dasatinib (Sprycel®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO016

Description

Dasatinib (Sprycel) is an orally administered tyrosine kinase inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
dasatinib (Sprycel)	20 mg tablets	Philadelphia chromosome-positive (Ph+) Chronic myeloid leukemia (CML)/ Ph+ Acute lymphoblastic leukemia (ALL)	90 tablets/30 days
	50 mg tablets		30 tablets/30 days
	70 mg tablets		30 tablets/30 days
	80 mg tablets		30 tablets/30 days
	140 mg tablets		30 tablets/30 days
	100 mg tablets	Chronic phase CML	30 tablets/30 days
	70 mg tablets	Gastrointestinal Stromal Tumors (GIST)	60 tablets/30 days
generic dasatinib	20 mg tablets	Philadelphia chromosome-positive (Ph+) Chronic myeloid leukemia (CML)/ Ph+ Acute lymphoblastic leukemia (ALL)	90 tablets/30 days
	50 mg tablets		30 tablets/30 days
	70 mg tablets		30 tablets/30 days
	80 mg tablets		30 tablets/30 days
	140 mg tablets		30 tablets/30 days
	100 mg tablets	Chronic phase CML	30 tablets/30 days
	70 mg tablets	Gastrointestinal Stromal Tumors (GIST)	60 tablets/30 days

Initial Evaluation

I. **Dasatinib (Sprycel)** may be considered medically necessary when the following criteria below are met:
   A. Prescribed by, or in coordination with, an oncologist; **AND**
   B. Request is for generic dasatinib; **OR**
      1. If request is for brand Sprycel, generic dasatinib has been ineffective, not tolerated, or is contraindicated; **AND**
   C. A diagnosis of one of the following:
      1. **Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL); AND**
         i. Adult member with resistance or intolerance to prior therapy; **AND**
            a. If resistance to prior TKI therapy:

i. Member does not have BCR-ABL mutations T315I, V299L, or F317L; **OR**

ii. Newly diagnosed pediatric member ≥1 year of age; **AND**

iii. Used in combination with chemotherapy; **OR**

2. **Ph+ Chronic myeloid leukemia (CML)**; **AND**
   i. Adult or pediatric member with newly diagnosed Ph+ CML in chronic phase; **OR**
   ii. Adult or pediatric member with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy; **AND**
      a. If resistance to prior TKI therapy:
         i. Member does not have BCR-ABL mutations T315I, V299L, and F317L; **OR**
3. **Gastrointestinal Stromal Tumors (GIST); AND**
   i. BCR-ABL KD mutational status contains PDGFRA D842V mutation; **AND**
   ii. Member has tried and failed imatinib (Gleevec) AND sunitinib (Sutent) AND regorafenib (Stivarga) for the treatment of gastrointestinal stromal tumors

II. Dasatinib (Sprycel) is considered investigational when used for all other conditions, including but not limited to:
   A. Pancreatic cancer - Metastatic

Renewal Evaluation

I. No increase in the rate of disease progression while on therapy

Supporting Evidence

I. Per NCCN guidelines dasatinib (Sprycel) is not active against cells harboring the ABL mutations T315I, V299L, and F317L. Thus for patients with disease resistant to TKI therapy it becomes important to identify potential ABL mutations that may underlie the observed resistance to treatment.

II. The efficacy of Sprycel was investigated in open label trials in adult patients with Ph+ CML or Ph+ ALL whose disease was resistant to, or were intolerant to, imatinib: 1,158 patients had chronic phase CML, 858 patients had accelerated phase, myeloid blast phase, or lymphoid blast phase CML, and 130 patients had Ph+ ALL. Overall, 80% of patients had imatinib-resistant disease and 20% of patients were intolerant to imatinib. The primary efficacy endpoint of major cytogenetic response (MCyR) in chronic phase CML was met in 63% of patients. The primary efficacy endpoint of major hematologic response (MaHR) in accelerated phase, myeloid blast phase, lymphoid blast phase CML, and Ph+ ALL was met in 44% of Sprycel patients by 7 years.

III. Prior therapy includes a minimum of 30 to 60 day trial of imatinib 400mg or more per day without a complete hematologic response or discontinuation of imatinib therapy due to toxicity. Dosing may be escalated to 180 mg once daily in patients who do not achieve a hematologic or cytogenic response at the recommended dosage.

IV. In clinical trials imatinib intolerance was defined as inability to tolerate 400 mg or more of imatinib per day or discontinuation of imatinib because of toxicity.

V. The approval for Sprycel for pediatric patients with Ph+ ALL was based on findings from a phase II trial (NCT01460160), which demonstrated a 3-year event-free survival (EFS) 64.1% (95% CI, 52.4%-74.7%) in 78 pediatric patients with newly diagnosed B-cell precursor Ph+ ALL. This trial compared dasatinib (Sprycel) plus chemotherapy versus chemotherapy alone in the external historical control trial. Another TKI, Gleevec, was approved for this same patient population in 2013. There is no head-to-head study comparing Gleevec to Sprycel for Ph+ ALL in pediatric patients. The NCCN guidelines recommend all tyrosine kinase inhibitors within the same 2a recommendation.

VI. Dasatinib (Sprycel) in the setting of newly diagnosed chronic phase CML in adults was approved based on the DASISION trial (NCT00481247) an open label, randomized trial comparing Sprycel to imatinib. The primary endpoint of rate of confirmed complete cytogenetic response (CCyR) within 12 months was achieved in 76.8% of Sprycel patients versus 66.2% of imatibib patients. After 60 months follow-up, median time to confirmed complete cytogenetic response was 3.1 months in 215 Sprycel responders and 5.8 months in 204 imatinib responders.

