Clinical Policy: Dasatinib (Sprycel, Phyrago)

Reference Number: CP.PHAR.72
Effective Date: 06.01.12
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Dasatinib (Sprycel®, Phyrago™) is a kinase inhibitor.

FDA Approved Indication(s)

Sprycel and Phyrago are indicated for the treatment of:

- Newly diagnosed adults 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 Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy

Sprycel is indicated for the treatment of:

- Pediatric patients 1 year of age and older with Ph+ CML in chronic phase
- Pediatric patients 1 year of age and older with newly diagnosed Ph+ ALL in combination with chemotherapy

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia and Acute Lymphoblastic Leukemia (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Ph+ (BCR-ABL1-positive) CML;
   b. Ph+ (BCR-ABL1-positive) ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age is one of the following (a or b):
   a. Sprycel: ≥ 1 year;
   b. Phyrago: ≥ 18 years;
4. Member does not have the following mutations: T315I/A, F317L/V/I/C or V299L;
5. One of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

6. For brand Sprycel or Phyrago requests, member must use generic dasatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):* ≠
   a. Pediatrics, age < 18 years: Dose does not exceed the weight-based dosing in Section V;
   b. Adults, age ≥ 18 years: Dose does not exceed 180 mg per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*
≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Gastrointestinal Stromal Tumor (off-label) (must meet all)**:**
1. Diagnosis of unresectable, recurrent, progressive, or metastatic gastrointestinal stromal tumor (GIST; a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist;
3. Age is one of the following (a or b):
   a. Sprycel: ≥ 1 years;
   b. Phyrago: ≥ 18 years;
4. Failure of imatinib (Gleevec®) or Ayvakit®, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization is required for imatinib and Ayvakit.*
5. For brand Sprycel or Phyrago requests, member must use generic dasatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).* ≠
   **Prescribed regimen must be FDA-approved or recommended by NCCN*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Bone Cancer (off-label) (must meet all)**:**
1. Diagnosis of metastatic chondrosarcoma or recurrent chordoma;
2. Prescribed by or in consultation with an oncologist;
3. Age is one of the following (a or b):
   a. Sprycel: ≥ 1 years;
   b. Phyrago: ≥ 18 years;
4. For chordoma, one of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

5. For brand Sprycel or Phyrago requests, member must use generic dasatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).* ≠
   **Prescribed regimen must be FDA-approved or recommended by NCCN*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Off-Label Indications (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia (MLNE) and ABL1 rearrangement in blast or chronic phase;
   b. KIT-positive metastatic or unresectable melanoma as second-line or subsequent therapy (i.e., following BRAF-targeted therapy);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age is one of the following (a or b):
   a. Sprycel: ≥ 1 years;
   b. Phyrago: ≥ 18 years;
4. One of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
5. For brand Sprycel or Phyrago requests, member must use generic dasatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).* ≠
   **Prescribed regimen must be FDA-approved or recommended by NCCN*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Sprycel or Phyrago for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Sprycel or Phyrago requests, member must use generic dasatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):* ≠
   a. Adults age ≥ 18 years, bone cancer, or GIST: New dose does not exceed 180 mg per day;
   b. Pediatrics age < 18 years for CML or ALL: New dose does not exceed weight-based dosing in Section V;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*
≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM - 12 months
Commercial - 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CML: chronic myelogenous leukemia
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
MLNE: myeloid/lymphoid neoplasms with eosinophilia
Ph+: positive Philadelphia chromosome

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

imatinib (Gleevec)	ALL:
	• Adult: 600 mg/day PO for relapsed / refractory Ph+ ALL
	• Pediatric: 340 mg/m^2/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL
	Chordoma: 400 mg PO BID
	CML:
	• Adult:
	  ○ 400-600 mg/day PO for chronic phase
	  ○ 600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID)
	• Pediatric: 340 mg/m^2/day PO for chronic phase
	GIST: 400 mg PO QD to 400 mg PO BID
	MLNE: 100-400 mg PO QD [NCCN]
		Adults: 800 mg/day
		Pediatrics: 600 mg/day

Ayvakit (avapritinib)	GIST: 300 mg PO QD	300 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Dose optimization is the consolidation of multiple units of lower strength to the fewest units required to achieve the desired daily dose/regimen based on commercially available dosage strengths. Requests for multiple units of a lower strength will be denied when the plan-approved QL for such medication is exceeded and higher strength units are commercially available to achieve the desired daily dose/regimen.

