Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1543 – Request to amend Medicare Benefits Schedule (MBS) item 73336 (BRAF mutation test for treatment of metastatic melanoma) to include reference to encorafenib

Applicant: **Pierre Fabre**

Date of MSAC consideration: **MSAC 74th Meeting, 22-23 November 2018**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

This streamlined co-dependent application requested:

- an amendment to the Medicare Benefits Schedule (MBS) item 73336 (*BRAF* mutation test) allowing its use to determine eligibility for treatment with encorafenib in patients with unresectable stage III or stage IV metastatic cutaneous melanoma; and
- Pharmaceutical Benefits Scheme (PBS) Authority Required (STREAMLINED) listing for the concurrent use of encorafenib and binimetinib for the treatment of *BRAF* V600 mutation positive unresectable Stage III or metastatic (Stage IV) melanoma.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported amending MBS item 73336 for *BRAF* mutation testing in patients with metastatic melanoma to also determine access to encorafenib under the Pharmaceutical Benefits Scheme.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted the PBAC's positive recommendation for Authority Required (STREAMLINED) listing of encorafenib in combination with binimetinib, for the treatment of *BRAF* V600 mutation-positive unresectable or metastatic melanoma, on a cost-minimisation basis against dabrafenib + trametinib and vemurafenib + cobimetinib.

The rationale for the inclusion of encorafenib in the same MBS item descriptor is that the identification of a *BRAF* V600 mutation in a patient does not imply treatment with a specific BRAF inhibitor; rather, it is indicative that they will respond to treatment with BRAF inhibitors. The addition of encorafenib to MBS item 73336 will allow final treatment

decisions to be made by clinicians in consideration of individual patient circumstances, resulting in optimal care for patients.

The proposed listing for item 73336 is as follows:

> A test of tumour tissue from a patient with unresectable stage III or stage IV metastatic cutaneous melanoma, requested by, or on behalf of, a specialist or consultant physician, to determine the requirements relating to BRAF V600 mutation status for access to dabrafenib, vemurafenib or encorafenib under the Pharmaceutical Benefits Scheme are fulfilled.

There is no change to the proposed MBS fee, costs to the MBS or testing strategy. Utilisation is not expected to increase, as this represents an additional treatment choice in the same patient population.

4. Background

MSAC has not previously considered this application.

MSAC has previously considered and supported public funding on the MBS for Applications 1172 & 1172.1 - Testing for *BRAF* mutation in patients with metastatic melanoma for access to vemurafenib and Application 1207 - Testing for V600 status in patients with locally advanced or metastatic melanoma for access to dabrafenib.

5. Prerequisites to implementation of any funding advice

All *BRAF* mutation tests must occur in National Association of Testing Authorities (NATA) accredited laboratories. Competence to perform the test is already being monitored through a Royal College of Pathologists of Australasia (RCPA) quality assurance program (QAP).

6. Proposal for public funding

The application sought to amend the existing BRAF MBS item 73336, to include reference to encorafenib (Table 1). The application proposed an equivalent fee to the current MBS item of $230.95.

Table 1 Current and proposed description of MBS item 73336

Item 73336	Description	Fee
Proposed listing	A test of tumour tissue from a patient with unresectable stage III or stage IV metastatic cutaneous melanoma, requested by, or on behalf of, a specialist or consultant physician, to determine the requirements relating to BRAF V600 mutation status for access to dabrafenib, vemurafenib or *encorafenib* under the Pharmaceutical Benefits Scheme are fulfilled.	$230.95

Source: (MBS, 2018), accessed August 2018

7. Proposed intervention's place in clinical management

Inclusion of encorafenib in the MBS item descriptor will allow identification of a *BRAF* V600 mutation in a patient, which is indicative that they will respond to treatment with BRAF inhibitors and allow final treatment decisions to be made by clinicians in consideration of individual patient circumstances, resulting in optimal care for patients.

8. Comparative effectiveness

BRAF V600 testing is usually ordered by the patient's surgeon or oncologist once a diagnosis is made. A biopsy sample is collected from the patient which is then normally processed into formalin-fixed, paraffin-embedded (FFPE) tissue blocks.

The testing strategy used in the COLUMBUS trial and the corresponding trial of the comparator medicine is presented in Table 2.

Table 2 Testing strategy used in COLUMBUS trial and comparator trials

Trial	Testing strategy
COLUMBUS (encorafenib + binimetinib) (COLUMBUS Part 1 CSR, 2017), pg. 103	A tumour tissue sample (archival or newly collected biopsy fixed in formalin) was required from all patients for pre-screening of BRAF V600 mutation status. A BioMerieux THxID™ BRAF diagnostic test that can identify both *BRAF* V600E and V600K gene mutations was used to select patients eligible for this study.
coBRIM (vemurafenib + cobimetinib) (Larkin, et al., 2014), pg. 89	BRAFV600 mutation testing must be performed with the cobas 4800 BRAF V600 mutation test. Only patients whose melanoma tumours test positive for the BRAFV600 mutation on the cobas® 4800 BRAF V600 mutation test will be eligible for enrolment in the clinical study if other eligibility criteria are met. Archival or newly obtained formalin-fixed paraffin-embedded (FFPE) tumour specimens may be utilized for the cobas® 4800 BRAF V600 mutation test.
COMBI-V (dabrafenib + trametinib) (COMBI-V CSR, 2014), pg. 103	Subjects will be screened prior to treatment to determine whether their tumour sample has a V600E or V600K mutation, indicating their eligibility for the study. Tumour BRAF mutation testing will be conducted using the bioMerieux BRAF THxID IUO assay (IDE: G120011) and testing will be performed in a central reference laboratory.
COMBI-D (dabrafenib + trametinib) (COMBI-D CSR, 2013), pg. 93	Subjects will be screened prior to treatment to determine whether their tumour sample has a V600E or V600K mutation, indicating their eligibility for the study. Tumour BRAF mutation testing will be conducted using the bioMerieux BRAF THxID IUO assay (IDE: G120011) and testing will be performed in a central reference laboratory.

9. Financial/budgetary impacts

The proposed amendment to the BRAF MBS item 73336 is anticipated to be cost neutral to the MBS.

10. Applicant's comments on MSAC's Public Summary Document

Pierre Fabre welcome the support of MSAC to amend MBS item 73336 for *BRAF* mutation testing in patients with unresectable or metastatic melanoma to determine access to encorafenib under the PBS.

11. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website