Analysis of medicines for the treatment of non-small cell lung cancer, including a predicted versus actual analysis of durvalumab

Drug utilisation sub-committee (DUSC)

September 2022

Abstract

Purpose

To review the utilisation of PBS listed medicines for non-small cell lung cancer (NSCLC), including an assessment of the predicted versus actual use of durvalumab.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Durvalumab was PBS listed for the treatment of NSCLC on 1 March 2020.

Data Source / methodology

Data extracted from the PBS database maintained by Department of Health and Aged Care, processed by Services Australia were used for the analyses.

Key Findings

- In 2021, there were 85,606 prescriptions dispensed to 8,225 patients for the treatment of NSCLC.
- There was a greater proportion of NSCLC patients treated with immunotherapies compared to targeted therapies.
- In 2021, pembrolizumab was the most common immunotherapy. Based on targeted therapy type, the most common therapies were alectinib (anaplastic lymphoma kinase inhibitor), osimertinib (epidermal growth factor receptor inhibitor) and entrectinib (c-ROS oncogene 1 inhibitor).
- There were 1,033 and 1,259 patients treated with durvalumab during the first and second year of listing respectively, which was [redacted] than estimated.
- There were 24,241 and 22,349 durvalumab prescriptions dispensed during the first and second year of listing respectively, which was [redacted] than estimated.
- Most patients treated with immunotherapies did not switch to another immunotherapy.

Purpose of analysis

To assess the utilisation of PBS listed medicines for the treatment of non-small cell lung cancer (NSCLC), including an assessment to compare the predicted versus actual utilisation of durvalumab, as requested by DUSC at its June 2022 meeting.

Background

Clinical situation

Lung cancer is one of the most common causes of cancer related death in Australia.[1] NSCLC is the most common lung cancer sub-type attributing to over 80% of all lung cancers.[2] NSCLC can be divided into two major histological types, comprising non-squamous and squamous cell carcinoma.

Histological type and genetic biomarkers can direct the treatment course. The relevant genetic biomarkers indicate the presence or absence of driver mutations, including epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) and c-ROS oncogene 1 (ROS1), for which specific inhibitor treatments are available. The presence of a high level of programmed cell death ligand 1 (PD-L1) expression, defined as greater than or equal to 50% of cells, is another molecular characteristic for which PD-L1 or programmed cell death protein 1 (PD-1) protein inhibitors are available.

In this review, utilisation of the following PBS subsidised medicines for the treatment of NSCLC were considered:

Immunotherapies: atezolizumab (first-line [1L] in combination with bevacizumab and second-line [2L] as monotherapy), durvalumab, nivolumab (1L in combination with ipilimumab and 2L as monotherapy) and pembrolizumab.

Targeted therapies:

- EGFR inhibitors: afatinib, erlotinib, gefitinib and osimertinib.
- ALK inhibitors: alectinib, brigatinib, ceritinib, crizotinib and lorlatinib.
- ROS1 inhibitors: crizotinib and entrectinib.

Chemotherapies for NSCLC were not included in this review.

[1] Australian Institute of Health and Welfare. Cancer data in Australia [Internet]. Canberra: Australian Institute of Health and Welfare, 2020 [cited 2020 Aug. 19]. Available from: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia
[2] Zarogoulidis K, Zarogoulidis P, Darwiche K, et al. Treatment of non-small cell lung cancer (NSCLC). J Thorac Dis. 2013;5 Suppl 4(Suppl 4):S389-S396. doi:10.3978/j.issn.2072-1439.2013.07.10

Pharmacology

Durvalumab is a monoclonal antibody that blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1). Expression of PD-L1 protein is an adaptive immune response that helps tumours evade detection and elimination by the immune system. Blockade of these interactions enhances antitumour immune responses. These antitumour responses may result in tumour elimination.[3]

Therapeutic Goods Administration (TGA) approved indications

Durvalumab is TGA indicated for:

- Locally advanced non-small cell lung cancer (NSCLC) whose disease has not progressed following platinum-based chemoradiation therapy.
- First-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC) in combination with etoposide and either carboplatin or cisplatin.
- Locally advanced or metastatic urothelial carcinoma who:
    - -Have disease have disease progression during or following platinum-containing chemotherapy.
    - -Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

[3] Imfinzi (durvalumab). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 2 October 2018, updated 27 October 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Dosage and administration

Table 1: Dosage and administration of medicines for NSCLC

Product	Dose and frequency of administration
Immunotherapies	
ATEZOLIZUMAB	<u>1L with bevacizumab</u> Induction of 1200 mg followed by bevacizumab, then paclitaxel and carboplatin every 3 weeks for four to six cycles. Maintenance of 1200 mg followed by bevacizumab every 3 weeks. <u>2L monotherapy</u> Intravenous infusion First infusion will be given over 60 minutes, following infusions are given over 30 minutes. • 840 mg administered by IV infusion every 2 weeks, • 1200 mg administered by IV infusion every 3 weeks or • 1680 mg administered by IV infusion every 4 weeks. [4]
DURVALUMAB	Intravenous infusion for 1 hour. 10 mg/kg every 2 weeks or 1500 mg every 4 weeks. [3]
NIVOLUMAB	<u>1L with ipilimumab</u> Intravenous infusion 360 mg nivolumab every 3 weeks, in combination with 1 mg/kg ipilimumab via intravenous infusion over 30 minutes every 6 weeks. <u>2L monotherapy</u> Intravenous infusion for 30 minutes • 3 mg/kg every 2 weeks, • 240 mg every 2 weeks or • 480 mg every 4 weeks.[5]
PEMBROLIZUMAB	Intravenous infusion for 30 minutes. Every three or six weeks depending on dose given.[6]

[4] Tecentriq (atezolizumab). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 27 July 2017, updated 12 May 2022. Available from < https://www.tga.gov.au/product-information-pi.>
[5] Opdivo (nivolumab). Australian Approved Product Information. Mulgrave: Bristol-Myers Squibb Australia Pty Ltd. Approved 11 January 2016, updated 18 July 2022. Available from < https://www.tga.gov.au/product-information-pi.>
[6] Keytruda (pembrolizumab). Australian Approved Product Information. Macquarie Park: Merck Sharp & Dome (Australia) Pty Limited. Approved 16 April 2015, updated 18 May 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Product	Dose and frequency of administration
Targeted therapies	
AFATINIB	40 mg tablet once daily.[7]
ALECTINIB	Four 150 mg capsules twice a day (total daily dose of 1200 mg), taken with food.[8]
BRIGATINIB	90 mg tablet once daily for the first 7 days. Thereafter, 180 mg tablet once daily.[9]
CERITINIB	450 mg capsule once daily with food.[10]
CRIZOTINIB	250 mg capsule taken twice daily.[11]
ENTRECTINIB	Adults: 600 mg given orally, once daily Children and adolescents: calculated based on body surface area (BSA) • Greater than 1.50 m^2 BSA: 600 mg once daily. • 1.11 to 1.50 m^2 BSA: 500 mg once daily. • 0.91 to 1.10 m^2 BSA: 400 mg once daily.[12]
ERLOTINIB	One 150 mg tablet daily taken at least one hour before or two hours after the ingestion of food.[13,14]
GEFITINIB	One 250 mg tablet once daily.[15,16]
LORLATINIB	100 mg taken orally once daily.[17]
OSIMERTINIB	80 mg tablet once daily.[18]

Source: TGA Consumer Medicines Information and Product Information.

