Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1642 – Programmed death ligand 1 testing for access to cemiplimab for the treatment of metastatic non-small cell lung cancer

Applicant: **sanofi-aventis Australia Pty Ltd**

Date of MSAC consideration: 83rd MSAC Meeting, 25-26 November 2021

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:

- An amendment of Medicare Benefits Schedule (MBS) item 72814 for testing of tumour tissue from patients with non-small cell lung cancer (NSCLC) to detect programmed death ligand 1 (PD-L1) to help determine eligibility for cemiplimab
- Pharmaceutical Benefits Schedule (PBS) listing of cemiplimab for the treatment of patients with metastatic NSCLC with PD-L1 tumour proportion score (TPS) ≥50%, who are negative for epidermal growth factor receptor (*EGFR*) wildtype and negative for anaplastic lymphoma kinase (ALK) and c-ROS proto-oncogene (ROS1).

2. MSAC's advice to the Minister

MSAC supported public funding for PD-L1 testing in patients with non-small cell lung cancer in alignment with PBAC's decision to recommend cemiplimab in this codependent submission.

Although the relevant MBS item descriptor implemented from 1 November 2021 did not need amending, MSAC supported related amendments to the MBS items for *EGFR*, *ALK* and *ROS1* testing to ensure that cemiplimab would only be prescribed as a first-line therapy for eligible patients who do not have any of these biomarkers (see Table 2).

Consumer summary

This application was from sanofi-aventis Australia Pty Ltd, to make a change to Medicare Benefits Schedule (MBS) item so that people with a type of lung cancer who have a particular protein in their cancer cells would then be eligible to access a drug called cemiplimab on the Pharmaceutical Benefits Scheme (PBS).

Cancer comes about when abnormal cells divide uncontrollably and destroy body tissue. Normally, our immune system fights foreign substances. But some cancer cells have high

amounts of PD-L1 (which stands for programmed death-ligand 1). This is a protein that allows the cancer cells to "trick" the immune system, and avoid being attacked as foreign, harmful substances.

Immunohistochemistry is a technique used to work out whether proteins such as PD-L1 are in cancer cells and, if so, how much is there. If cancer cells have a high amount of PD-L1, the person may benefit from a treatment called immunotherapy. This therapy boosts the body's natural defences, using substances made by the body or in a laboratory, to find and destroy cancer cells.

Pembrolizumab and cemiplimab are therapeutic antibodies that stop PD-L1 from working. Currently, in order for people with lung cancer to be eligible to receive pembrolizumab, they have a test for PDL1, which is funded through the MBS. This application was submitted so that evidence could be examined to see whether cemiplimab could also be added to the treatment options listed in the MBS item for the test (that is, to help decide which patients could be treated with either pembrolizumab or cemiplimab).

MSAC considered that the specific test and tested population in the evidence base for both pembrolizumab and cemiplimab were the same, and so supported the application.

However, on 1 November 2021, just before the November MSAC meeting, MBS item 72814 for PD-L1 testing in patients diagnosed with lung cancer was updated to remove mention of pembrolizumab. MSAC had previously agreed with this change to the MBS item which means that neither cemiplimab nor pembrolizumab need to be mentioned.

MSAC considered that, as already applies to pembrolizumab, cemiplimab should not be used before other types of targeted lung cancer treatment. As the MBS already includes tests to help identify which patients should first receive these other targeted treatments, MSAC supported amendments to these test items to ensure that patients are not suitable for these treatments before being treated with cemiplimab.

MSAC's advice to the Commonwealth Minister for Health

Although supporting the application, MSAC advised that no further changes to MBS item 72814 were needed. However, MSAC advised that MBS items for other tests be amended to identify PBS-listed immunotherapies and thus include cemiplimab as well as pembrolizumab.

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

MSAC noted that this application is related to an immunohistochemical (IHC) test to determine if the requirements relating to PD-L1 status for access to pembrolizumab (a PD1 inhibitor) under the PBS are fulfilled.

MSAC noted that the purpose of this submission was to request a minor amendment to MBS item 72814, to add cemiplimab as an alternative to pembrolizumab.

