6.08 DASATINIB
20 mg, 50 mg, 70 mg and 100 mg tablets, Sprycel®, Bristol Myers Squibb Australia Pty Ltd

1 Purpose of Application

1.1 The minor re-submission requested an amendment to the existing PBS listings of dasatinib for first-line treatment of patients with chronic myeloid leukaemia.

2 Requested listing

2.1 The submission requested a change in the type of authority required (from written authority to telephone authority) for subsequent continuing treatment applications. The Pre-PBAC Response accepted that the listing of dasatinib should be aligned and modelled on the same requirements as imatinib (item 9113P and item 9114Q).

3 Background

3.1 There are currently three tyrosine kinase inhibitor (TKI) agents listed on the PBS for the first-line treatment of chronic myeloid leukaemia in the chronic phase – dasatinib, imatinib and nilotinib.

3.2 At its July 2011 meeting, the PBAC recommended the listing of dasatinib (20 mg, 50 mg, 70 mg and 100 mg tablets) and nilotinib (150 mg capsules) on the PBS as a Authority Required benefits for first-line treatment of chronic phase Philadelphia positive chronic myeloid leukaemia on a cost-minimisation basis compared with imatinib 400 mg. PBS listing was effective on 1 April 2012.

3.3 At its July 2014 meeting, the PBAC considered a minor submission requesting an amendment to the current first-line PBS restriction for dasatinib for treatment of patients with chronic myeloid leukaemia (CML) to ensure consistency with the first-line listing for the alternative TKI imatinib, and to make it easier for patients to continue receiving dasatinib whilst they continue to respond to treatment in the first-line setting.

3.4 The PBAC rejected the requested amendment noting the current high PBS expenditure on TKIs in CML and expressed a desire to consider the request in a manner that is informed by drug utilisation data.

3.5 The PBAC noted that it would be prepared to reconsider an amendment if drug utilisation data provided by the sponsor and/or the Drug Utilisation Sub-Committee on patient persistence rates for dasatinib and imatinib indicate no discernible difference.

Summary of evidence provided in re-submission

3.6 The sponsor provided data comparing the persistence to treatment with dasatinib versus imatinib using Kaplan-Meier analysis. The analyses were based on a 10% patient sample obtained from the Department of Human Services for PBS reimbursed scripts from January 2005 to October 2015.

3.7 Only the patient's first persistence episode within the analysis time period was measured. Three cases were tested including: (1) Base case - Dasatinib 100mg (30 tabs) vs. Imatinib 400mg (30 tabs) using 60 day drop off definition; (2) Sensitivity Analysis 1 - Dasatinib 100mg (30 tabs) vs. Imatinib 400mg (30 tabs) using 90 day drop off definition; and (3) Sensitivity Analysis 2 - Dasatinib any strength vs. Imatinib any strength using 180 day drop off definition. No statistically significant differences in the time on treatment were found between dasatinib and imatinib across the base case and sensitivity analyses. For the time period between April 2012 and October 2015, the base case result was HR [redacted] (95%CI: [redacted], [redacted]); P-value = [redacted].

For more detail on PBAC's view, see section 6 "PBAC outcome"

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted and welcomed the input from, individuals (3) and organisations (1). The comments described the experiences of prescribers in prescribing PBS-listed tyrosine kinase inhibitors for first-line CML.

4.3 The PBAC noted the comments received from the Haematology Society of Australia and New Zealand (HSANZ). The PBAC noted that prescribers have found the current requirement of obtaining a written authority to be unnecessarily cumbersome in the context of approval continuing treatment. The HSANZ indicated that similar drugs for treating the same condition require the telephone authority method which is generally faster than obtaining a written authority via post. The PBAC noted that this advice was supportive of the evidence provided in the submission.

5 Estimated PBS usage & financial implications

5.1 The sponsor estimated there to be no financial implications to the PBS, as a consequence of changing the authority method from Authority Required (Written) to Authority Required (Telephone).

For more detail on PBAC's view, see section 6 "PBAC outcome"

6 PBAC Outcome

6.1 The PBAC recommended that the authority required type for dasatinib be changed from Authority Required (written) to Authority Required (telephone) for subsequent continuing treatment applications for first-line treatment of CML. The requirements for initial treatment (Authority Required – Written) and first continuing treatment applications (Authority Required– Written) remain unchanged, this aligns with the current requirements for imatinib.

6.2 The PBAC agreed with the submission that the requested amendment to the restriction should not have any financial implications for the PBS.

Outcome:
Recommended

7 Recommended listing

7.1 Amend existing listing

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name Manufacturer	
DASATINIB				
DASATINIB 20 MG TABLET, 60	1	5	Sprycel	BQ
DASATINIB 50 MG TABLET, 60	1	5	Sprycel	BQ
DASATINIB 70 MG TABLET, 60	1	5	Sprycel	BQ
DASATINIB 100 MG TABLET, 30	1	5	Sprycel	BQ

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Condition:	Chronic Myeloid Leukaemia (CML)
PBS Indication:	Chronic Myeloid Leukaemia (CML)
Treatment phase:	Subsequent continuing
Restriction Level / Method:	☐ Restricted benefit ☒ Authority Required - In Writing ☒ Authority Required - Telephone ☐ Authority Required – Emergency ☐ Authority Required - Electronic ☐ Streamlined