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from the TGA (Product Information) and the TGA (Consumer Medicines Information).

[7] Giotrif (afatinib). Australian Approved Product Information. North Ryde: Boehringer Ingelheim Pty Limited. Approved 7 November 2013, updated 17 December 2020. Available from < https://www.tga.gov.au/product-information-pi.>
[8] Alecensa (alectinib). Australian Approved Product Information. Sydney: Roche Products Pty Limited. Approved 14 March 2017, updated 7 May 2021. Available from < https://www.tga.gov.au/product-information-pi.>
[9] Alunbrig (brigatinib). Australian Approved Product Information. Sydney: Takeda Pharmaceuticals Australia Pty Ltd. Approved 6 March 2019, updated 3 June 2022. Available from < https://www.tga.gov.au/product-information-pi.>
[10] Zykadia (ceritinib). Australian Approved Product Information. Macquarie Park: Novartis Pharmaceuticals Australia Pty Limited. Approved 31 March 2016, updated 23 March 2022. Available from < https://www.tga.gov.au/product-information-pi.>
[11] Xalkori (crizotinib). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 27 September 2013, updated 10 September 2020. Available from < https://www.tga.gov.au/product-information-pi.>
[12] Rozlytrek (entrectinib). Australian Approved Product Information. Sydney: Roche Products Pty Limited. Approved 15 May 2020, updated 25 March 2022. Available from < https://www.tga.gov.au/product-information-pi.>
[13] Erlotinib Apotex (erlotinib). Australian Approved Product Information. Kew East: Accelagen Pty Ltd. Approved 13 August 2020. Available from < https://www.tga.gov.au/product-information-pi.>
[14] Erlotinib Sandoz (erlotinib). Australian Approved Product Information. Macquarie Park: Sandoz Pty Ltd. Approved 2 September 2020. Available from < https://www.tga.gov.au/product-information-pi.>
[15] Iressa (gefitinib). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 28 April 2003, updated 13 January 2021. Available from < https://www.tga.gov.au/product-information-pi.>
[16] Cipla Gefitinib (gefitinib). Australian Approved Product Information. South Melbourne: Cipla Australia Pty Ltd. Approved 23 April 2020, updated 30 April 2021. Available from < https://www.tga.gov.au/product-information-pi.>
[17] Lorviqua (lorlatinib). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 19 November 2019, updated 22 December 2021. Available from < https://www.tga.gov.au/product-information-pi.>
[18] Tagrisso (osimertinib). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 3 August 2016, updated 14 September 2021. Available from < https://www.tga.gov.au/product-information-pi.>

PBS listing details (as at August 2022)

Table 2: PBS listing of durvalumab

Item	Name, form & strength	Max amount	Rpts	DPMA	Brand name and manufacturer
11915D	durvalumab, 120 mg/2.4 mL injection, 2.4 mL vial 500 mg/10 mL injection, 10 mL vial	1500 mg	4	$12,012.07	Imfinzi® AstraZeneca Pty Ltd
11911X	durvalumab, 120 mg/2.4 mL injection, 2.4 mL vial 500 mg/10 mL injection, 10 mL vial	1500 mg	4	$12,220.65	

Note: Special Pricing Arrangements apply.
Source: the PBS website.

Restriction

Durvalumab is an Authority Required (Streamlined) listing under Section 100 (Efficient Funding of Chemotherapy) for the treatment of unresectable Stage III NSCLC.

Treatment phase: Initial treatment

- Clinical criteria:
  - Patient must have received platinum based chemoradiation therapy, AND
  - The condition must not have progressed following platinum based chemoradiation therapy, AND
  - Patient must have a WHO performance status of 0 or 1, AND
  - Patient must not have previously received PBS-subsidised treatment with this drug for this condition, AND
  - The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition.

Treatment phase: Continuing treatment

- Clinical criteria:
  - Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND
  - Patient must not have developed disease progression while being treated with this drug for this condition, AND
  - The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition, AND
  - The treatment must not exceed 12 months in total for this condition under the initial and continuing restriction combined, AND
  - The treatment must be once in a lifetime with this drug for this condition.

For details of the current PBS listing refer to the PBS website.

Date of listing on PBS

Durvalumab was PBS listed for the treatment of NSCLC on 1 March 2020.

Changes to listing

October 2021: Removal of grandfather treatment phase.

August 2022: The existing listing of durvalumab was amended following the PBAC's recommendation at its March 2022 meeting for the listing of durvalumab 1500 mg Q4W regimen for the treatment of NSCLC. The maximum amount was increased from 1200 mg to 1500 mg, the number of repeats was reduced from 8 to 4 and the administrative note, 'No increase in the maximum number of repeats may be authorised' was removed.

Current PBS listing details are available from the PBS website.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

November 2018 PBAC meeting

The submission requested a Section 100 (Efficient Funding of Chemotherapy), Authority Required (Streamlined) listing for durvalumab for treatment of Stage III NSCLC in patients who have not progressed after platinum-based chemoradiation therapy (CRT). The submission requested PBS listing on the basis of a cost-utility analysis comparing durvalumab to placebo or 'watch and wait' monitoring plus best supportive care.

The PBAC noted that the DUSC considered the estimates of utilisation presented in the submission to be inaccurate. The main issues identified by the DUSC were:

- The proportion of NSCLC of all lung cancers was likely to be closer to 80% than the 70.3% applied in the estimates.
- No justification was provided for the estimate of the proportion of patients undergoing first-line chemoradiation. The submission assumed that 70%, 80% and 90% of eligible patients would receive chemoradiation in Year 1, Year 2 and Years 3-6. The DUSC did not agree that the number of patients receiving chemoradiation would substantially change with the introduction of durvalumab. The DUSC considered that the proportion of patients receiving chemoradiation was reasonable for Year 1, but was overestimated for subsequent years.
- The submission initially estimated that the total cost to Government would be more than $100 million in Year 6. However, the DUSC noted that the financial implications did not account for cost-offsets associated with the lower use of subsequent immunotherapies.

The Pre-PBAC response included a revised estimated use and financial implications and applied the following changes as well as the lower price offered as part of the Pre-PBAC response:

- 80% of lung cancers were assumed to be NSCLC.

- Proportion of patients receiving first line chemoradiation 70% in Year 1, 75% in year 2 and 80% in Years 3-6.

The Pre-PBAC response did not include cost-offsets from later line immunotherapy use. The PBAC considered the DUSC advice on the proportion of patients who would receive first-line chemoradiation to be reasonable.

