Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1607 – 17p deletion testing for access to acalabrutinib in patients with relapsed or refractory chronic lymphocytic leukaemia

Applicant: **AstraZeneca Pty Ltd**

Date of MSAC consideration: **MSAC 78th Meeting, 3 April 2020**

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

1. Purpose of application

An application for a streamlined codependent consideration requested:

- Pharmaceutical Benefits Schedule (PBS) listing of acalabrutinib for the treatment of patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)
- an amendment of Medicare Benefits Schedule (MBS) item 73343 to include acalabrutinib in the list of medicines for which fluorescence *in situ* hybridization (FISH) testing for the detection of *17p* deletion (*del(17p)*) can be used to determine eligibility for access to PBS subsidised treatment.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of *17p* deletion (*del(17p)*) testing, MSAC supported the modification of existing MBS item 73343 to include reference to acalabrutinib in alignment with the PBS listing of this medicine as recommended by the Pharmaceutical Benefits Advisory Committee (PBAC) in March 2020.

The MSAC-supported descriptor was:

Detection of 17p chromosomal deletions by fluorescence in situ hybridization, of a patient with relapsed or refractory chronic lymphocytic leukaemia or small lymphocytic lymphoma, on a peripheral blood or bone marrow sample, requested by a specialist or consultant physician, to determine if the requirements for access to idelalisib, ibrutinib, venetoclax ***or acalabrutinib*** *on the Pharmaceutical Benefits Scheme are fulfilled.*

MSAC recently supported other amendments to MBS item descriptor 73343 which are not implemented (see PSD for Application 1560, MSAC 77th Meeting, 28-29 November 2019 and PSD for Application 1544, MSAC 77th Meeting, 28-29 November 2019).

Consumer summary

AstraZeneca Pty Ltd applied for funding through the Medicare Benefits Schedule (MBS) for some people with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) to have funded chromosome *17p* deletion testing to help them know whether they can receive subsidised access to the medicine acalabrutinib when listed on the Pharmaceutical Benefits Scheme (PBS). CLL and SLL are two closely related blood cancers.

17p deletion testing is a genetic test that checks if people are missing part of their genetic material in their chromosome 17. It is a common genetic change in several types of cancer.

The test for *17p* deletion is already listed on the MBS to help determine access to several medicines which can help people who have CLL or SLL and who also have a *17p* deletion. Acalabrutinib is the most recent medicine to be proposed for listing on the PBS for such patients.

In March 2020, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended the listing of acalabrutinib on the PBS as a second-line treatment for some people with CLL or SLL, including if they have a *17p* deletion.

MSAC's advice to the Commonwealth Minister for Health

The Medical Services Advisory Committee (MSAC) has previously advised that *17p* deletion testing is safe, clinically effective and cost-effective. As the PBAC has recommended the listing of acalabrutinib on the PBS, MSAC supported the funding of *17p* deletion testing to help patients with CLL or SLL know whether they have access to PBS-subsidised acalabrutinib.

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

MSAC noted that this was a streamlined minor submission for proposed (further) amendment of MBS item 73343 to allow *17p* deletion testing of certain patients with CLL or SLL to help determine eligibility for acalabrutinib under the PBS.

MSAC noted that the March 2020 PBAC meeting recommended that acalabrutinib be listed on the PBS as a second-line treatment for CLL or SLL.

The medicines (ibrutinib, idelalisib, and venetoclax) are already listed on the PBS for second-line treatment for CLL or SLL. One of the eligibility criteria for their PBS subsidy is the presence of a chromosomal *17p* deletion, which requires testing to detect its presence. MSAC recalled that it had previously supported *17p* deletion testing as being safe, clinically effective and cost-effective in patients with CLL or SLL, which resulted in MBS item 73343.

MSAC agreed with the applicant's proposals that there should be no consequential changes to the MBS fee, costs to the MBS, or testing strategy. However, MSAC recalled that, during its November 2019 meeting in the context of MSAC Application 1544, it had supported an amended fee for *17p* deletion testing to allow for a different technology to be used, and confirmed that the amended fee is still appropriate. It was noted that the applicant for MSAC Application 1607 would not have been aware of this decision at the time of providing its minor submission.

Other discussion
MSAC noted that the Department will be seeking policy approval for MSAC Application 1560, which is an amendment of MBS item 73343 to allow testing for access to ibrutinib for first-line treatment for patients with CLL/SLL, and Application 1544 which sought to amend item 73292 to extend genome-wide microarray (GWMA) to people with CLL, SLL and multiple myeloma (MM).

MSAC noted that implementation of all of the related CLL/SLL/MM and *17p* testing (FISH/GWMA) MBS items needs to avoid any unintended contradictions over time, including with respect to their coordinated PBS restrictions. MSAC suggested that the Department should review the timing of the implementation of the various inter-related applications to ensure the item descriptors and fees remain appropriately aligned, and thus update the MSAC Executive.