MSAC noted that, in November 2021, PBAC recommended the listing of cemiplimab (Libtayo®), sponsored by sanofi-aventis Australia Pty Ltd, for the treatment of patients with previously untreated metastatic NSCLC with PD-L1 tumour proportion score ≥50%.

MSAC noted that PBAC considered the claims that cemiplimab demonstrated non-inferior comparative effectiveness and safety compared to pembrolizumab were reasonable.

MSAC noted that the relevant cemiplimab clinical trial, R2810 ONC 1624 (Study 1624; NCT03088540) used the same PD-L1 test as pembrolizumab trials, the Dako PD-L1 IHC 22C3 pharmDx test (Dako 22C3 assay). The Dako 22C3 assay was used to determine

eligibility for enrolment in the KEYNOTE 024 trial. MSAC recalled that this test was evaluated in previous applications.

Regarding safety and quality assurance, MSAC noted that the listing of another similar drug on the PBS would not make any difference to the laboratories apart from a different TPS threshold for eligibility.

MSAC considered that there would be no changes to the utilisation of the PD-L1 IHC item, as the PBS listing will simply provide an alternative therapy.

MSAC noted that no changes to the fee were requested.

MSAC noted that on 1 November 2021, item 72814 was updated to remove the restriction of PD-L1 status as a requirement for access to pembrolizumab in patients diagnosed with NSCLC consistent with the revised PBS restriction for pembrolizumab. Item 72814 continues to be available for clinical guidance, as best practice (Table 1).

Table 1 MBS item 72814 as effective from 1 November 2021

CATEGORY 6 – PATHOLOGY SERVICES
72814 Immunohistochemical examination by immunoperoxidase or other labelled antibody techniques using the programmed cell death ligand 1 (PD-L1) antibody of tumour material from a patient diagnosed with non-small cell lung cancer. **Fee:** $74.40 **Benefit:** 75% = $55.90 85% = $63.35

MSAC supported this change and advised that no amendment is necessary to item 72814 to accommodate cemiplimab.

Other discussion

MSAC noted related items 73337, 73341 and 73344 were also updated on 1 November 2021 to specify pembrolizumab. In supporting these changes and to accommodate cemiplimab, MSAC advised that that these items should be amended as follows in Table 2 (additions in **bold** and deletions in strikethrough).

Table 2 MSAC supported amendments for related MBS items (additions in bold and deletions in strikethrough):

CATEGORY 6 – PATHOLOGY SERVICES
73337 A test of tumour tissue from a patient diagnosed with non-small cell lung cancer, shown to have non-squamous histology or histology not otherwise specified, requested by, or on behalf of, a specialist or consultant physician, to determine: a. if the requirements relating to epidermal growth factor receptor (EGFR) gene status for access to an EGFR tyrosine kinase inhibitor under the Pharmaceutical Benefits Scheme are fulfilled; or b. if the requirements relating to EGFR status for access to **an immunotherapy listed** ~~pembrolizumab~~ under the Pharmaceutical Benefits Scheme are fulfilled. **Fee:** $397.35 **Benefit:** 75% = $298.05 85% = $337.75
73341 Fluorescence in situ hybridisation (FISH) test of tumour tissue from a patient with locally advanced or metastatic non-small cell lung cancer, which is of non-squamous histology or histology not otherwise specified, with documented evidence of anaplastic lymphoma kinase (ALK) immunoreactivity by immunohistochemical (IHC) examination giving a staining intensity score > 0, and with documented absence of activating mutations of the epidermal growth factor receptor (EGFR) gene, requested by a specialist or consultant physician, to determine: a. if requirements relating to ALK gene rearrangement status for access to an anaplastic lymphoma kinase inhibitor under the Pharmaceutical Benefits Scheme are fulfilled; or b. if requirements relating to ALK status for access to **an immunotherapy listed** ~~pembrolizumab~~ under the Pharmaceutical Benefits Scheme are fulfilled. **Fee**: $400.00 **Benefit**: 75% = $300.00 85% = $340.00
73344 Fluorescence in situ hybridization (FISH) test of tumour tissue from a patient with locally advanced or metastatic non-small-cell lung cancer, which is of non-squamous histology or histology not otherwise specified, with documented evidence of ROS proto-oncogene 1 (ROS1) immunoreactivity by immunohistochemical (IHC) examination giving a staining intensity score of 2+ or 3+; and with documented absence of both activating mutations of the epidermal growth factor receptor (EGFR) gene and anaplastic lymphoma kinase (ALK) immunoreactivity by IHC, requested by a specialist or consultant physician, to determine: a. if requirements relating to ROS1 gene arrangement status for access to crizotinib or entrectinib under the Pharmaceutical Benefits Scheme are fulfilled; or b. if requirements relating to ROS1 status for access to **an immunotherapy listed** ~~pembrolizumab~~ under the Pharmaceutical Benefits Scheme are fulfilled. **Fee:** $400.00 **Benefit:** 75% = $300.00 85% = $340.00

