

30 June 2009

Listing of two new pharmaceuticals (Entecavir and Dasatinib) approved

PHARMAC is pleased to announce the approval of the proposal to list two new pharmaceuticals; entecavir (Baraclude) for the treatment of Hepatitis B infection and dasatinib (Sprycel) for the treatment of Chronic Myeloid Leukaemia.

In summary, from 1 August 2009:

- Entecavir (Baraclude) 0.5 mg tablets will be listed in Section B and Section H of the Pharmaceutical Schedule. Note the 1.0 mg strength tablet will not be listed.
- In Section B entecavir will be listed under Special Authority restrictions for first-line treatment in Hepatitis B treatment-naïve patients.
- Entecavir will be dispensed through community pharmacies and DHB hospital pharmacies with a community pharmacy claiming contract.
- Dasatinib (Sprycel) tablets will be listed in Section B and Section H of the Pharmaceutical Schedule.
- In Section B Dasatinib will be listed subject to Special Authority restrictions for patients with Chronic Myeloid Leukaemia (CML).
- Approval for subsidies for dasatinib will be upon application to PHARMAC.
- Dasatinib will be dispensed and distributed directly to patients by Healthcare Logistics Limited (HCL).
- Confidential rebate arrangements between PHARMAC and Bristol-Myers Squibb (NZ) Limited will apply to entecavir and dasatinib.

Details of the Decision

From 1 August 2009:

- Baraclude (entecavir 0.5 mg tablets) will be listed in the Antivirals (Infections – agents for Systemic Use) therapeutic group in Section B and Part II of Section H of the Pharmaceutical Schedule at the following price and subsidy (ex-manufacturer, excl. GST):

Chemical	Form and Strength	Brand	Pack size	Price and subsidy
Entecavir	Tab 0.5 mg	Baraclude	30	\$400.00

- The listing of entecavir in Section B will be subject to the following Special Authority restriction:

SAXXX Special Authority for Subsidy

Initial application only from a gastroenterologist or infectious disease specialist. Approvals valid without further renewal unless notified for applications meeting the following criteria:

- 1 Patient has confirmed Hepatitis B infection (HBsAg positive for more than 6 months); and
- 2 Patient is Hepatitis B nucleoside analogue treatment-naïve; and
- 3 Entecavir dose 0.5 mg/day; and
- 4 Any of the following:
 - 4.1 ALT greater than upper limit of normal; or
 - 4.2 Bridging fibrosis of cirrhosis (Metavir stage 3 or greater) on liver histology; and
- 5 Any of the following:
 - 5.1.HBeAg positive; or
 - 5.2 patient has $\geq 2,000$ IU HBV DNA units per ml and fibrosis (Metavir stage 2 or greater) on liver histology; and
- 6 All of the following:
 - 6.1 No continuing alcohol abuse or intravenous drug use; and
 - 6.2 Not co-infected with HCV, HIV or HDV; and
 - 6.3 Neither ALT nor AST greater than 10 times upper limit of normal; and
 - 6.4 No history of hypersensitivity to entecavir; and
 - 6.5 No previous documented lamivudine resistance (either clinical or genotypic).

Notes:

- Entecavir should be continued for 6 months following documentation of complete HBeAg seroconversion (defined as loss of HBeAg plus appearance of anti-HBe plus loss of serum HBV DNA) for patients who were HBeAg positive prior to commencing this agent. This period of consolidation therapy should be extended to 12 months in patients with advanced fibrosis (Metavir Stage F3 or F4).
 - Entecavir should be taken on an empty stomach to improve absorption.
- A confidential rebate arrangement between PHARMAC and Bristol-Myers Squibb (NZ) Limited will apply to entecavir
- Sprycel (dasatinib 20 mg, 50 mg and 70 mg tablets) will be listed in the Protein-tyrosine Kinase Inhibitors (Oncology Agents and Immunosuppressants) therapeutic group in Section B and in Part II of Section H of the Pharmaceutical Schedule at the following prices and subsidies (ex-manufacturer, excl. GST):

Chemical	Form and Strength	Brand	Pack size	Price and subsidy
Dasatinib	Tab 20 mg	Sprycel	60	\$3,774.06
Dasatinib	Tab 50 mg	Sprycel	60	\$6,214.20
Dasatinib	Tab 70 mg	Sprycel	60	\$7,692.58

- Sprycel (dasatinib 100 mg tablet) will be listed in the Protein-tyrosine Kinase Inhibitors (Oncology Agents and Immunosuppressants) therapeutic group in Section B and in Part II of Section H of the Pharmaceutical Schedule as soon as possible following Medsafe registration at the following price and subsidy (ex-manufacturer, excl. GST):

Chemical	Form and Strength	Brand	Pack size	Price and subsidy
Dasatinib	Tab 100 mg	Sprycel	30	\$6,214.20

- The listing of dasatinib in Section B will be subject to the following Special Authority restriction:

SAXXX Special Authority for Subsidy

Special Authority approved by PHARMAC.