Appendix E: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CML	Adults: • Chronic phase: 100-140 mg/day PO • Accelerated, myeloid phase, or lymphoid blast phase: 140-180 mg/day PO Pediatrics: Initial weight-based dosing PO QD: • Weight 10 to < 20 kg: 40 mg • Weight 20 to < 30 kg: 60 mg • Weight 30 to < 45 kg: 70 mg • Weight ≥ 45 kg: 100 mg Dose escalation PO QD: • Starting dose 40 mg can be escalated to 50 mg • Starting dose 60 mg can be escalated to 70 mg • Starting dose 70 mg can be escalated to 90 mg • Starting dose 100 mg can be escalated to 120 mg	Adults: 180 mg/day Pediatrics: 120 mg/day

Indication	Dosing Regimen	Maximum Dose
ALL	Adults: 140-180 mg/day PO Pediatrics: Weight-based dosing PO QD • Weight 10 to < 20 kg: 40 mg • Weight 20 to < 30 kg: 60 mg • Weight 30 to < 45 kg: 70 mg • Weight ≥ 45 kg: 100 mg	Adults: 180 mg/day Pediatrics: 100 mg/day

VI. Product Availability

Tablets: 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, 140 mg

VII. References

1. Sprycel Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; February 2023. Available at: https://packageinserts.bms.com/pi/pi_sprycel.pdf. Accessed January 22, 2024.
2. Phyrago Prescribing Information. New Brighton, MN: Nanocopoeia; December 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216099s000lbl.pdf. Accessed December 29, 2023.
3. Dasatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 12, 2024.
4. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 2.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed January 22, 2024.
5. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed January 22, 2024.
6. National Comprehensive Cancer Network Guidelines. Pediatric Acute Lymphoblastic Leukemia Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed January 22, 2024.
7. National Comprehensive Cancer Network Guidelines. Gastrointestinal Stromal Tumors (GISTs) Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed January 22, 2024.
8. National Comprehensive Cancer Network Guidelines. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed January 22, 2024.
9. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed January 22, 2024.
10. National Comprehensive Cancer Network Guidelines. Melanoma: Cutaneous Version 3.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed January 22, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: HIM nonformulary language removed; references reviewed and updated.	02.11.20	05.20
2Q 2021 annual review: added off-label indication myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement in chronic phase; added generic redirection language to "must use" since oral oncology product; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); added standard oral oncology generic redirection language; references reviewed and updated.	02.21.21	05.21
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; WCG.CP.PHAR.72 to be retired and approval durations consolidated to 6 months; per NCCN for CML and ALL added exclusions for mutations that are contraindicated, for GIST added Ayvakit and removed Sutent and Stivarga as prior therapy options; for CML, AML, chordoma, and myeloid/lymphoid neoplasms added that member has contraindication, intolerance, or disease progression on imatinib or allowed by-passing of redirection if state regulations do not allow step therapy in certain oncology settings; references reviewed and updated.	01.27.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	
2Q 2023 annual review: for MLNE added NCCN supported use in the blast phase; added off-label use in melanoma; modified continued approval duration for Medicaid and HIM lines of business from 6 to 12 months; references reviewed and updated.	01.06.23	05.23
RT4: Added brand Phyrago for adult use to all indications; updated Appendix D to include Oklahoma.	01.03.24	
2Q 2024 annual review: no significant changes; for dosing limits added clarification that dose optimization is required in each criteria set; added Appendix D to define dose optimization; for Appendix E, updated state OH description to include Commercial line of business; references reviewed and updated.	01.10.24	05.24

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.