4. Background

In April 2017, MSAC supported the listing of *del(17p)* testing as a codependent test to support access to the kinase inhibitors idelalisib and ibrutinib, which were both earlier recommended by PBAC for listing on the PBS for the treatment of patients with relapsed or refractory CLL or relapsed or refractory SLL whose disease is characterised by a chromosome *17p* deletion (see Public Summary Document [PSD] for Application 1456, MSAC 69th Meeting, 6-7 April 2017).

In November 2018, MSAC supported amending MBS item 73343 to include *del(17p)* deletion testing in patients with relapsed or refractory CLL to determine access to venetoclax under the PBS (see PSD for Application 1456, MSAC 74th Meeting, 22-23 November 2018).

In November 2019, MSAC supported the modification of existing MBS item 73343, to expand the eligible population for this test to include previously untreated patients and to limit the testing to no more frequently than one test per year. MSAC advised that implementation of this advice should not necessarily be impeded by the implementation of its related advice from Application 1544 (see PSD for Application 1560, MSAC 77th Meeting, 28-29 November 2019).

Also in November 2019, MSAC supported the amendment of MBS item 73343 to allow for genome wide micro-array (GWMA) testing, with a consequential increase in fee (see PSD for Application 1544, MSAC 77th Meeting, 28-29 November 2019). Implementation of this proposed amendment is also progressing, but likely to occur after any changes resulting from Application 1560, outlined above.

There are a number of MSAC supported amendments to MBS item 73343 (in Applications 1544 and 1560) that require Government consideration. Should these amendments receive policy approval, the following proposed MBS item descriptor would be:

MBS Item 73343	Category 6 – PATHOLOGY SERVICES
	Group P7 Genetics
Detection of 17p chromosomal deletions by fluorescence *in situ* hybridization **in a patient** or **analysis of chromosomes by genome-wide micro-array in diagnostic studies of** a patient with ~~**relapsed or refractory**~~ chronic lymphocytic leukaemia or small lymphocytic lymphoma, on a peripheral blood or bone marrow sample or **lymph node tissue sample**, requested by a specialist or consultant physician, to determine if the requirements for access to idelalisib, ibrutinib or venetoclax on the Pharmaceutical Benefits Scheme are fulfilled. ~~**Fee: $230.95 Benefit: 75% = $173.25 85% = $196.35**~~ **Fee: $589.90 Benefit: 75% = $442.45 85% = $506.50** ---------- **Explanatory note:** **This item number should not be used more than once per year per patient.** **This test is not intended for monitoring purposes.**	

5. Proposal for public funding

As per Application 1560, the application stated that the FISH test is well-established in Australia. In 2020, there are at least eight different Australian molecular pathology service providers that routinely offer *17p* deletion testing for patients with CLL. Australian molecular pathology service providers currently use a number of different commercial test kits, including the Vysis CLL probe which was used in the ASCEND study.

Australian pathology service providers participate in a local quality assurance program that is administered by the Royal College of Pathologists of Australasia Quality Assurance Programs Pty Limited (RCPAQAP). This program runs annually with three patient-derived samples (RCPAQAP, 2018).

The application stated that, of the 13 laboratories participating in the program, four utilised the Cytocell TP53 deletion probe set, four utilised the MetaSystems ATM/TP53 probe set from the CLL panel, three used the Vysis ATM/TP53 probe set from the CLL panel and two laboratories used the Cytocell ATM/TP53 combined probe set from the Cytocell CLL panel. The 2018 RCPA QAP demonstrated a concordance rate of 100%, 92% and 100% in Cases 1, 2 and 3, respectively.

6. Proposed intervention's place in clinical management

The inclusion of acalabrutinib in the proposed MBS item 73343 descriptor would not impact the position of FISH testing for *17p* deletions in patients with CLL.

7. Comparative effectiveness

17p deletion testing in ASCEND
The primary data source for the streamlined codependent submission to the PBAC was the randomised Phase III ASCEND trial. ASCEND demonstrated that treatment with acalabrutinib is superior in terms of efficacy and similar in terms of safety to the trial investigator's choice of idelalisib plus rituximab or bendumustine plus rituximab (IR/BR).

Based on a matching adjusted indirect comparison across ASCEND and the RESONATE randomised trial of ibrutinib, the submission to PBAC also claimed that acalabrutinib is non-inferior in terms of efficacy and safety to ibrutinib, the current standard of care.

The primary endpoint in ASCEND was progression free survival (PFS), which demonstrated a statistically significant improvement in independent review committee (IRC)-assessed PFS for acalabrutinib compared with IR/BR, with a 69% reduction in risk of disease progression

or death (hazard ratio =0.31, 95% CI: 0.20, 0.49, p<0.0001). The median estimated PFS for acalabrutinib was not reached; the median estimated PFS for IR/BR was 16.5 months (95% CI: **redacted**).

In ASCEND, central laboratory testing using the Vysis® CLL FISH probe was performed to determine which patients in the study had a *17p* deletion.

8. Financial/budgetary impacts

The application did not propose a change to the eligible population for the test and did not expect the requested amendment to result in any change to the utilisation of the MBS item in terms of number of tests or cost to the MBS.

9. Applicant comments on MSAC's Public Summary Document

The applicant had no comment.

10. Further information on MSAC

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