Clinical Policy: Dasatinib (Sprycel)

Reference Number: CP.PHAR.72
Effective Date: 06/12 Revision Log
Last Review Date: 07/17

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for dasatinib (Sprycel®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Sprycel is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of chronic myeloid leukemia (CML);
2. CML is Philadelphia chromosome positive (Ph+) or BCR-ABL1 positive;
3. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Newly diagnosed CML in chronic phase;
      ii. Chronic, accelerated or blast phase CML with history of resistance or intolerance to imatinib;
   b. Off-label NCCN recommended use (any of the following):
      i. Chronic phase CML with history of resistance or intolerance to nilotinib;
      ii. As a single agent for accelerated or myeloid blast phase CML;
      iii. In combination with steroids as primary treatment for lymphoid blast phase CML;
      iv. In combination with induction chemotherapy followed by stem cell transplant for blast phase CML;
      v. Post stem cell transplant;
      vi. Positive for Y253H, E255K/V or F359V/C/I mutation.
4. Dose does not exceed 180 mg/day.

Approval duration: 6 months

B. Acute Lymphoblastic Leukemia (must meet all):

1. Diagnosis of acute lymphoblastic leukemia (ALL);
2. ALL is Ph+;
3. Member meets a or b:
   a. FDA approved use: following resistance or intolerance to prior therapy:
   b. Off-label NCCN recommended use (any of the following):
      i. Induction or consolidation therapy;
      ii. Maintenance therapy (a or b):

a) In combination with vincristine and prednisone with or without methotrexate and mercaptopurine;
b) Post stem cell transplant;

iii. Relapsed or refractory disease (a, b or c):
a) As a single agent;
b) In combination with an induction regimen not previously given;
c) If positive for a Y253H, E255K/V, or F359V/C/I mutation;

4. Dose does not exceed 180 mg/day.

Approval duration: 6 months

C. Other diagnoses/indications:

1. Additional NCCN recommended uses meeting NCCN categories 1, 2a or 2b are covered for the following indications per the CP.PHAR.57 Global Biopharm policy:
   a. Gastrointestinal stromal tumor.

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Sprycel (dasatinib) is a kinase inhibitor. Dasatinib, at nanomolar concentrations, inhibits the following kinases: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRβ. Based on modeling studies, dasatinib is predicted to bind to multiple conformations of the ABL kinase. *In vitro,* dasatinib was active in leukemic cell lines representing variants of imatinib mesylate-sensitive and resistant disease. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines overexpressing 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.

Formulations:

Tablet, oral administration

- Sprycel: 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, 140 mg

FDA Approved Indications:
Sprycel (dasatinib) is a kinase inhibitor/oral tablet formulation indicated for treatment of adults with:

- Newly diagnosed Ph+ CML in chronic phase.
- Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.
- Ph+ ALL with resistance or intolerance to prior therapy.

Appendices
Appendix A: Abbreviation Key
ALL: acute lymphoblastic leukemia
CML: chronic myelogenous leukemia
Ph+: positive Philadelphia chromosome

Reviews, Revisions, and Approvals	Date	Approval Date
Updated re-auth questions for disease progression, loss of response, and toxicity. Updated all approval periods to 6 months or up to 12 months (CML only)	07/13	07/13
Annual Clinical Review Updated approval timeframe in Figure 1 algorithm Added cytogenetic response question Figure 2 and 3 algorithms Added to and updated background	07/14	07/14
Reworked narrative for CML and ALL per NCCN guidelines. Removed requests for documentation from all algorithms. Resistance (Appendix B) used in Figures 1 and 2. Combined Figures 2 and 3 (CML); modified monitoring per NCCN guidelines – see corresponding narrative and Appendix C. Restructured safety section into list per package insert.	06/15	07/15
Policy converted to new template. Age removed under FDA approved use per new oncology template guidelines (but retained if specified in the NCCN recommended uses). Criteria specifying "Ph+" for ALL and "Ph+ and/or BCRABL1 positive" for CML follows NCCN compendial recommendations. Detailed resistance and therapeutic response criteria removed. NCCN compendial uses for CML and ALL added if not considered covered by the CML/ALL FDA approved uses. The remaining NCCN compendial use for GIST is added.	06/16	07/16
Added NO at beginning of II.A.2, which was erroneously left off.	02/17	
CML NCCN: 1) "myeloid" is inserted to describe blast phase CML; 2) "In combination with steroids as primary treatment for CML in lymphoid blast phase" is added; 3) "for relapse" is deleted from "post stem cell transplant therapy" 4) CML positive for a Y253H, E255K/V, or F359V/C/I mutation is added; 5) continuing treatment with Sprycel is deleted from initial criteria.	06/17	07/17

Reviews, Revisions, and Approvals	Date	Approval Date
ALL NCCN: 1) Specific regimens are deleted; 2) "After complete response to induction therapy is achieved following transplantation" is replaced with "maintenance therapy post stem cell transplant"; 3) "with or without methotrexate and mercaptopurine" is added to the maintenance vincristine regimen; 4) mutation history is separated from the "relapsed/refractory disease" heading and moved below it. Maximum dose added."No disease progression of unacceptable toxicity" is replaced with "Member is responding positively to therapy". Reasons to discontinue are removed. Approval periods changed from 3/6 to 6/12 mos.		

References

1. Synribo Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; April 2017. Available at http://packageinserts.bms.com/pi/pi_sprycel.pdf. Accessed June 15, 2017.
2. Dasatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed June 15, 2017.
3. Chronic myelogenous leukemia (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed June 19, 2017.
4. Acute lymphoblastic leukemia (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed June 19, 2017.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.