The PBAC did not recommend the listing of durvalumab as an adjuvant (consolidation) treatment for Stage III NSCLC patients who have not progressed following chemoradiotherapy. The PBAC noted that some patients (~25%) are cured by chemo-radiotherapy and hence consolidation treatment with durvalumab would expose this group of patients to treatment without benefit. The PBAC however acknowledged that adjuvant treatment with durvalumab may reduce the risk of recurrence of NSCLC in some patients who have not been cured by chemo-radiotherapy. However, given the immaturity of the trial data and the unknown impact of subsequent treatment with an immunotherapy agent on progression, the extent of effect on overall survival could not be determined. The Committee considered that the uncertainty surrounding the magnitude of benefit of durvalumab in this setting resulted in a highly uncertain and potentially very high incremental cost-effectiveness ratio.

The PBAC noted the high estimated financial impact of subsidising durvalumab for the proposed listing, although considered that the financial impact was overestimated as it did not account for a reduction in the use of subsequent lines of PD-(L)1 therapies. The PBAC considered that there would be substantial cost offsets from PD-(L)1 use in later stage NSCLC resulting from a PBS listing of durvalumab in stage III NSCLC, which would affect the current risk sharing arrangements (RSA) in the current joint Deed of Agreement for atezolizumab, nivolumab and pembrolizumab in NSCLC. The PBAC considered that if durvalumab was made available on the PBS, there would only be a modest increase in the overall number of patients treated for NSCLC, provided sequential treatment with different PD-(L)1 therapies was precluded.

For further details refer to the Public Summary Document from the November 2018 PBAC meeting.

July 2019 PBAC meeting

The PBAC did not recommend the listing of durvalumab as a consolidation treatment in Stage III unresectable NSCLC in patients who have not progressed after platinum-based CRT.

The PBAC considered the total cost of subsidising durvalumab in this setting to be very high and uncertain. The PBAC considered that the financial impact was overestimated in terms of the eligible patient population and inadequate inclusion of cost-offsets associated with avoiding subsequent immunotherapy.

The PBAC considered it would be appropriate for the patient estimates to apply an uptake of CRT of 70% and an uptake rate for durvalumab of 90% across all years.

The PBAC recalled that in November 2018, it considered that there would be substantial cost-offsets from PD-(L)1 inhibitor use in later stage NSCLC resulting from a PBS listing of durvalumab in stage III NSCLC, which would affect the current RSA in the shared subsidisation cap in the Deeds of Agreement for atezolizumab, nivolumab and pembrolizumab in NSCLC (paragraph 7.13, durvalumab PSD, November 2018 meeting). The PBAC considered the cost-offsets were underestimated in the financial estimates and that it would be appropriate to assume that 70% of patients that initiate treatment with durvalumab would avoid subsequent use of PD-(L)1 inhibitors in the metastatic setting.

The PBAC reaffirmed its November 2018 advice that if durvalumab was made available on the PBS, there would only be a modest increase in the overall number of patients treated for NSCLC, provided sequential treatment with different PD-(L)1 therapies was precluded. The PBAC also reaffirmed its previous advice that due to a lack of evidence to support the sequential use of immunotherapies, precluding prior and subsequent use of PD-(L)1 inhibitors remained appropriate. The PBAC further considered it was appropriate for durvalumab to share the RSA subsidisation cap in the current Deeds of Agreement for locally advanced/metastatic NSCLC for PD-(L)1 therapies.

The PBAC considered that any resubmission could be a minor resubmission and would be required to:

- Revise the patient estimates applying the uptake rates.
- Revise the financial estimates for grandfathered patients to take into account only the number of patients accessing treatment at the time of PBAC reconsideration and a reduced cost per patient to account for treatment already received.

For further details refer to the Public Summary Document from the July 2019 PBAC meeting.

November 2019 PBAC meeting

The PBAC recommended the listing of durvalumab, on the basis that it should be available only under special arrangements under Section 100 (Efficient Funding of Chemotherapy). The PBAC recommended durvalumab be made available for the treatment of unresectable Stage III NSCLC in patients whose disease had not progressed following CRT. The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of durvalumab would be acceptable with a small (around 5%) reduction to the price proposed in the resubmission.

The PBAC noted the revised financial estimates applied the treatment cost per patient for nivolumab to estimate the net reduction in cost of PD-(L)1 inhibitors but there are alternative PD-(L)1 inhibitors available in the first-line and second-line setting (pembrolizumab, atezolizumab). The PBAC noted the PD-(L)1 inhibitor costs for the offset patients (in both the first-line or second-line setting) are already accounted for in current subsidisation caps for NSCLC. The PBAC was also of the view that nivolumab should not be considered the most likely therapy for the purposes of the estimated offset population, as the PBAC has previously considered that the majority of patients were likely to switch to first line treatment with PD-(L)1 inhibitors once these are available.

For further details refer to the Public Summary Document from the November 2019 PBAC meeting

March 2022 PBAC meeting

The PBAC recommended the listing of the durvalumab 1500 mg Q4W regimen for the treatment of NSCLC. The PBAC considered creating a separate listing with a maximum amount of 1500 mg and four repeats to provide for 1500 mg Q4W dosing may lead to unnecessary complexity and potential ambiguity in the listings.

Instead, the PBAC recommended amending the existing listing as follows:

- Increase the maximum amount from 1200 mg to 1500 mg.
- Reduce the number of repeats from 8 to 4.
- remove administrative advice: 'No increase in the maximum number of repeats may be authorised'.

The PBAC considered the market share estimates were reasonable and, due to the small cost differences, were unlikely to have a significant impact on the overall financial impact.

For further details refer to the Public Summary Document from the March 2022 PBAC meeting.

Previous reviews by the DUSC

Commercial-in-confidence

[redacted]

End commercial-in-confidence

February 2017

Erlotinib and Gefinitib for NSCLC: predicted versus actual analysis

In 2014, 598 patients commenced erlotinib or gefitinib for first-line treatment of Stage IIIB (locally advanced) or Stage IV (metastatic) NSCLC harbouring EGFR mutations. In 2015, 347 patients commenced 1L erlotinib or gefitinib therapy. The number of patients who received 1L TKIs was similar to expected in 2014 and lower than expected in 2015. Median length on 1L TKI treatment was similar to predicted. The observed prevalence of EGFR mutations (17.9%) was similar to predicted (15%). A small proportion of patients (7.4%) initiating TKI

therapy in 2014 had supplies of chemotherapy between supplies of TKI, indicating use beyond progression or in combination with chemotherapy, which is outside the PBS restriction.

For details of the DUSC consideration of erlotinib and gefitinib refer to the Public Release Document from the February 2017 DUSC meeting.

June 2020

Nivolumab for NSCLC: predicted versus actual analysis

DUSC reviewed the use of nivolumab for the treatment of NSCLC. Since PBS listing, 5,331 patients were supplied nivolumab for NSCLC, and in 2019, 25,816 prescriptions of nivolumab were supplied to 2,327 patients. The utilisation of nivolumab had decreased as other immunotherapies had been PBS listed for NSCLC. The alteration of the PBS restriction to allow flat dosing from September 2019 was changing prescribing, as patients were being supplied higher doses less often.

