BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

Dasatinib oral tablet
PHYRAGO® (dasatinib) oral tablet
SPRYCEL® (dasatinib) oral tablet
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 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.

Criteria:

➢ **Criteria for initial therapy:** Sprycel (dasatinib), Phyrago (dasatinib), or generic dasatinib are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Gastroenterologist depending upon indication or use

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. **For Sprycel, Phyrago, or generic dasatinib:** Adult patient (18 years of age or older) with:
        i. Newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase

ii. Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
iii. Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy

b. **For Sprycel and generic dasatinib only:** Pediatric patient (1 year of age or older) with:
i. Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase. [**Note:** Phyrago (dasatinib) is not indicated in pediatric individuals]
ii. Newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy [**Note:** Phyrago (dasatinib) is not indicated in pediatric individuals]

c. 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

3. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
a. Liver function tests (bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase)
b. Serum potassium, magnesium, and uric acid are within normal range

4. **For brand Sprycel and Phyrago (dasatinib):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **generic dasatinib** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual is not using significant interacting drugs such as H2 antagonists (e.g., cimetidine, ranitidine, etc.) or proton pump inhibitors (e.g., omeprazole, lansoprazole, etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Sprycel (dasatinib), Phyrago (dasatinib), or generic dasatinib are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Gastroenterologist depending upon indication or use

2. Individual's condition has responded while on therapy with response defined as the following:
a. Documented evidence of efficacy, disease stability and/or improvement
b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. **For brand Sprycel and Phyrago (dasatinib):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **generic dasatinib** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed significant adverse drug effects that may exclude continued use such as:
    a. Myelosuppression (e.g., neutropenia, thrombocytopenia, anemia)
    b. Bleeding
    c. Marked fluid retention
    d. Pleural effusion
    e. Pulmonary arterial hypertension
    f. Stevens-Johnson syndrome
    g. Erythema multiforme
    h. Hepatotoxicity as measured by elevations in bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase

6. Individual is not using significant interacting drugs such as H2 antagonists (e.g., cimetidine, ranitidine, etc.) or proton pump inhibitors (e.g., omeprazole, lansoprazole, etc.)

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:

Dasatinib (generic and brand Sprycel) is a kinase inhibitor is indicated for the treatment of adults with newly diagnosed with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase; adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib; adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy; and for the treatment of pediatric patients 1 year of age and older with Ph+ CML in chronic phase; and pediatric patients 1 year of age and older with newly diagnosed Ph+ ALL in combination with chemotherapy. Phyrago (dasatinib) is indicated for the treatment of adults with newly diagnosed with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase; adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib; adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy. It is not indicated for pediatric use.

Dasatinib inhibits several kinases. It is predicted to bind to multiple conformations of the ABL kinase. *In vitro*, dasatinib was active in leukemic cell lines representing variants of imatinib-sensitive and -resistant disease.

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Dasatinib inhibited the growth of CML and ALL cell lines that overexpress BCR-ABL. Under the conditions of the assays, dasatinib was able to overcome imatinib-resistance resulting from BCR-ABL kinase domain mutations, activation of alternate signaling pathways involving the SRC family kinases (LYN, HCK), and multi-drug resistance gene overexpression.

Definitions:

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

Accelerated Phase CML:

Modified Criteria used at MD Anderson Cancer Center (most commonly used in clinical trials)
Peripheral blood blasts ≥ 15% and < 30% Peripheral blood blasts and promyelocytes combined ≥ 30% Peripheral blood basophils ≥ 20% Platelet count ≤ 100 x 10^9/L unrelated to therapy Additional clonal cytogenetic abnormalities in Ph+ cells
Semin Hematol 1988;25:49-61 Br J Haematol 1997;99:30-35 Blood 1993;82:691-703 Blood 2002;99:1928-1937

Blast Phase CML:

World Health Organization Criteria	International Bone Marrow Transplant Registry
Blasts ≥ 20% of peripheral white blood cells or of nucleated bone marrow cells Extramedullary blast proliferation Large foci or clusters of blasts in the bone marrow biopsy	≥ 30% blasts in the blood, marrow, or both Extramedullary infiltrates or leukemic cells
NCCN Chronic myeloid leukemia. Version 1.2018, July 26, 2017	

Treatment options based on BCR-ABL1 mutation profile:

Contraindicated Mutations	Therapy
AA337T, P465S	Asciminib
T315I/A, F317L/V/I/C, V299L	Dasatinib
T315A, Y253H, E255K/V, F359V/C/I	Nilotinib
T315A, V299L, G250E, F317L	Bosutinib
None	Ponatinib, Omacetaxine, allogeneic HCT, or clinical trial

- Patients with disease that is resistant to primary treatment with imatinib should be treated with nilotinib, dasatinib, or bosutinib in the second-line setting, taking into account BCR-ABL1 kinase domain mutation status
- Patients with disease that is resistant to primary treatment with bosutinib, nilotinib, or dasatinib could be treated with an alternative TKI (other than imatinib) in the second-line setting.

