PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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RYDAPT® (midostaurin)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Rydapt (midostaurin) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Hematologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Acute myeloid leukemia (AML) who are FLT3 mutation positive (both ITD and TKD mutations) used in **EITHER** of the following:
        i. In combination with standard cytarabine and daunorubicin induction
        ii. In combination with standard cytarabine consolidation chemotherapy

     b. Aggressive systemic mastocytosis (ASM)

     c. Systemic mastocytosis with associated hematologic neoplasm (SM-AHN)

     d. Mast cell leukemia (MCL) with or without an associated hematologic neoplasm

     e. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. **For AML**: FLT3 mutation diagnosis was made using an FDA-approved test
     b. Negative pregnancy test in a woman of reproductive potential
     c. Eastern Cooperative Oncology Group (ECOG) Performance Status is 0-1

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Rydapt (midostaurin) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Hematologist

  2. Individual's condition responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

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3. Individual has been adherent with the medication

4. Individual has not developed any adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Known or suspected interstitial lung disease or pneumonitis
        ii. ANC persistently low for > 21 days and is suspected to be due to Rydapt
        iii. Platelet count persistently low for > 21 days and is suspected to be due to Rydapt
        iv. Hemoglobin persistently low for > 21 days and is suspected to be due to Rydapt

5. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Rydapt (midostaurin), a multi-kinase inhibitor, is indicated, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by a FDA approved test; and it is also indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL). Rydapt (midostaurin) is not indicated as a single-agent induction therapy for the treatment of patients with AML.

AML is a rare and aggressive cancer of the blood and bone marrow, about 21,000 individuals are diagnosed with AML each year in the US. About a third of these have a FLT3 gene mutation, which is associated with lower survival rates than other forms of AML.

Mastocytosis is a group of disorders where mast cells accumulate in one or more tissues or organs. Mastocytosis is considered to be a myeloproliferative neoplasm. There are two major categories of mastocytosis: cutaneous mastocytosis, in which the mast cells accumulate in the skin only, and systemic mastocytosis (SM) where the mast cells accumulate in skin, bone marrow, liver, spleen, gastrointestinal tract, and lymph nodes. Subtypes of SM include indolent systemic mastocytosis and advanced systemic mastocytosis. The indolent forms of SM are more benign diseases and are associated with a good prognosis. Isolated bone marrow mastocytosis and smoldering systemic mastocytosis are examples of indolent systemic mastocytosis. While indolent systemic mastocytosis is considered a relatively benign disease, there is a risk of progression to advanced systemic mastocytosis.

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Advanced systemic mastocytosis includes aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematologic neoplasm (SM-AHN), mast cell leukemia (MCL), mast cell sarcoma (MCS), and extracutaneous mastocytosis. These more advanced forms of SM have a poor prognosis.

Rydapt (midostaurin) inhibits multiple receptor tyrosine kinases. Studies have shown that midostaurin or its major active metabolites inhibit the activity of wild type FLT3, FLT3 mutant kinases (ITD and TKD), KIT (wild type and D816V mutant), PDGFRα/β, VEGFR2, as well as members of the serine/threonine kinase PKC (protein kinase C) family. Rydapt (midostaurin) inhibits FLT3 receptor signaling and cell proliferation, and it induces apoptosis in leukemic cells expressing ITD and TKD mutant FLT3 receptors or overexpressing wild type FLT3 and PDGF receptors. It also inhibits KIT signaling, cell proliferation and histamine release and induce apoptosis in mast cells.

Resources:

Rydapt (midostaurin) product information, revised by Novartis Pharmaceuticals Corporation 11-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 1.2022 – Updated December 202, 2021 Available at https://www.nccn.org. Accessed May 13, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Systemic Mastocytosis Version 1.2022 – Updated April 14, 2022. Available at https://www.nccn.org. Accessed May 13, 2022.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.