For details of the DUSC consideration of nivolumab refer to the Public Release Document from the June 2020 DUSC meeting.

October 2020

Alectinib for NSCLC: predicted versus actual analysis

DUSC reviewed the use of alectinib for the treatment of NSCLC. In 2018, 254 patients were dispensed 1,715 alectinib scripts. In 2019, 322 patients were dispensed 2,546 alectinib scripts. The overall utilisation of alectinib was higher than expected. The growth in the number of dispensed scripts was greater compared to the number of patients as the treatment duration was longer than predicted. For patients treated with ALK inhibitors, most were treated with alectinib or switched from a different treatment to alectinib.

For details of the DUSC consideration of alectinib refer to the Public Release Document from the October 2020 DUSC meeting.

Methods

Data extracted from the PBS claims database maintained by the Department of Health and Aged Care and processed by Services Australia were used for the analyses. Prescription data were extracted from 1 January 2016 up to and including 30 June 2022.

These data were used to determine the prescription and patients counts for the NSCLC market counted by supply quarter and calendar year. These counts were categorised into therapy type: immunotherapy and targeted therapy. Drug names were ascertained based on their item code. Crizotinib is currently PBS listed as both an ALK and ROS1 inhibitor, for which there are separate item codes. Similarly, atezolizumab and nivolumab are currently PBS listed as 1L and 2L therapies for NSCLC, for which there are separate item codes for.

Bevacizumab was PBS listed as a combination therapy with atezolizumab for 1L therapy. However, on 1 June 2021, it became an unrestricted listing with different item codes with a change in brand name.[19] As the indication for NSCLC utilisation cannot be ascertained following its change to an unrestricted listing, utilisation data for bevacizumab was only extracted up until 31 May 2021.

For durvalumab, PBS claims data were used to determine the number of incident and prevalent patients, number of prescriptions supplied, and to analyse patient demographics such as age and gender. Initiating and prevalent patients were counted by quarter of supply. An initiating patient was defined based on their first date of supply of durvalumab.

A drug sequence analysis was conducted to examine the utilisation pattern of immunotherapies. The first prescribed drug was recorded and if patients were subsequently supplied other drugs, these were noted to form the patient's drug chronological sequence.

The treatment duration of durvalumab was ascertained. A Kaplan-Meier curve was generated to present treatment duration. A cohort of initiating patients were selected from 1 June 2020, to account for the wash out period of grandfathered patients, up to and including 30 November 2020. These patients were followed until 30 June 2022, with patients censored if they were still continuing treatment. Another Kaplan Meier curve was generated accounting for breaks in treatment. A patient was considered to be on a treatment break if they did not receive a supply in more than two sets of standard treatment days. The median standard treatment days was calculated to be 14 days.

Date of death data were linked to the PBS claims data based on the unique patient identifier. This was used to determine the proportion of patients who ceased durvalumab treatment due to death. Date of death data were last updated 20 December 2021. As this

[19] Department of Health and Aged Care. Pharmaceutical Benefits Scheme (PBS). Bevacizumab on the PBS. Available from <https://www.pbs.gov.au/info/news/2021/07/bevacizumab-on-the-pbs>

analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data.[20]

Data manipulation was undertaken using SAS.

[20] PBS statistics. Australian Government Services Australia. Canberra. Available from <http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>.

Results

Analysis of drug utilisation

Overall utilisation

Figure 1 and Table 3 shows the number of prescriptions supplied for the treatment of NSCLC by supply quarter and calendar year, respectively.

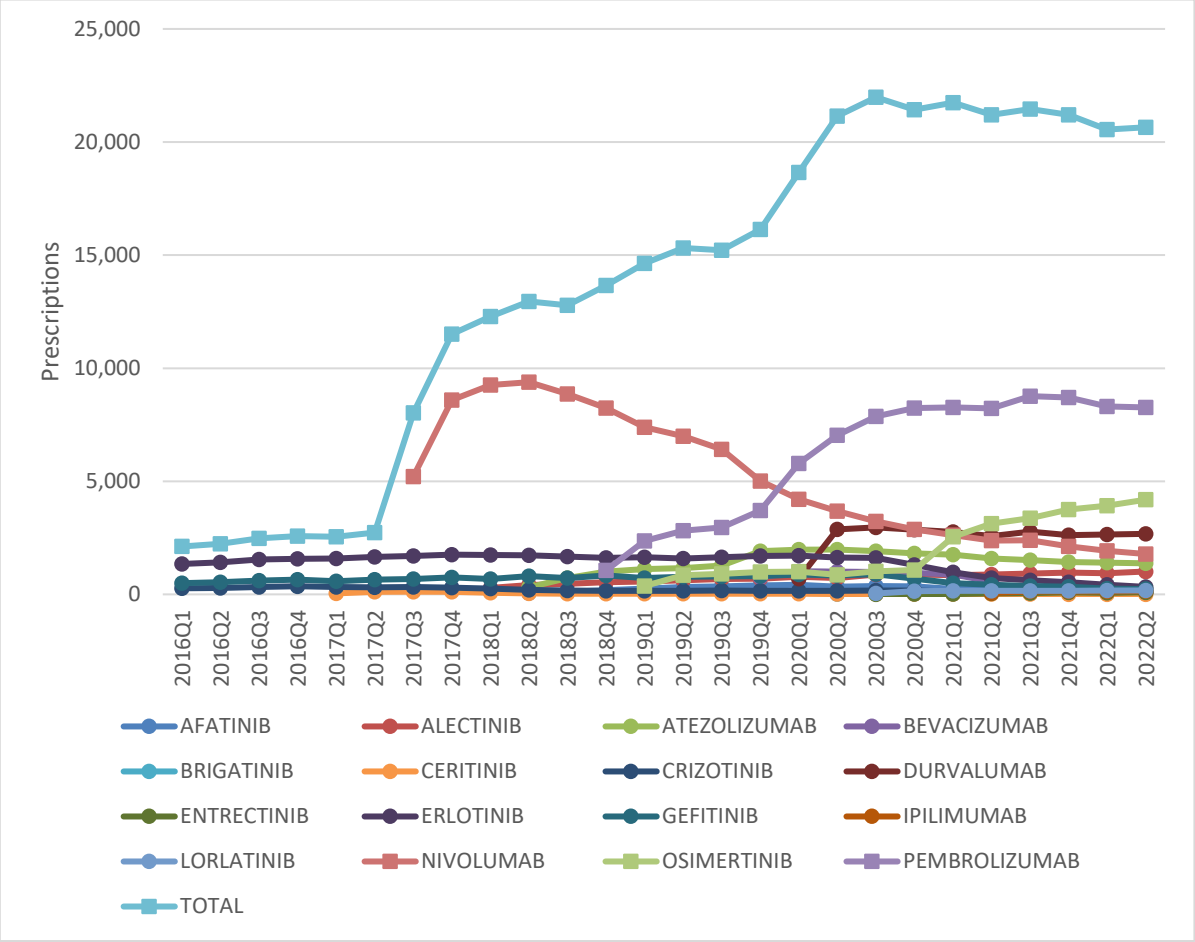

Figure 1: Number of prescriptions supplied for the treatment for NSCLC by supply quarter

As shown in Figure 1, based on the number of prescriptions supplied, the drug that has accounted for the largest NSCLC market share has varied over time, including erlotinib (prior to 2017Q3), nivolumab (from 2017Q3 to 2020Q1) and pembrolizumab (from 2020Q1 onwards).