4. Background

MSAC has not previously considered this application.

MSAC had previously considered PD-L1 testing to help determine eligibility for pembrolizumab: for treatment of locally advanced or metastatic NSCLC (MSAC application 1614); and treatment-naïve patients with locally advanced or metastatic NSCLC (MSAC applications 1440, 1440.1). MSAC supported PD-L1 testing in treatment-naïve patients with locally advanced or metastatic NSCLC application 1440.1.

From 1 November 2021 item 72814 has been updated to remove the restriction of PD-L1 status as a requirement for access to pembrolizumab in patients diagnosed with NSCLC. Item 72814 will be performed for clinical guidance, as best practice, rather than to determine eligibility for pembrolizumab.

5. Prerequisites to implementation of any funding advice

PD-L1 IHC testing is already in use under MBS item 72814. The National Pathology Accreditation Advisory Council Advice advised that there is an existing external quality assurance program.

6. Proposal for public funding

The proposed MBS item descriptor reflects the existing item with a minor amendment to include cemiplimab as an alternative treatment (Table 3). No fee changes were requested to the current MBS item 72814.

Table 3 Applicant- proposed wording for MBS item 72814 (addition in bold)

CATEGORY 6 – PATHOLOGY SERVICES **Group P5 - Tissue Pathology**
72814 Immunohistochemical examination by immunoperoxidase or other labelled antibody techniques using the programmed cell death ligand 1 (PD-L1) antibody of tumour material from a patient diagnosed with non-small cell lung cancer, to determine if the requirements relating to PD-L1 status for access to pembrolizumab **or cemiplimab** under the Pharmaceutical Benefits Scheme are fulfilled. Fee: $74.50 Benefit: 75% = $55.90 85% = $63.35

Source: Table 1, p1 of the minor streamlined codependent submission

7. Comparative effectiveness

Clinical utility standard
The relevant cemiplimab clinical trial (Study 1642) was conducted using the same PD-L1 test (Dako 22C3 test) as for pembrolizumab (manufactured by Dako). The same Dako 22C3 assay used to determine eligibility for enrolment in the KEYNOTE-024 trial.

8. Financial/budgetary impacts

There will be no changes to the utilisation of this item or additional financial cost to the MBS. The number of items processed for PD-L1 IHC testing since listing on the MBS 1 November 2018 is shown in Table 4 by calendar year.

Table 4 Services for PD-L1 IHC testing Item 72814 (2018 – April 2021)

Calendar year	State								Total
	NSW	VIC	QLD	SA	WA	TAS	ACT	NT	
2018	97	29	57	3	0	0	5	0	191
2019	1,820	605	373	139	156	23	37	8	3,161
2020	2,232	748	340	291	140	67	32	5	3,855
YTD April 2021	627	291	145	141	88	31	4	4	1,331
Total	4,776	1,673	915	574	384	121	78	17	8,538

Source: Table 2, p1 of the minor streamlined codependent submission

The application stated that the reimbursement of cemiplimab will not change the market growth rate of patients initiating PD-L1 therapies. It will provide an alternative monotherapy option that is equivalent in efficacy and safety to pembrolizumab monotherapy. The proposed minor amendment to MBS item 72814 will not drive further uptake of PD-L1 IHC tests, as testing is already available to access pembrolizumab.

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