BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

RYDAPT® (midostaurin)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for RYDAPT (midostaurin)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist or Hematologist

Indication
- Newly diagnosed acute myeloid leukemia (AML) with FLT3 mutation-positive, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy

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- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL)
- Other oncologic direct treatment uses listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- For AML: FLT3 mutation diagnosis confirmed using an FDA-approved test
- Negative pregnancy test for women of reproductive potential
- Eastern Cooperative Oncology Group (ECOG) Performance Status is 0–1

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety
- No concomitant use of strong CYP3A4 inducers (e.g., carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort, etc.)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (FLT3 mutation status, pregnancy test, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist or Hematologist

Clinical Response
- No evidence of disease progression or unacceptable toxicity

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Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No development of adverse drug effects that may exclude continued use such as:
  - Known or suspected interstitial lung disease or pneumonitis
  - ANC persistently low for greater than 21 days and suspected to be due to Rydapt
  - Platelet count persistently low for greater than 21 days and suspected to be due to Rydapt
  - Hemoglobin persistently low for greater than 21 days and suspected to be due to Rydapt
- No concomitant use of strong CYP3A4 inducers (e.g., carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort, etc.)

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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.

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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.

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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

NCCN recommendation definitions:
Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

National Cancer Institute Common Terminology for Adverse Events (NCI CTCAE) severity: Grade 1 = mild symptoms; 2 = moderate symptoms; 3 = severe symptoms; 4 = life-threatening symptoms.

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description

0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

Resources:

Rydapt (midostaurin) product information, revised by Novartis Pharmaceuticals Corporation 05-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 2.2025 – Updated January 27, 2025. Available at https://www.nccn.org. Accessed April 18, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Systemic Mastocytosis Version 1.2025 – Updated February 21, 2025. Available at https://www.nccn.org. Accessed April 18, 2025.

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.