Table 3: Number of NSCLC prescriptions supplied by drug and calendar year

Drug	2016	2017	2018	2019	2020	2021	2022	Total
NIVOLUMAB		13,799	35,747	25,816	13,992	9,499	3,717	102,570
PEMBROLIZUMAB			1,062	11,846	28,933	33,959	16,574	92,374
ERLOTINIB	5,874	6,705	6,755	6,562	6,258	2,857	755	35,766
OSIMERTINIB				3,113	3,952	12,808	8,105	27,978
DURVALUMAB					9,398	10,735	5,333	25,466
ATEZOLIZUMAB			2,033	5,472	7,663	6,297	2,778	24,243
GEFITINIB	2,285	2,657	3,037	3,112	3,291	1,620	494	16,496
ALECTINIB			1,715	2,546	3,248	3,614	1,950	13,073
BEVACIZUMAB				746	3,974	1,443		6,163
CRIZOTINIB	1,248	1,258	784	640	654	515	203	5,302
AFATINIB			354	1,344	1,484	884	366	4,432
LORLATINIB					181	620	342	1,143
CERITINIB		395	179	97	62	46	11	790
IPILIMUMAB						314	265	579
BRIGATINIB					96	191	149	436
ENTRECTINIB					23	204	161	388
Total	9,407	24,814	51,666	61,294	83,209	85,606	41,203	357,199
Growth from previous year		164%	108%	19%	36%	3%		

Notes:

- 2022 figures are year-to-date 30 June.
- The PBS listing of bevacizumab became unrestricted 1 June 2021.

In Table 3, nivolumab accounted for the highest total number of NSCLC prescriptions supplied. The highest percentage growth in the number of NSCLC prescriptions was observed between 2016 to 2017 (164%), due to the PBS listings of nivolumab and ceritinib in 2017.

Figure 2 and Table 4 shows the number of patients supplied treatment for NSCLC by supply quarter and calendar year, respectively.

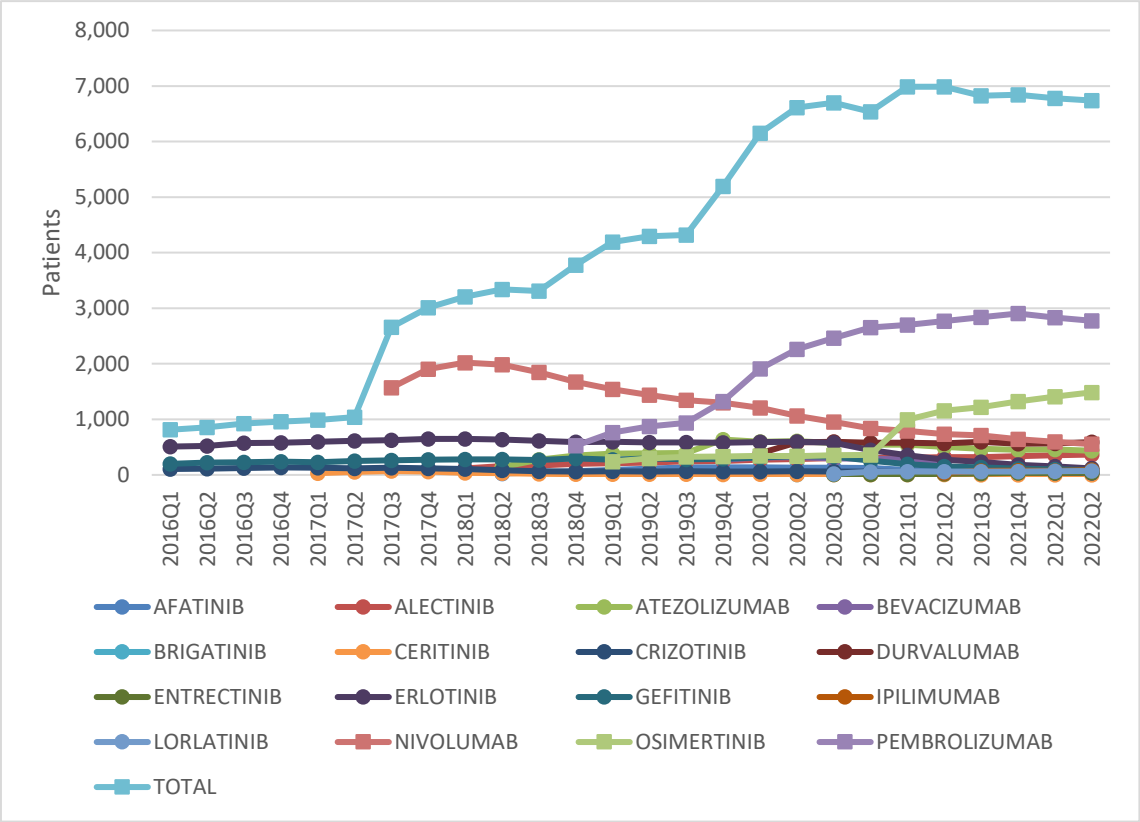

Figure 2: Number of patients supplied treatment for NSCLC by supply quarter

As shown in Figure 2, based on the number of patients treated for NSCLC the most common drug for the treatment of NSCLC has varied over time, including erlotinib (prior to 2017Q3), nivolumab (from 2017Q3 to 2020Q1) and pembrolizumab (from 2020Q1 onwards).

Table 4: Number of patients supplied treatment for NSCLC by drug and calendar year

Drug	2016	2017	2018	2019	2020	2021	2022	Total
PEMBROLIZUMAB			525	1,944	4,295	5,048	3,545	15,357
NIVOLUMAB		2,247	3,244	2,327	1,565	1,095	680	11,158
ERLOTINIB	856	983	962	903	823	383	155	5,065
OSIMERTINIB				438	506	1,743	1,643	4,330
ATEZOLIZUMAB			488	1,004	1,035	854	572	3,953
DURVALUMAB					932	1,031	728	2,691
GEFITINIB	360	398	434	440	445	214	105	2,396
ALECTINIB			254	322	374	397	401	1,748
BEVACIZUMAB				275	588	322		1,185
CRIZOTINIB	183	195	116	99	84	65	42	784
AFATINIB			83	192	202	115	77	669
IPILIMUMAB						120	114	234
LORLATINIB					57	94	79	230
CERITINIB		108	45	22	13	10	≤5	203
ENTRECTINIB					10	47	48	105
BRIGATINIB					25	32	32	89
Total	1,399	3,931	6,151	7,966	10,954	11,570	8,226	50,196
Growth from previous year		181%	56%	30%	38%	6%		

Notes:

- 2022 figures are year-to-date 30 June.
- The PBS listing of bevacizumab became unrestricted 1 June 2021.
- Where the patient count is between 1 and 4 (inclusive), a figure data point is set to ≤5 to protect patient confidentiality.

