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

dasatinib (Sprycel)	Indication	Quantity Limit	DDID
20 mg tablets	Philadelphia chromosome-positive (Ph+) Chronic myeloid leukemia (CML)/ Ph+ Acute lymphoblastic leukemia (ALL)	90 tablets/30 days	120505
50 mg tablets		30 tablets/30 days	120506
70 mg tablets		30 tablets/30 days	120504
80 mg tablets		30 tablets/30 days	163348
140 mg tablets		30 tablets/30 days	163349
100 mg tablets	Chronic phase CML	30 tablets/30 days	135944
70 mg tablets	Gastrointestinal Stromal Tumors (GIST)	60 tablets/30 days	120504

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. 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 who 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. 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.

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.

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.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guideline in Oncology. Soft Tissue Sarcoma Version 2.2019. February 7, 2019.

Policy Implementation/Update:

Date Created	March 2017
Date Effective	March 2017
Last Updated	February 2019
Last Reviewed	01/2018, 02/2019

Action and Summary of Changes	Date
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