



PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Sprycel® (dasatinib tablets for oral use – Bristol-Myers Squibb)

TAC APPROVAL DATE: 03/20/2019

OVERVIEW

Sprycel, a tyrosine kinase inhibitor (TKI), is indicated for the treatment of adults with: newly-diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP); chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including Gleevec® (imatinib tablets, generic); and Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy.¹ Additionally, Sprycel is indicated for the treatment of pediatric patients ≥ 1 year of age with Ph+ CML in CP and newly-diagnosed Ph+ ALL in combination with chemotherapy. Currently, there are four other TKIs approved for the treatment of CP Ph+ CML: Gleevec, Sprycel® (dasatinib tablets), Bosulif® (bosutinib tablets), Tasigna® (nilotinib capsules), and Iclusig® (ponatinib tablets).²⁻⁵ These agents are indicated for the treatment of CP Ph+ CML in various phases; some TKIs are indicated after resistance or intolerance to prior therapy. Iclusig is approved for patients with T315I-positive CML and in adult patients with CML for whom no other TKI therapy is indicated.⁵ Gleevec also has indications related to use in ALL.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CML (version 1.2019 – August 1, 2018) state that for patients with CP CML with a low-risk score, the primary treatment recommended includes a first-generation TKI (Gleevec or generic imatinib 400 mg QD [Category 1]), or a second-generation TKI (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]).⁶ For patients with CP CML with an intermediate- or high-risk score, a second-generation TKI is preferred (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]). A first-generation TKI (Gleevec or generic imatinib 400 mg QD) is an alternative [Category 2A]. Iclusig is an option for patients with a T315I mutation and for with disease that has not responded to multiple TKIs or in whom another TKI is not indicated.

The NCCN guidelines for ALL (version 1.2018 – March 12, 2018) recommend Sprycel in a variety of clinical scenarios including induction therapy, maintenance, relapsed or refractory ALL and for use in specific mutations.⁷

The NCCN soft tissue sarcoma guidelines (version 2.2019 – February 4, 2019) indicate that Sprycel is a treatment option for patients with GIST as an additional option for patients who are no longer experiencing benefit from imatinib, Sutent® (sunitinib capsules), or Stivarga® (regorafenib tablets).⁸ It is noted that data are limited with Sprycel (e.g. unpublished, Phase II, small numbers, retrospective). However, it was suggested that Sprycel may be a more effective option for patients with the D842V mutation.⁸

The NCCN guidelines on bone cancer (version 1.2019 – August 1, 2018) recommend dasatinib for patients with chondrosarcoma or chordoma.³⁰

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Sprycel. All approvals are provided for 3 years in duration.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sprycel is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Acute Lymphoblastic Leukemia (ALL) That is Philadelphia Chromosome Positive (Ph+).**
Approve for 3 years.
2. **Chronic Myeloid Leukemia (CML) That is Philadelphia Chromosome Positive (Ph+).**
Approve for 3 years.

Other Uses with Supportive Evidence

3. **Gastrointestinal Stromal Tumor (GIST).** Approve for 3 years if the patient meets the following criteria (A, B, and C):
A) Patient has tried imatinib; AND
B) Patient has tried Sutent® (sunitinib capsules); AND
C) The patient has tried Stivarga® (regorafenib tablets).
4. **Chondrosarcoma or chordoma.** Approve for 3 years.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Sprycel has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Breast Cancer.** In one study (n = 75) Sprycel had limited activity in patients with advanced human epidermal growth factor receptor 2 (HER2)-positive and/or hormone-receptor (HR)-positive breast cancer.¹⁰ Of 69 evaluable patients, 3 patients had confirmed partial responses and 6 patients had stable disease for at least 16 weeks; all nine of these tumors were HR-positive (two were also HER2-positive).¹⁰ In one Phase II study (n = 31) Sprycel did not exhibit significant antitumor activity in patients with heavily pretreated metastatic breast cancer.¹¹ The trial was closed early because of a statistical boundary that required at least four patients (13%) without disease progression to continue accrual. None of the tumors showed the predefined optimal level of Src inhibition at Week 4. Sprycel is not addressed in the NCCN breast cancer guidelines (version 4.2018 – February 8, 2019).¹²
2. **Chronic Lymphocytic Leukemia (CLL).** In one Phase II study (n = 15) Sprycel demonstrated some activity in patients with relapsed and refractory CLL.¹² Partial responses were achieved in 3 of the 15 patients (20%). Among the remaining 12 patients, 5 patients had nodal responses, and 1

patient had a nodal and lymphocyte response but with severe myelosuppression. Another small Phase II study (n = 20) investigated one cycle of Sprycel monotherapy.¹³ Additional studies are needed. Sprycel is not cited in the NCCN chronic lymphocytic leukemia/small lymphocytic lymphoma guidelines (version 4.2019 – March 15, 2019).¹⁴