In Table 4, most NSCLC patients were treated with pembrolizumab. The highest percentage growth in the number of patients treated for NSCLC was observed between 2016 and 2017 (181%), due to the PBS listings of nivolumab and ceritinib in 2017.

Utilisation by type of NSCLC therapy

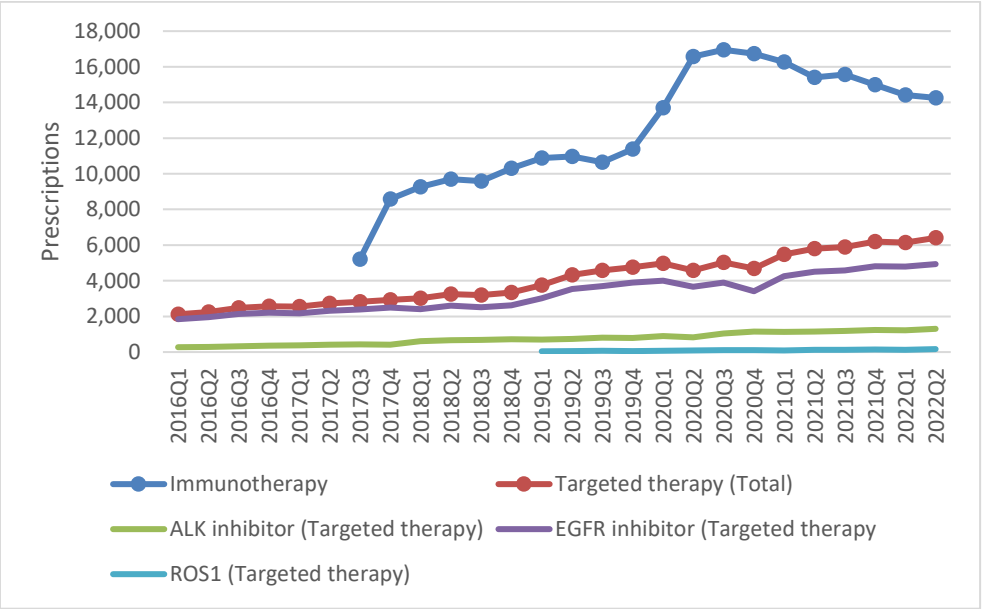

Figure 3: Number of prescriptions supplied for the treatment for NSCLC by therapy type and supply quarter

As shown in Figure 3, immunotherapies accounted for a greater proportion of prescriptions supplied for the treatment of NSCLC compared to targeted therapies.

Table 5: Annual growth in the number of prescriptions supplied by NSCLC therapy type and calendar year

	2017 vs 2016	2018 vs 2017	2019 vs 2018	2020 vs 2019	2021 vs 2020
Immunotherapy		181%	13%	46%	-3%
Targeted therapy	17%	16%	36%	11%	21%
ALK inhibitor	32%	62%	14%	28%	21%
EGFR inhibitor	15%	8%	39%	6%	21%
ROS1 inhibitor				60%	29%

In Table 5, the highest percentage growth in the number of prescriptions supplied for immunotherapies (181%) was observed between 2017 and 2018, whereas for targeted therapies (36%), this was observed between 2018 and 2019.

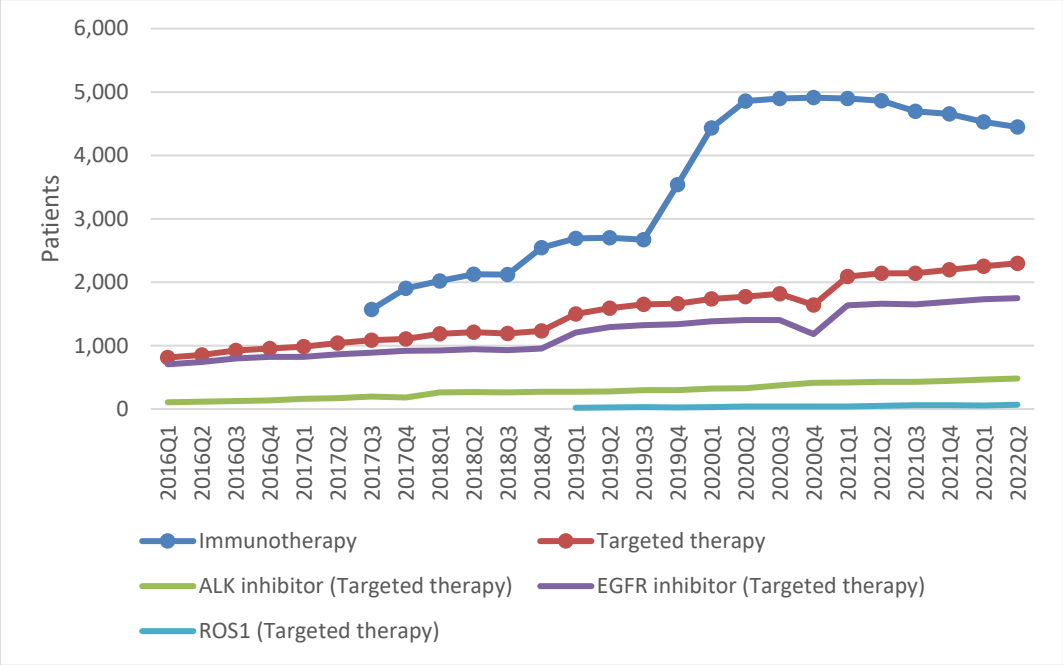

Figure 4: Number of patients treated for NSCLC by therapy type and supply quarter

As shown in Figure 4, most NSCLC patients were treated with immunotherapies compared to targeted therapies. An increase of approximately 2,600 to 4,800 patients treated per supply quarter with immunotherapies was observed between 2019Q3 and 2020Q2, which is likely due to extension of pembrolizumab listing from monotherapy to include combination therapy with platinum chemotherapy and pemetrexed (recommended at the July 2019 PBAC meeting).

Table 6: Annual growth in the number of patients treated for NSCLC therapy type and calendar year

	2017 vs 2016	2018 vs 2017	2019 vs 2018	2020 vs 2019	2021 vs 2020
Immunotherapy		89%	31%	53%	0.3%
Targeted therapy	20%	12%	28%	5%	22%
ALK inhibitor	66%	37%	-2%	26%	10%
EGFR inhibitor	14%	7%	33%	0%	24%
ROS1 inhibitor				39%	44%

In Table 6, the highest percentage growth in the number of patients treated with immunotherapies (89%) was observed between 2017 to 2018, whereas for targeted therapies (28%), this was observed between 2018 and 2019.

