BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**7/20/17**
LAST REVIEW DATE:	**8/02/18**
LAST CRITERIA REVISION DATE:	**8/02/18**
ARCHIVE DATE:	

RYDAPT® (midostaurin) oral capsule

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.

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. Individual is 18 years of age or older

  2. A confirmed diagnosis of **ONE** of the following:
     - Acute myeloid leukemia (AML) who are FLT3 mutation positive used in **EITHER** of the following:
       - Induction therapy in combination with standard cytarabine and daunorubicin
       - Consolidation therapy in combination with cytarabine
       - Single agent therapy after consolidation therapy
     - Aggressive systemic mastocytosis (ASM)
     - Systemic mastocytosis with associated hematologic neoplasm (SM-AHN)
     - Mast cell leukemia (MCL)

  3. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - **For AML**: FLT3 mutation diagnosis was made using an FDA-approved test
     - Pregnancy test in a woman of reproductive potential

  4. There are **NO** contraindications:
     - Contraindications include:
       - Hypersensitivity to midostaurin or to any excipients

  5. Will not be used as single agent for induction therapy for AML

  6. Will not be use with strong CYP3A4 inducers such as Carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort

  7. Woman patient of child bearing potential should use effective contraception during and after therapy and for at least 4 months after the last dose

  8. Woman patient who is breast feeding an infant or child should stop breast feeding during and for at least 4 months after therapy

  9. Male patient with a female partner of reproductive potential should use effective contraception during treatment and for 4 months after the last dose

  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's condition responded while on therapy

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- Response is defined as:
  - No evidence of disease progression
  - No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Known or suspected interstitial lung disease or pneumonitis
     - ANC persistently low for > 21 days and is suspected to be due to Rydapt
     - Platelet count persistently low for > 21 days and is suspected to be due to Rydapt
     - Hemoglobin persistently low for > 21 days and is suspected to be due to Rydapt

4. There are no significant interacting drugs

Renewal duration: 12 months

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). Package Insert. Revised by manufacturer 04/2017. Accessed 05-23-2017.

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.

Lim KH, Tefferi A, Lasho TL, et al. Systemic mastocytosis in 342 consecutive adults: survival studies and prognostic factors. Blood. 2009 June 4; 113 (23):5727-5736

Rotolo A, Familiari U, Nicoli P, et al. Systemic Mastocytosis: An Intriguing Disorder. 2012 Hematology - Science and Practice, Dr. Charles Lawrie (Ed.), ISBN: 978-953-51-0174-1, InTech, Available from: http://www.intechopen.com/books/hematology-science-andpractice/mast-cell-disease

Cohen SS, Stine Skovbo S, Vestergaard H, et al. Epidemiology of systemic mastocytosis in Denmark. British Journal of Haematology, 2014, 166 (4): 521–528

Pardanani A. Systemic mastocytosis in adults: 2015 update on diagnosis, risk stratification, and management. Annual Clinical Updates in Hematological Malignancies. Am J Hematol 2015 March; 90 (5):251-262

Arock M, Akin C, Hermine O, Valent P. Current treatment options in patients with mastocytosis: status in 2015 and future perspectives. Eur J Haematology 2015, 94 (6): 474–490

NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia. Version 1.2018, Feb 7, 2018. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

UpToDate: Mastocytosis (cutaneous and systemic): Epidemiology, pathogenesis, and clinical manifestations. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/mastocytosis-cutaneous-and-systemic-epidemiology-pathogenesis-and-clinical-manifestations?search=systemic%20mastocytosis&source=search_result&selectedTitle=1~94&usage_type=default&display_rank=1

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UpToDate: Systemic mastocytosis: Management and prognosis. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/systemic-mastocytosis-management-and-prognosis?search=systemic%20mastocytosis&source=search_result&selectedTitle=2~94&usage_type=default&display_rank=2#H29

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.