CONSULTATION

PHARMAC
Pharmaceutical Management Agency

22 October 2013

Proposal for sole supply of imatinib for indications other than Gastro Intestinal Stromal Tumours (GIST)

PHARMAC is seeking feedback on a proposal to:

- List AFT's brand of imatinib mesilate 100 mg capsules (Imatinib-AFT) in Section B, and Part II of Section H, of the Pharmaceutical Schedule from 1 April 2014; and
- Award Imatinib-AFT' brand of imatinib mesilate Sole Subsidised Supply status in the community and DHB hospitals for all indications, other than Gastro Intestinal Stromal Tumours (GIST), from 1 July 2014 to 30 June 2017; and
- Amend the Special Authority restriction applying to imatinib mesilate 100 mg tablet (Glivec) in Section B of the Pharmaceutical Schedule from 1 July 2014.

The effect of this proposal, if approved, would be that

1) The Glivec brand of imatinib mesilate tablets would no longer be funded for patients with Chronic Myeloid Leukaemia (CML) and any other indications approved under Exceptional Circumstances (EC)/Named Patient Pharmaceutical Assessment (NPPA); instead the Imatinib-AFT brand of imatinib mesilate capsules would be fully funded for these patients.
2) The direct distribution of imatinib mesilate (Glivec) to patients with CML would cease; these patients would need to obtain their supply of imatinib mesilate (Imatinib-AFT) through their usual retail pharmacy. Imatinib-AFT would be listed without restriction. (Special Authority criteria or otherwise).
3) Glivec would remain fully funded, but only for patients with unresectable and/or metastatic malignant GIST. Funding of Glivec for GIST would be widened to include patients with c-kit negative disease. GIST patients would continue to receive Glivec by direct distribution.

Further details of this proposal, including how to provide feedback and background information including proposed transition timelines and how the brand switch and change in distribution arrangements would be managed for non-GIST patients, can be found on the following pages.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **5 pm, Tuesday 12 November 2014** to:

Jackie Evans
Senior Therapeutic Group Manager
PHARMAC
PO Box 10 254
Wellington 6143

Email: jackie.evans@pharmac.govt.nz
Fax: 04 460 4995

All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request.

Details of the proposal

- From 1 April 2014, AFT's brand of imatinib mesilate 100 mg capsules (Imatinib-AFT) would be listed in Section B, and Part II of Section H, of the Pharmaceutical Schedule at the following subsidy and price (ex-manufacturer and excluding GST):

Chemical	Presentation	Brand	Pack size	Price and subsidy
Imatinib mesilate	Cap 100 mg	Imatinib-AFT	60	$298.90

- The following Note would be applied to Imatinib-AFT listed in Section B, and Part II of Section H, of the Pharmaceutical Schedule:

  > Note: The Glivec brand of imatinib mesilate (supplied by Novartis) remains funded for patients with unresectable and/or metastatic malignant GIST.

- Imatinib-AFT would be dispensed 3 months all-at-once.

- Award Sole Subsidised Supply Status (the only funded brand in the community) and Hospital Supply Status (the only available brand in DHB hospitals, subject to a 1% discretionary variance limit), for all indications other than Gastro Intestinal Stromal Tumours (GIST), to Imatinib-AFT from 1 July 2014 to 30 June 2017; and
- From 1 July 2014, the Special Authority applying to Novartis' brand of imatinib mesilate 100 mg tablets (Glivec) listed in Section B of the Pharmaceutical Schedule would be amended as follows (changes in strikethrough).

  Glivec
  SAXXX Special Authority for Subsidy
  Special Authority approved by the ~~CML/~~GIST Co-ordinator
  Notes: Application details may be obtained from PHARMAC's website http://www.pharmac.govt.nz, and prescriptions should be sent to:
  The CML/GIST Co-ordinator
  PHARMAC
  PO Box 10 254
  Wellington
  Phone: (04) 460 4990
  Facsimile: (04) 916 7571
  Email: ~~mary.chesterfield~~**cmlgistcoordinator**@pharmac.govt.nz

  ~~Special Authority criteria for CML – access by application~~

a) ~~Funded for patients with diagnosis (confirmed by a haematologist) of a chronic myeloid leukaemia (CML) in blast crisis,accelerated phase, or in chronic phase.~~
b) ~~Maximum dose of 600 mg/day for accelerated or blast phase, and 400 mg/day for chronic phase CML.~~
c) ~~Subsidised for use as monotherapy only.~~
d) ~~Initial approvals valid seven months.~~
e) ~~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.~~

~~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 × 109/L, platelets > 100 × 109/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 × 109/L, platelets > 20 × 109/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.~~

Special Authority criteria for GIST – access by application

a) Funded for patients:
    1) with a diagnosis (confirmed by an oncologist) of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST); ~~and~~
    2) ~~who have immunohistochemical documentation of c-kit (CD117) expression by the tumour.~~
b) Maximum dose of 400 mg/day.
c) Applications to be made and subsequent prescriptions can be written by an oncologist.
d) Initial and subsequent applications are valid for one year. The re-application criterion is an adequate clinical response to the treatment with imatinib (prescriber determined)

- Patients with an existing CML Special Authority approval would receive their last delivery of Glivec via direct distribution on 26 March 2014; this delivery would comprise two months stock of Glivec. After this date patients would need to obtain a prescription for imatinib mesilate (Imatinib-AFT) from their doctor or haematologist and obtain their medicine from a retail pharmacy.