Clinical criteria:	The condition must be in the chronic phase of chronic myeloid leukaemia, AND Patient must have received initial continuing PBS-subsidised treatment with this drug as a first line therapy for this condition; OR Patient must have experienced intolerance, not a failure of response, to PBS-subsidised treatment with imatinib as a first line therapy for this condition; OR Patient must have experienced intolerance, not a failure of response, to PBS-subsidised treatment with nilotinib as a first line therapy for this condition, AND Patient must have maintained a major cytogenic response; OR Patient must have maintained a peripheral blood level of BCR-ABL of less than 1%, AND The treatment must not exceed a total maximum of 24 weeks of therapy with a PBS-subsidised treatment with a tyrosine kinase inhibitor for this condition under this restriction, AND The treatment must be the sole PBS-subsidised therapy for this condition.
Prescriber Instructions	Subsequent authority applications for continuing therapy with dasatinib may be made on the telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).
Administrative Advice *(not included in LI)*	The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of tyrosine kinase inhibitors (TKI) agents for the chronic phase of chronic myeloid leukaemia. Where the term TKI agent appears in the following notes and restrictions it refers to imatinib mesylate, dasatinib or nilotinib. Patients are eligible for PBS-subsidised treatment with only one TKI agent at any one time and must not be receiving concomitant interferon alfa therapy. Eligible patients may only swap between TKI agents if they have not failed prior PBS-subsidised treatment with that agent. 1. Continuing treatment with imatinib mesylate, dasatinib or nilotinib - first-line First continuing applications are to be written and must include a pathology report demonstrating the patient has responded to the initial course of treatment. Second and subsequent authority applications for continuing therapy with imatinib mesylate, dasatinib or nilotinib may be made on the telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Patients must maintain a major cytogenetic response or have a peripheral blood BCR-ABL of less than 1% to receive continuing therapy. Nilotinib is not approved for patients in blast crisis. 2. Initial second line treatment From 1 April 2012, under the PBS, a patient will be able to be prescribed either dasatinib or nilotinib within the initial 18 month treatment period as second-line therapy, as long as only one agent is approved at a time and providing the patient did not fail that drug as first-line therapy. During the initial 18 month treatment period, switching between approved second-line agents may only occur for reasons of intolerance, not failure of

	response. 3. Initial third line treatment Third-line treatment with a TKI can only be approved when imatinib is used for first-line treatment. Patients will only be approved for PBS-subsidised treatment with one third-line agent. From 1 April 2012, under the PBS, a patient will be able to be prescribed either dasatinib or nilotinib providing the patient did not fail that drug as first or second line therapy and for nilotinib the patient is not in blast crisis. 4. Continuing treatment for second and third line treatment All continuing applications are to be written and must include a pathology report demonstrating the patient has responded to PBS-subsidised treatment as follows: (i) within 18 months of the commencement of treatment, at which time patients in whom a major cytogenetic response or peripheral blood BCR-ABL level of less than 1% has been demonstrated may receive authorisation for a further 12 months of treatment; and (ii) at no greater than 12 month intervals thereafter, to demonstrate that the major cytogenetic response or peripheral blood BCR-ABL level of less than 1% has been sustained. During second line continuing treatment beyond the initial 18 month treatment period, switching between approved second line TKI agents may only occur for reason of intolerance. Where there is failure of response, switching may only occur through application for prescription of a third line agent. 3. For imatinib mesylate, dasatinib and nilotinib During continuing therapy beyond the initial 18 month treatment period, switching between approved first-line agents may only occur for reason of intolerance. Where there is failure of response, switching may only occur through application for prescription of second-line agents. Where a patient has previously received PBS-subsidised treatment with imatinib mesylate, dasatinib or nilotinib no approval will be granted for PBS-subsidised re-treatment in the chronic phase of chronic myeloid leukaemia, where that patient has at any time failed to meet the response criteria whilst on that TKI agent
	5. Authority approval requirements Response criteria to initial treatment with imatinib mesylate, dasatinib or nilotinib: For the purposes of assessing response to PBS-subsidised treatment with imatinib mesylate, dasatinib or nilotinib either cytogenetic analysis indicating the number of Philadelphia positive [t (9;22)] cells in the bone marrow measured by standard karyotyping, or quantitative PCR indicating the relative level of BCR-ABL transcript in the peripheral blood using the international scale, must be submitted. For bone marrow analyses, where the standard karyotyping is not informative for technical reasons, a cytogenetic analysis performed on the bone marrow by the use of fluorescence in situ hybridisation (FISH) with BCR-ABL specific probe must be submitted. The cytogenetic or peripheral blood quantitative PCR analyses must be submitted within 18

	months of the commencement of treatment with imatinib mesylate, dasatinib or nilotinib (patients in whom a major cytogenetic response or peripheral blood BCR-ABL level of less than 1% is demonstrable by 18 months are eligible to receive continuing treatment with that agent). 5. Definitions of response A major cytogenetic response is defined as less than 35% Philadelphia positive bone marrow cells. A peripheral blood BCR-ABL level of less than 1% on the international scale (Blood 108: 28-37, 2006) also indicates a response, at least the biological equivalent of a major cytogenetic response. 6. Definitions of loss of response Loss of a previously documented major cytogenetic response (demonstrated by the presence of greater than 35% Ph positive cells on bone marrow biopsy), during ongoing tyrosine kinase inhibitor (TKI) therapy. Loss of a previously demonstrated molecular response (demonstrated by peripheral blood BCR-ABL levels increasing consecutively in value by at least 5 fold to a level of greater than 0.1% confirmed on a subsequent test), during ongoing tyrosine kinase inhibitor therapy. Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

The sponsor had no comment.