Utilisation of NSCLC immunotherapies

The following immunotherapies are listed 1L for stage IV (metastatic) NSCLC:

- Atezolizumab + bevacizumab (in combination with platinum-based chemotherapy)
- Nivolumab + ipilimumab (in combination with platinum-based chemotherapy for the first two cycles)
- Pembrolizumab

Atezolizumab monotherapy and nivolumab monotherapy are 2L immunotherapies following platinum-based chemotherapy for locally advanced or metastatic NSCLC.

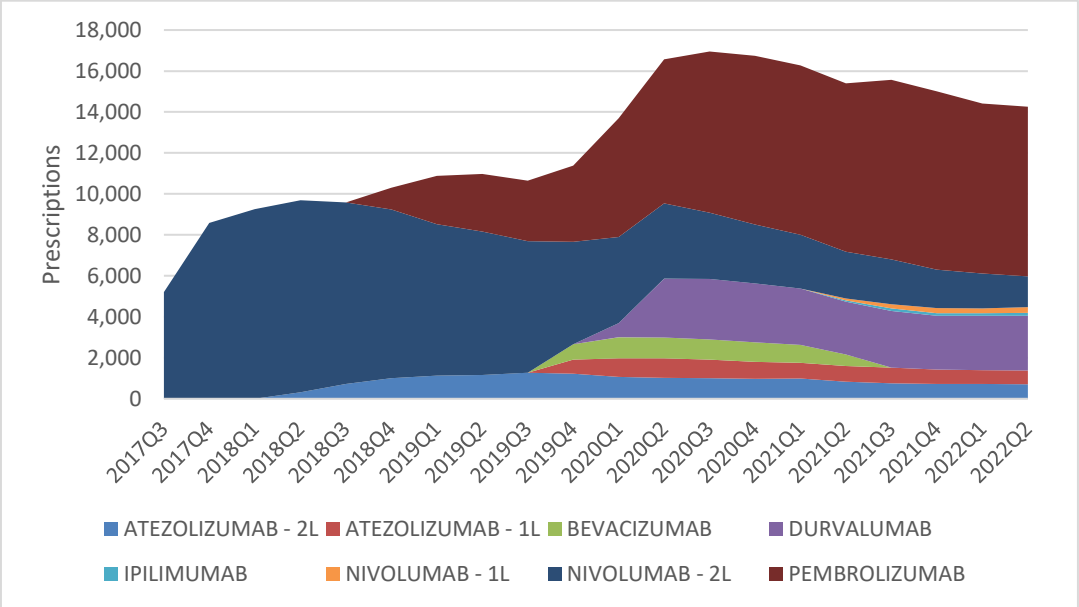

Figure 5: Number of NSCLC immunotherapy prescriptions by supply quarter

As shown in Figure 5 based on prescription counts, pembrolizumab was the most common immunotherapy overall for NSCLC. Nivolumab monotherapy was previously the most common immunotherapy, however, its utilisation has decreased following the PBS listing of other immunotherapies. Despite nivolumab monotherapy utilisation decreasing over time, it remains the more commonly utilised 2L immunotherapy compared to atezolizumab. Durvalumab is the second-most common immunotherapy, overtaking nivolumab monotherapy from 2021 onwards.

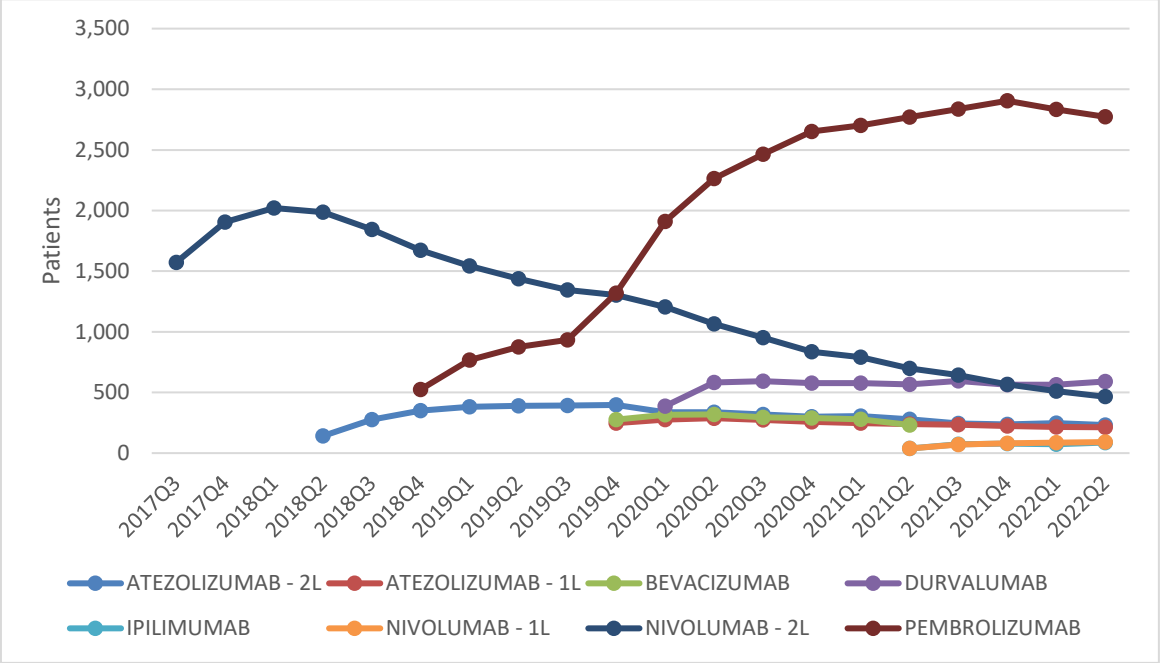

Figure 6: Number of patients treated with NSCLC immunotherapies by supply quarter

As shown in Figure 6, pembrolizumab was the most common immunotherapy for NSCLC patients. Nivolumab monotherapy was previously the most common immunotherapy, however, its utilisation has decreased following the introduction of other immunotherapies. Despite nivolumab monotherapy utilisation decreasing over time, a greater proportion of patients were treated with nivolumab as 2L therapy compared to atezolizumab. In relation to other NSCLC immunotherapies, durvalumab was the third-most common treatment, however it appears to have overtaken nivolumab in the most recent supply quarter.

Utilisation of NSCLC targeted therapies

ALK inhibitors

Alectinib, brigatinib, ceritinib, crizotinib and lorlatinib are PBS listed for stage IIIB (locally advanced) or stage IV (metastatic) NSCLC. Criteria for treatment include the requirements for monotherapy, non-squamous type NSCLC or not otherwise specified (NOS) NSCLC, WHO performance status of 2 or less and evidence of ALK gene arrangement in tumour material of 15% or greater positive cells by fluorescence in situ hybridisation (FISH) testing.

Alectinib, brigatinib, ceritinib and crizotinib are line agnostic ALK inhibitors. At the time of this review (August 2022), lorlatinib is a 2L treatment with patients required to have progressed treatment with an ALK other than crizotinib. It is noted that PBAC recommended a line agnostic listing for lorlatinib at its December 2021 Meeting.

As shown in Figure 7 and 8 below, alectinib remains the most common ALK inhibitor supplied to patients since its PBS listing (1 January 2018).