3. **Colorectal Cancer (CRC).** In one Phase II study (n = 19) Sprycel did not demonstrate clinical activity in previously treated patients with metastatic CRC.¹⁶ The study was terminated after the first stage due to lack of efficacy.¹⁶ A Phase I study (n = 12) investigated Sprycel in metastatic colorectal cancer.¹⁷ More data are needed. Sprycel is not addressed in the NCCN colon cancer guidelines¹⁸ nor in the NCCN rectal cancer guidelines.¹⁹
4. **Head and Neck Squamous Cell Carcinoma.** In one Phase II study (n = 15), Sprycel failed to demonstrate significant activity in patients with advanced head and neck squamous cell carcinoma, despite c-Src inhibition.²⁰
5. **Lung Cancer.** In one Phase II study (n = 21), Sprycel had no activity in patients with epidermal growth factor receptor (EGFR)-mutant lung adenocarcinoma with acquired resistance to Tarceva® (erlotinib tablets) and Iressa® (gefitinib tablets).²¹ No complete or partial responses were observed.
6. **Malignant Mesothelioma.** In one Phase II study (n = 46), single-agent Sprycel had no activity in malignant mesothelioma and was associated with pulmonary toxicities that prohibit its use in an unselected population.²²
7. **Melanoma.** In one Phase II study (n = 39) Sprycel demonstrated minimal activity in patients with chemotherapy-naïve unresectable stage 3/4 melanoma.²³ A total of two patients had confirmed partial responses lasting 64 and 24 weeks. A total of three patients had minor responses lasting 136, 64, and 28 weeks. The median progression-free survival (PFS) was 8 weeks; the 6-month PFS rate was 13%. Additional studies are needed. Sprycel is not addressed in the NCCN cutaneous melanoma guidelines (version 2.2019 – March 12, 2019).²⁴
8. **Non-Small Cell Lung Cancer (NSCLC).** In one Phase II study (n = 34) Sprycel demonstrated modest clinical activity that was lower than that observed in patients with NSCLC who received chemotherapy.²⁵ In one Phase I/II study (n = 34) Sprycel demonstrated modest clinical activity when used in combination with Tarceva in patients with advanced NSCLC.²⁶ Two partial responses and one bone response were observed; the disease control rate was 63%. Additional studies are needed. Sprycel is not addressed in the NCCN NSCLS guidelines (version 4.2017).²⁷
9. **Prostate Cancer, Metastatic Castration-Resistant.** Data are available regarding Sprycel in patients with castration-resistant prostate cancer.²⁸⁻³⁰ A Phase III, multicenter, multinational, randomized, double-blind, placebo-controlled trial involved adult males with chemotherapy-naïve, metastatic, castration-resistant prostate cancer who were randomized to receive docetaxel (75 mg/m² intravenously [IV] every 3 weeks plus oral prednisone 5 mg BID) plus either Sprycel (100 mg QD) or placebo until disease progression or until unacceptable toxicity occurred (n = 1,522).³⁰ After a median follow-up to 19 months, 914 patients had died. The median overall survival was 21.5 months for patients who were given Sprycel and 21.2 months for patients given placebo (P = 0.90). This trial does not support the addition of Sprycel to docetaxel in this population. Sprycel is not addressed in the NCCN prostate cancer guidelines (version 1.2019 – March 6, 2019).³¹

10. **Small Cell Lung Cancer.** In one Phase II study (n = 45) Sprycel did not reach the specified efficacy criteria in patients with chemosensitive relapsed small cell lung cancer; the study was terminated.³²
11. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes.	02/24/2016
Annual revision	No criteria changes.	03/01/2017
Annual revision	Removed the criteria allowing for approval if the patient has been started on Sprycel for an indication or condition addressed as an approval in the Recommended Authorization section (FDA-approved indication or other uses with supportive evidence section).	03/07/2018
Annual revision	Approval is now given for patients with chordoma and chondrosarcoma for 3 years.	03/20/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; TAC – Therapeutic Assessment Committee; CML – Chronic myelogenous leukemia; ALL – Acute lymphoblastic leukemia.