VII. Treatment of Ph+ CML in chronic phase in pediatric patients ≥1 year of age was evaluated in two pediatric studies: an open-label, non-randomized dose-ranging trial (NCT00306202) and an open label, non-randomized, single-arm trial (NCT00777036). With a median follow-up of 4.5 years in newly diagnosed patients, the median durations of CCyR, MCyR, and major molecular response (MMR) could not be estimated as more than half of the responding patients had not progressed at the time of data cut-off. With a median follow-up of 5.2 years in imatinib-resistant or -intolerant patients, the median durations of CCyR, MCyR, and MMR could not be estimated as more than half the responding patients had not progressed at the time of data cut-off.

VIII. In the setting of GIST, NCCN guidelines recommend following imatinib and sutinib, therapy with regorafenib (Cat 1). Regorafenib may then be followed by dasatinib (Sprycel) (Cat 2a). Dasatinib (Sprycel) is thus recommended as a fourth line agent in the setting of D842V mutation status.

IX. Dasatinib (Sprycel) has been studied in patients of various ages, ranging all the way down to 1 year old, in the treatment of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL). The COG AALL-0622 trial included patients 1-30 years of age (n=60) with Ph+ ALL that were considered at standard risk (i.e., allogenic hematopoietic stem-cell transplantation was not recommended yet). Patients were treated with an intensive chemotherapy regimen combined with dasatinib 60 mg/m2. Patients received dasatinib 60 mg/m2 continuously if they completed therapy through week 23 without dose-limiting toxicities. Results demonstrated the 3-year event-free survival (EFS) rate was 84.6% + 5.7%. There were no deaths resulting from toxicity

and the combination of dasatinib plus intensive chemotherapy was found to be safe. Long term follow-up of dasatinib (Sprycel) in the treatment of Ph+ ALL was completed in various durations and chemotherapy regimens. Those studies demonstrated consistent, positive results compared to AALL-0622 regarding event-free survival (74.6%, median follow-up of 53 months). In addition, various long-term follow-up studies demonstrated similar overall survival rates (e.g., around 40%). Grade 3 and 4 adverse events observed include bleeding, pleural and/or pericardial effusions, diarrhea, infections, and elevated transaminases with none being a concern. Overall, these are lower quality trials (i.e., small population, surrogate markers); however, there is moderate confidence in the data as there are multiple trials that overall porin in the direction of positive results.

Investigational or Not Medically Necessary Uses

I. Pancreatic Cancer Metastatic
   A. Sprycel is currently being evaluated for use in metastatic pancreatic cancer and is the subject of ongoing clinical trials. A phase 2 study of dasatinib (Sprycel) added to gemcitabine for subjects with locally-advanced pancreatic cancer (LAPC) was recently completed.

** The Moda Split Fill program is a physician-centric, patient engagement program intended to provide enhanced patient and physician support while accomplishing the goals of minimizing waste and avoiding incremental healthcare costs due to medication intolerance and unexpected change or termination of therapy regimen. Under the Split Fill program, the identified medications are programmed for fills of up to a 14 or 15-day supply for the duration of the first three months (86 or 90 days) of therapy. This program affords additional interactions with a specialty pharmacist, allowing more frequent assessments of side effects and barriers to adherence. Each fill is administered at half of the member cost-share, thereby reducing the economic burden if they must discontinue therapy mid-month.*

References

1. Sprycel [package insert]. Princeton, NJ. Bristol-Myers Squibb Company. December 2018
2. Trent JC,Wathen K, von Mehren M, et al. A phase IIstudy of dasatinib for patients with imatinib-resistant gastrointestinal stromal tumor (GIST) [abstract]. J Clin Oncol 2011; 29 (15_Suppl): Abstract 10006
   Demetri GD, Lo Russo P, MacPherson IR, et al. Phase Idose-escalation and pharmacokinetic study of dasatinib in patients with advanced solid tumors. Clin Cancer Res 2009; 15:6232-6240.
3. Dewaele B, Wasag B, Cools J, et al. Activity of dasatinib, a dual SRC/ABL kinase inhibitor, and IPI-504, a heat shock protein 90 inhibitor, against gastrointestinal stromal tumor-associated PDGFRAD842V mutation. Clin Cancer Res. 2008;14(18):5749-58.
4. Demetri GD, Reichardt P, Kang YK, et al. Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomized, placebo-controlled, phase 3 trial. Lancet. 2013;381(9863):295-302.
   National Comprehensive Cancer Network. NCCN Clinical Practice Guideline in Oncology. Soft Tissue Sarcoma Version 2.2019. February 7, 2019.

Policy Implementation/Update:

Action and Summary of Changes	Date
Added supporting evidence for dasatinib in the treatment of Ph+ ALL.	02/2025
Added generic dasatinib to the policy and required a t/f of generic dasatinib prior to use of branded product	09/2024
Updated to new format. Added new indication in pediatric patients with newly diagnosed Ph+ ALL. Added patient specific mutation assessment in the relapsed CML and ALL settings.	02/2019
Removed pregnancy question and adult only language as this is now approved for pediatric indications. Added regorafenib as an additional prior agent in GIST indication, as well as assessing patient specific mutation that received benefit in GIST in the salvage setting.	01/2018
Previous Reviews	03/2017