Transition timelines

- The implementation process and timelines, should this proposal be approved, would be as follows:

    - **Mid December 2013 –** anticipated notification of a decision on this proposal if approved. We would communicate directly with all patients recommending that they visit their haematologist or other doctor (for EC/NPPA patients) prior to 31

May 2014 to discuss the proposed brand switch, change in distribution arrangements and obtain a prescription for imatinib mesilate (Imatinib-AFT) to present at a retail pharmacy. There would be no change for GIST patients.

- **26 March 2014** - CML patients, with existing Special Authority approvals for imatinib, would receive their last direct delivery of Glivec. This would comprise 2 months stock. GIST patients would continue to receive direct deliveries of Glivec as usual beyond this date.

- **1 April 2014** – Listing of Imatinib-AFT 100mg capsules. There would be no change to the listing of Glivec.

- **From 1 June 2014 onwards** (exact date depends on how much stock each patient has) – CML and EC/NPPA patients would need to have prescriptions for imatinib mesilate filled at a retail pharmacy. Patients would be dispensed 3 months' supply of imatinib mesilate (Imatinib-AFT) all at once. Patients would need to pay a $5 co-payment for this supply. There would be no change for GIST patients.

- **1 July 2014** – The Special Authority for Glivec would be amended, such that this brand would continue to be funded only for patients with GIST.

- **1 July 2014 to 30 June 2017** – Imatinib-AFT would be the sole subsidised brand of imatinib mesilate in the community (Sole Subsidised Supply Status) and the only available brand in DHB hospitals, subject to a 1% discretionary variance limit (Hospital Supply Status), for all indications other than GIST. There would be no change for GIST patients; the Glivec brand would remain fully funded for them.

Background

Imatinib mesilate 100 mg tablets are currently funded under Special Authority (access by application) for patients with Chronic Myeloid Leukaemia (CML) and Gastrointestinal Stromal Tumours (GIST). A confidential rebate applies to the currently funded brand of imatinib mesilate (Glivec, Novartis). Patients obtain their supplies of Glivec via a central pharmacy direct distribution mechanism, funded by Novartis, and managed by PHARMAC staff.

Imatinib mesilate is funded for up to 400 mg/day in GIST and chronic phase CML or up to 600 mg/day in accelerated or blast phase CML. Doses of up to 800 mg/day imatinib mesilate are approved by Medsafe for use in all phases of CML, but this dose is not currently funded.

In August 2012 PHARMAC issued a request for proposals for the sole subsidised supply of imatinib mesilate in the community and DHB hospitals noting that the incumbent brand, Glivec, would remain funded for patients with gastrointestinal stromal tumours only. PHARMAC notes that Novartis' patent NZ525254 is directed at the use of Glivec for the treatment of GIST and expires in 2021.

Currently, approximately 225 patients with CML, and 80 patients with GIST, access funded imatinib mesilate via direct distribution. There are a further 11 patients funded through the EC/NPPA schemes who obtain their imatinib mesilate via a nominated retail pharmacy (mainly for chronic eosinophilic leukaemia and Philadelphia chromosome-positive acute lymphoblastic leukaemia).

There are a number of outstanding funding applications for imatinib mesilate: PTAC has considered funding requests for patients with c-kit negative GIST and patients with Philadelphia

chromosome positive acute lymphoblastic leukaemia (ALL) and funding of doses up to 600 mg/day for chronic phase CML. Under this proposal all these patient groups would be able to access fully funded imatinib as there would be no dose limit on the funding of Imatinib-AFT.

The proposal to award sole supply to Imatinib-AFT for non-GIST indications would provide savings to the Combined Pharmaceuticals Budget of approximately $12 million per year; these savings could be used to fund other new medicines.

Managing the proposed brand switch

Imatinib-AFT capsules have been approved by Medsafe and have demonstrated bioequivalence to currently funded Glivec tablets; that means that the rate and the extent of the absorption of imatinib mesilate is the same for both brands. Whilst there are some differences in the excipients these are not expected to result in any difference in the side effect profiles of the two brands. Imatinib-AFT capsules are available overseas and no increase in side effects has been reported compared with Glivec.

The proposal to award sole supply for imatinib mesilate for all indications other than GIST has been reviewed by the Cancer Treatments Subcommittee of PTAC. In summary, the Subcommittee considered that compliance with imatinib mesilate was an issue and considered that size and aesthetics of any new brand was important. It considered Imatinib-AFT capsules were acceptable. The Subcommittee recommended PHARMAC encourage patients to visit their haematologists to discuss the proposed switch. The Subcommittee has also recommended to widen access to imatinib mesilate for patients with c-kit negative GIST with high priority.

If this proposal is approved by the PHARMAC Board, PHARMAC will work with clinicians, Leukemia and Blood Cancer NZ, pharmacists and patients to manage the brand switch. PHARMAC would keep patients directly informed of the proposal, and any decisions made, in order to enable them to schedule appointments with their haematologists to discuss the potential brand switch. All CML patients would receive a ‘double delivery’ of Glivec in March 2014, which would give them at least 2 months to obtain a prescription for imatinib mesilate and have it dispensed from a retail pharmacy.

Poor adherence to oral tyrosine kinase therapy such as imatinib mesilate is a significant factor that contributes to cytogenetic relapse and treatment failure in patients with CML; therefore, it is very important that prescribers, and other healthcare professionals working with CML patients, routinely discuss and address barriers to adherence for these patients.