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Definitions for response and relapse in CML:

CHR	Complete normalization of peripheral blood counts with leukocyte count < 10 x 10^9/L Platelet count < 450 x 10^9/L No immature cells (such as myelocytes, promyelocytes, or blasts) in peripheral blood No signs & symptoms of disease, with disappearance of palpable splenomegaly
CyR	Complete CyR (CCyR): no Ph+ metaphases (correlates to *BCR-ABL (IS)* ≤ 1% (> 0.1-1%)) Major CyR: 0-35% Ph+ metaphases Partial CyR (PCyR): 1-35% Ph+ metaphases Minor CyR: > 35%-65% Ph+ metaphases
MR	Early MR (EMR) – *BCR-ABL1 (IS)* ≤ 10% at 3 and 6 months Major MR (MMR) – *BCR-ABL1 (IS)* ≤ 0.1% or ≥ 3 log reduction in *BCR-ABL1* mRNA from the standardized baseline, if qPCR (IS) is not available Deep molecular response (DMR): MR4.0: *BCR-ABL1 (IS)* ≤ 0.01% or MR4.5: *BCR-ABL1 (IS)* ≤ 0.0032%
Relapse	Any sign of loss of response defined as hematologic or cytogenetic Any sign of loss of CCyR or its molecular response corelate defined as an increase in *BCR-ABL1* transcript >1% 1 log increase in *BCR-ABL1* transcript levels with loss of MMR
CHR: complete hematologic response CyR: cytogenetic response MR: molecular response IS: International scale – the ratio of the BCR-ABL1 transcriptions to ABL1 transcripts	

Molecular response International Scale:

	International Scale (IS)
MR 2	Detectable disease at a level of ≤ 1% on the IS (≥ 2 log reduction from the standardized baseline). This level of response roughly corresponds to a "complete cytogenetic response"
MR 3	Detectable disease at a level of ≤ 0.1% on the IS (≥ 3 log reduction from the standardized baseline). This level of response has been termed a "major molecular response"
MR 4	Either detectable disease at a level of ≤ 0.01% on the IS (≥ 4 log reduction) **or** undetectable disease in cDNA with ≥ 10,000 ABL1 transcripts. This level of response requires that the assay being used is sensitive enough to detect a single abnormal transcript amongst 10,000 normal ABL1 transcripts
MR 4.5	Either detectable disease at a level of ≤ 0.0032% on the IS (≥ 4.4 log reduction) **or** undetectable disease in cDNA with ≥ 32,000 ABL1 transcripts. This level of response requires that the assay being used is sensitive enough to detect a single abnormal transcript amongst 32,000 normal ABL1 transcripts

Monitoring Response to TKI Therapy and Mutational Analysis:

Test	Recommendation
Bone marrow cytogenetic	• At diagnosis • Failure to reach response milestone • Any signs of loss of response (defined as hematologic or cytogenetic relapse
Quantitative RT-PCT (qPCR) using IS	• At diagnosis • Every 3 months after initiating treatment. After *BCR-ABL1* (IS) ≤ 1 % (> 0.1-1%) has been achieved, every 3 months x 2 y and every 3-6 months thereafter • If there is a 1-log increase in *BCR-ABL1* transcript levels with MMR, qPCR should be repeated in 1-3 months
BCR-ABL1 kinase domain mutation analysis	• Chronic phase ➢ Failure to reach response milestone ➢ Any signs of loss of response (defined as hematologic or cytogenetic relapse

	➢ 1-log increase in *BCR-ABL1* transcript levels and loss of MMR • Disease progression to accelerated or blast phase

Resources:

Dasatinib tab product information, revised by Apotex Corp. 09-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 05, 2024.

Phyrago (dasatinib) tab product information, revised by Nanocopoeia. 12-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 01, 2025.

Sprycel (dasatinib) tab product information, revised by E. R. Squibb & Sons, LLC. 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 05, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Lymphoblastic Leukemia Version 3.2024 – Updated December 20, 2024. Available at https://www.nccn.org. Accessed February 01, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Pediatric Acute Lymphoblastic Leukemia Version 2.2025 – Updated December 16, 2024. Available at https://www.nccn.org. Accessed February 01, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Myeloid Leukemia Version 3.2025 – Updated November 27, 2024. Available at https://www.nccn.org. Accessed February 01, 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.