have elapsed since receiving the induction regimen ‡; **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)

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes ‡ [2,7]

- Patient has eosinophilia with FGFR1 or FLT3 rearrangement; **AND**
  - Patient has chronic or blast phase myeloid or lymphoid neoplasms; **AND**
    - Used as a single agent; **OR**
  - Patient has blast phase lymphoid, myeloid, or mixed lineage neoplasms; **AND**
    - Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible)

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

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based on the following criteria:

- Patient continues to meet the 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

- 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 cytarabine. ** Induction consists of two 28-day cycles followed by consolidation consisting of four 28-day cycles for a total of 6 cycles of therapy.* **Patients requiring re-induction for residual disease may repeat two cycles of induction.*
Systemic Mastocytosis (ASM, SM-AHN, MCL)	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, May 2023. Accessed February 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) midostaurin. National Comprehensive Cancer Network, 2024. 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 2024.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 2.2024. National Comprehensive Cancer Network, 2024. 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 2024.
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 1.2024. National Comprehensive Cancer Network, 2024. 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 2024.

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
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
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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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