PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Rydapt Prior Authorization Policy
- Rydapt® (midostaurin capsules – Novartis)

REVIEW DATE: 02/10/2021

OVERVIEW

Rydapt, a tyrosine kinase inhibitor, is indicated in adults for the following uses:[1]

- **Acute myeloid leukemia (AML), newly diagnosed, that is FMS-like tyrosine kinase 3 (*FLT3*) mutation-positive** as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
- **Aggressive systemic mastocytosis (AMS), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL)**.

AML

AML is a heterogeneous hematologic malignancy characterized by clonal expansion of myeloid blasts in the peripheral blood, bone marrow, and/or other tissues.[2] Undifferentiated blast cells proliferate in bone marrow instead of maturing into normal blood cells. Among adults, it is the most common form of acute leukemia and accounts for the largest number of annual deaths from leukemias in the US. An estimated 19,940 individuals will be diagnosed with AML in 2019 and 11,180 are projected to die from the condition. The median age at diagnosis is 67 years. Diagnosis occurs at ≥ 65 years of age for 54% of patients with around one-third of patients diagnosed at ≥ 75 years of age. The incidence of AML increase as the population ages. Environmental factors such as prolonged exposure to petrochemicals, solvents such as benzene, pesticides, and ionizing radiation have been established to increase the risks for AML, as well as myelodysplastic syndrome (MDS).[2] The cure rates of AML have improved with this outcome noted in 35% to 40% of adult patients who are ≤ 60 years of age and 5% to 15% for patients who are > 60 years of age.[3] However, among patients who are older and unable to receive intensive chemotherapy the survival rates are dismal with a median survival of only 5 to 10 months. Various gene mutations are present in adults with AML. The prognosis of AML is worse for patients with *FLT3* mutations which comprise approximately 30% to 40% of AML cases. Two major classes of activating *FLT3* mutations have been identified in patients with AML which include the ITD and TKD point mutations. *FLT3*/ITD mutations occur in approximately 30% of cases and are more common than *FLT3*/TKD mutations, which occur in approximately 10% of patients.

Systemic Mastocytosis (SM)

Mastocytosis describes a rare group of disorders that are caused by too many mast cells in the body.[4-10] c-Kit mutations are implicated in some types of mastocytosis, including SM.[9] There are four major subtypes of SM: indolent SM (ISM), SM-AHN, ASM, and MCL.[8] The prognosis of ASM is highly variable, with a median survival of 3.5 to 7 years depending on the study. The only definitive therapy for ASM remains hematopoietic stem cell transplant (HSCT).[7] In general, the prognosis and treatment of SM-AHN is governed by the associated hematologic disorder while controlling the symptoms of mastocytosis. In SM-AHN, HSCT confers the greatest survival benefit in all forms of advanced SM, with a 3-year survival probability of 74% according to a large global retrospective study. The prognosis of SM-AHN remains poor, with a median survival estimated to be 2 to 4.4 years, depending on the study. MCL is by far the most aggressive form of SM, with median survival of approximately 6 months. HSCT offers a potentially curative role in appropriate patients with MCL, yet reports have failed to demonstrate reproducible evidence of durable eradication of the disease.

Guidelines

Various guidelines from the National Comprehensive Cancer Network (NCCN) address use of Rydapt.

- **Acute Myeloid Leukemia:** The NCCN guidelines on AML (version 2.2021 – November 12, 2020), recommend Rydapt + intravenous chemotherapy (e.g., cytarabine, daunorubicin) among the treatment options for induction, re-induction, and post-remission therapy.[3] It was noted that while Rydapt was not FDA-approved for maintenance therapy, the pivotal trial was designed for consolidation and maintenance Rydapt for a total of 12 months.
- **Myeloid/Lymphoid Neoplasms with Eosinophilia:** The NCCN guidelines myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes (version 3.2021 – August 21, 2020) recommend Rydapt for patients with FGFR1 or FLT3 rearrangements in chronic phase.[11]
- **Systemic Mastocytosis:** In the NCCN has guidelines for systemic mastocytosis (version 1.2020 – May 21, 2020).[12] Rydapt is recommended for the treatment of aggressive systemic mastocytosis (category 2A), for the treatment of systemic mastocytosis with an associated hematologic neoplasm (category 2A), and for mast cell leukemia (category 2A).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Rydapt. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rydapt approval requires Rydapt to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 3 years.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rydapt is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Acute Myeloid Leukemia (AML).** Approve for 3 years if the patient meets the following criteria (A B and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient is *FLT3*-mutation positive AML as detected by an approved test; AND
   - **C)** Patient is receiving Rydapt in one of the following settings (i, ii, iii, or iv):
     - **i.** Induction therapy in combination with cytarabine and daunorubicin; OR
     - **ii.** After standard-dose cytarabine induction/reinduction, along with cytarabine and daunorubicin; OR
     - **iii.** Post remission or consolidation therapy in combination with cytarabine; OR
     - **iv.** Maintenance therapy.

2. **Aggressive Systemic Mastocytosis (ASM).** Approve for 3 years if the patient is ≥ 18 years of age.

3. **Systemic Mastocytosis Associated with Acute Hematologic Neoplasm (SM-AHN).** Approve for 3 years if the patient is ≥ 18 years of age.

4. **Mast Cell Leukemia (MCL).** Approve for 3 years if the patient is ≥ 18 years of age.

Other Uses With Supportive Evidence

5. **Myeloid or Lymphoid Neoplasms with Eosinophilia.** Approve for 3 years if the patient meets one of the following (A or B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets one of the following (i or ii):
      i. Patient has an FGFR1 rearrangement; OR
      ii. Patient has an FLT3 rearrangement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rydapt is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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4. Pardanani A. Systemic mastocytosis in adults: 2019 update on diagnosis, risk stratification and management. *Am J Hematol*. 2019;94(3):363-377.
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7. Van Anrooij B, Oude Elberink JNG, Span LF, et al. Midostaurin in indolent systemic mastocytosis patients: an open-label phase 2 trial. *J Allergy Clin Immunol*. 2018;142(3):1006-1008.
8. Kim ES. Midostaurin: first global approval. *Drugs*. 2017;77:1251-1259.
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10. Kasamon Y, Ko CW, Subramaniam S, et al. FDA approval summary: midostaurin for the treatment of advanced systemic mastocytosis. *Oncologist*. 2018;23:1511-1519.
11. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Clinical Practice Guidelines in Oncology (version 3.2021 – August 21, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 8, 2021.
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