Notes: Application details may be obtained from PHARMAC's website

<http://www.pharmac.govt.nz>, and prescriptions should be sent to:

The Co-ordinator
PHARMAC
PO Box 10 254
Wellington

Phone: (04) 460 4990
Facsimile: (04) 916 7571
Email: mary.chesterfield@pharmac.govt.nz

Special Authority criteria for CML – access by application to PHARMAC

- 1) Funded for patients with diagnosis (confirmed by a haematologist) of a chronic myeloid leukaemia (CML) in blast crisis, accelerated phase, or in chronic phase.
- 2) Maximum dose of 140 mg/day for accelerated or blast phase and 100 mg/day for chronic phase CML.
- 3) Subsidised for use as monotherapy only.
- 4) Initial approvals valid seven months.
- 5) Subsequent approval(s) are granted on application and are valid for six months. The first reapplication (after seven months) should provide details of the haematological response. The third reapplication should provide details of the cytogenetic response after 14-18 months from initiating therapy. All other reapplications should provide details of haematological response, and cytogenetic response if such data is available. Applications to be made and subsequent prescriptions can be written by a haematologist or an oncologist.

Note: Dasatinib is indicated for the treatment of adults with chronic, accelerated or blast phase CML with resistance or intolerance to prior therapy including imatinib.

Guideline on discontinuation of treatment for patients with CML

- a) Prescribers should consider discontinuation of treatment if, after 6 months from initiating therapy, a patient did not obtain a haematological response as defined as any one of the following three levels of response:
 - 1) complete haematologic response (as characterised by an absolute neutrophil count (ANC) > $1.5 \times 10^9/L$, platelets > $100 \times 10^9/L$, absence of peripheral blood (PB) blasts, bone marrow (BM) blasts < 5% (or FISH Ph+ 0-35% metaphases), and absence of extramedullary disease); or
 - 2) no evidence of leukaemia (as characterised by an absolute neutrophil count (ANC) > $1.0 \times 10^9/L$, platelets > $20 \times 10^9/L$, absence of peripheral blood (PB) blasts, bone marrow (BM) blasts < 5% (or FISH Ph+ 0-35% metaphases), and absence of extramedullary disease); or
 - 3) return to chronic phase (as characterised by BM and PB blasts < 15%, BM and PB blasts and promyelocytes < 30%, PB basophils < 20% and absence of extramedullary disease other than spleen and liver).
- b) Prescribers should consider discontinuation of treatment if, after 18 months from initiating therapy, a patient did not obtain a major cytogenetic response defined as 0-35% Ph+ metaphases.

- Dasatinib, when used in the community subject to Special Authority approval, will be distributed directly to patients by Health Care Logistics funded by Bristol-Myers Squibb (NZ) Limited. This process is similar to that currently applying to Imatinib (Glivec) for patients with CML or GIST and Multiple Sclerosis treatments.
- A confidential rebate arrangement between PHARMAC and Bristol-Myers Squibb (NZ) Limited will apply to dasatinib.

Changes made to the Proposal and Feedback Received

The proposal to list entecavir and dasatinib was the subject of a consultation letter dated 30 April 2009. We appreciate all the feedback we received and acknowledge the time people took to respond. All consultation responses received by 14 May 2009 were considered in their entirety in making the decision on the proposal.

Consultation feedback on the proposal was generally supportive. The following changes were made to the proposal following consultation:

- The listing date was amended from 1 July 2009 to 1 August 2009; and
- Listing of the entecavir 1.0 mg tablet was removed. This strength is only used in treatment-experienced Hepatitis B patients; however, the proposal was for entecavir to be funded in treatment-naïve patients. We note that the proposed Special Authority criteria consulted on clearly stated that funding was for treatment naïve patients with an entecavir dose of 0.5 mg per day.

Some responders questioned why dasatinib was to be funded for all CML patients when it was only indicated for second line treatment (i.e. imatinib resistant/intolerant CML).

We have received and assessed an application for dasatinib to be funded as a second-line treatment, and this change makes such funding available.

The Pharmaceutical Schedule sets out the rules applying to subsidy payments rather than defining treatment protocols which require a particular course of action. We are aware that the Special Authority criteria for dasatinib would enable funding for first line use, however, funding availability should not necessarily be taken as a recommendation that such use should occur. It is the treating clinician's decision whether or not to use dasatinib first or second line.

With any funding proposal we are interested in the balance of benefit and risk (both clinical and economic) versus other potential funding options. In this case we are comfortable with the extent of funding provided.

Other issues raised by consultation responders, including requests for the funding of an alternative tyrosine kinase inhibitor (nilotinib, Novartis NZ Limited) in addition to dasatinib, and, funding of dasatinib for all BCR-ABL positive leukaemias thus encompassing both CML and Acute Lymphoblastic Leukaemia (ALL), require further assessment by PHARMAC and have not been implemented at this time.

More information

If you have any queries about these changes please contact the PHARMAC helpline on 0800 66 00 50 (9 am to 5 pm weekdays).