



Therapeutic Class ReviewSM

Oncology – dasatinib (Sprycel[®])

December 2006

New Product for Review:

dasatinib (SprycelTM) [Bristol-Myers Squibb]

model

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: 3

1- dossier w/missing components

2- all components present, except pharmacoeconomic

3- all components present (comprehensive)

Available Therapeutic Alternatives: Chronic myeloid leukemia (CML) and Philadelphia positive acute lymphoblastic leukemia (Ph+ ALL)

Preferred/Formulary	Non-preferred/non-formulary
COVERED UNDER PHARMACY BENEFIT	
imatinib mesylate (Gleevec [®]) [Novartis]	interferon alfa-2a (Roferon-A [®]) [Roche]
	dasatinib (Sprycel TM) [Bristol-Myers Squibb]
COVERED UNDER MEDICAL BENEFIT	
cytarabine (Cytosar-U)*	

*interferon alfa used in combination with cytarabine

Disease Overview:

CML:

- CML accounts for approximately 15% of all leukemias, with an incidence of 1 to 2 cases per 100,000 people.
- CML is a blood cancer that originates in the stem cells, causing overproduction of white blood cells.
- Imatinib (Gleevec) is the current standard of care. Bone marrow transplantation is the only curative treatment, but carries significant risk.

Ph + ALL:

- Ph + ALL accounts for approximately 2.3% of all leukemias.
- Ph + ALL results from uncontrolled proliferation and expansion of immature lymphoid cells in the blood, bone marrow, and other organs.
- Imatinib (Gleevec) is the current standard of care. Bone marrow transplantation is the only curative treatment, but carries significant risk.

Executive Summary

- Dasatinib (Sprycel) received accelerated approval for the treatment of CML and Ph+ ALL in patients resistant or intolerant to imatinib (Gleevec) based on:
 - Cytogenetic and hematologic response rates (intermediate endpoint).
 - Limited availability of treatment options for patients intolerant/resistant to imatinib (Gleevec).
- There is no overall survival information available for dasatinib (Sprycel).
- Dasatinib (Sprycel) will most likely be marketed as:
 - The only alternative in patients with CML or Ph+ ALL who fail or do not tolerate therapy with imatinib (Gleevec).
 - A well-tolerated option with lower potential for resistance.
- In vitro studies in patients with CML have demonstrated resistance to dasatinib (Sprycel) which resulted in disease progression.
- Post marketing studies have uncovered reports of cardiotoxicity with imatinib (Gleevec). It is not currently known if this toxicity will also be seen with long-term dasatinib (Sprycel) use.
- Potential off-label uses include use:
 - in pediatric patients;
 - as a first-line option;
 - for solid tumors;
 - for multiple myeloma.

Evidence

- There is no useful evidence regarding the efficacy of dasatinib (Sprycel) in the treatment of CML or Ph+ ALL.
 - Trials were of open-label design.
 - No comparators (placebo or best standard of care).
 - Intermediate endpoints were used (no overall survival data).
 - Preliminary data reported is of short duration (data reported at 12 weeks to 6 months).
- The most common adverse events observed to date in dasatinib (Sprycel) clinical trials include myelosuppression, gastrointestinal events, and fluid retention. Long-term safety and safety relative to other treatment options are not known.
- Considerations in subpopulations:
 - Pediatrics: There is no useful evidence to establish the safety and efficacy of dasatinib (Sprycel) in patients < 18 years of age.
 - Geriatrics: Current clinical experience with dasatinib (Sprycel) has not identified differences in safety or efficacy between younger and older (> 65 years of age) patients.

- Race, ethnicity, and/or gender: Current clinical experience with dasatinib (Sprycel) has not identified differences in safety or efficacy based on race, ethnicity, or gender.

Conclusion

- Dasatinib (Sprycel) is non-preferred/non-formulary because:
 - Clinical trial results are based on surrogate endpoints instead of overall survival.
 - Evidence is based on open-label, unpublished trials appraised as not useful.
 - There are no long term trials evaluating safety.
 - There are no trials evaluating comparative efficacy.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
dasatinib (Sprycel) ¹	6/2006	1. Ph+ ALL (resistant to prior therapy) 2. CML, all phases (resistant or intolerant to imatinib [Gleevec])	70 mg by mouth b.i.d.	\$4871	
imatinib (Gleevec) ²	5/2001	1. Chronic myeloid leukemia (Philadelphia chromosome +) 2. Gastrointestinal stromal tumor	Adults: 400 mg to 800 mg by mouth daily Children: 260 mg/m ² /day	\$6833	ALL, hypereosinophilic syndrome, Myelofibrosis, Polycythemia vera, Rheumatoid arthritis
interferon alfa-2a (Roferen-A) ³	10/1984	1. Chronic myeloid leukemia (Philadelphia chromosome +) 2. AIDS related Kaposi's sarcoma 3. Hairy cell leukemia 4. Chronic hepatitis C	Adults: 9 MIU IM/SQ daily Children: 2.5-5 MIU/m ² /day IM	\$3914	Malignant melanoma, renal cell carcinoma, angiosarcoma, Behcet's syndrome, carcinoid syndrome, carcinoma of the cervix, colorectal cancer, condyloma acuminatum, cryoglobulinemia, dyserythropoiesis, genital herpes simplex, hemangioma, hepatitis B, hepatitis D, HIV infection, liver carcinoma, malignant glioma, melanoma, Japanese encephalitis, malignant tumor of Islets of Langerhans, multiple myeloma, multiple sclerosis, non-Hodgkin's lymphoma, renal cell carcinoma, primary cutaneous T-cell lymphoma, skin cancer, subacute sclerosing panencephalitis, urticaria, thrombocytopenia

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of August 2006 for 1 month of therapy.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

Products (Continued)

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
cytarabine (Cytosar-U) ⁴	12/1998	1. Chronic myeloid leukemia, Blast phase 2. Meningeal leukemia; Treatment and Prophylaxis 3. Acute lymphoid leukemia 4. Acute myeloid leukemia	Optimal dose not defined	Covered under medical benefit	Hodgkin's disease, malignant meningitis, non-Hodgkin's lymphoma, Burkitt's lymphoma, CML, malignant lymphoma, mantle cell lymphoma, microglioma, myelodysplastic syndrome, neoplastic pleural effusion, progressive multifocal leukoencephalopathy, retinoblastoma, small cell carcinoma of the lung

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of August 2006 for 1 month of therapy.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

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