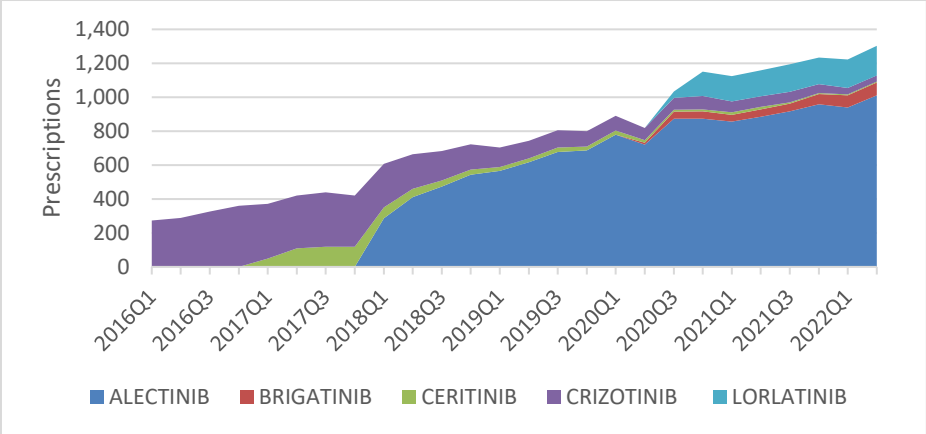

Figure 7: Number of prescriptions supplied for ALK inhibitors by supply quarter

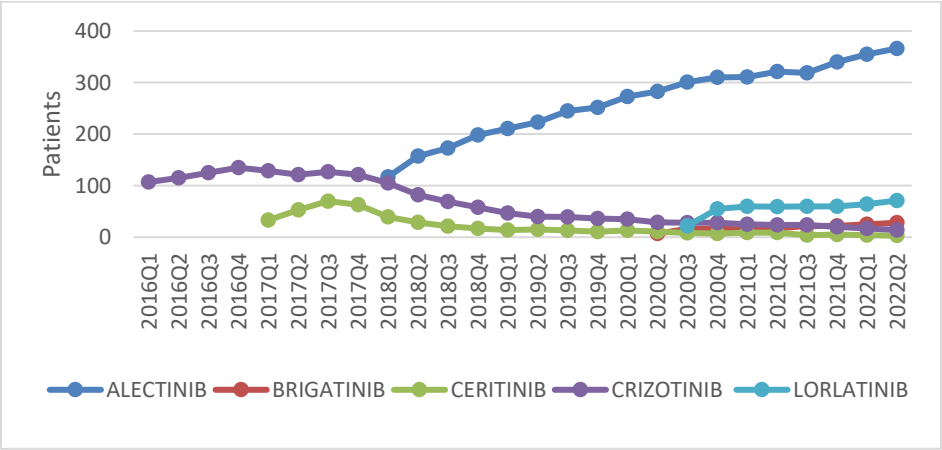

Figure 8: Number of patients treated with ALK inhibitors by supply quarter

EGFR inhibitors

Afatinib, erlotinib, gefitinib and osimertinib are PBS listed for stage IIIB (locally advanced) or stage IV (metastatic) NSCLC. Criteria for treatment include the requirements for monotherapy, non-squamous type NSCLC or NOS NSCLC, WHO performance status of 2 or less, evidence of an activating EGFR gene mutation known to confer sensitivity to treatment with EGFR tyrosine kinase inhibitors (TKI) in tumour material and to be 1L EGFR TKI therapy or if not have developed an intolerance to another EGFR TKI of a severity necessitating permanent treatment withdrawal.

Osimertinib is also listed for 2L EGFR TKI therapy, where patients must have evidence of EGFR T790M mutation in tumour material at the point of progression on or after 1L EGFR TKI treatment.

As shown in Figure 9 and 10 below, osimertinib was the most common treatment for EGFR mutations. On 1 January 2021 (recommended at the July 2020 PBAC Meeting), the listing for osimertinib was extended for 1L therapy.

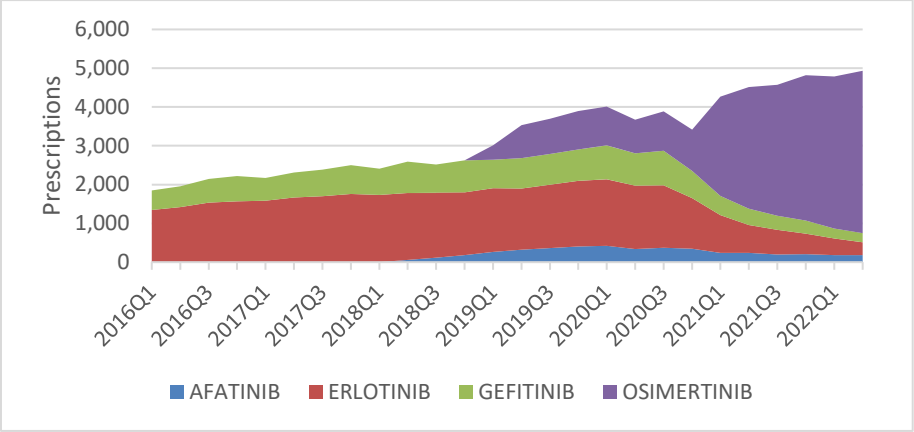

Figure 9: Number of prescriptions supplied for EGFR inhibitors by supply quarter

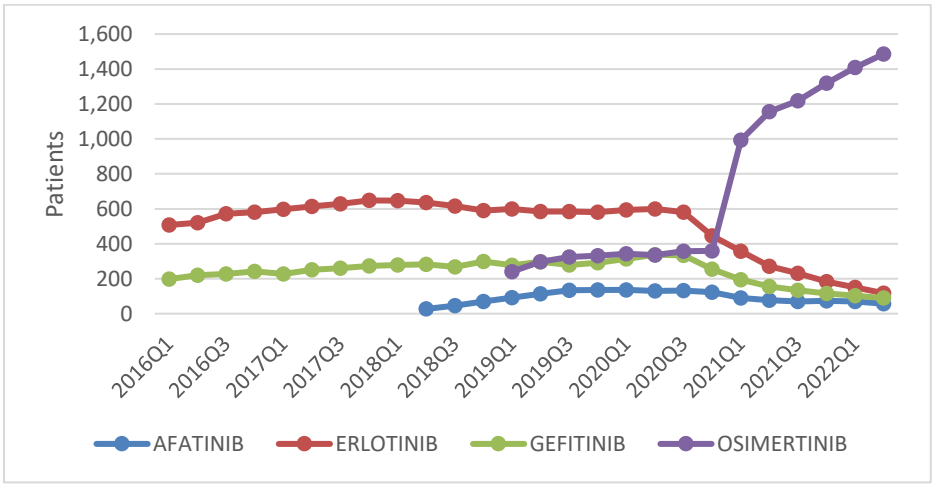

Figure 10: Number of patients treated with EGFR inhibitors by supply quarter

ROS1 inhibitors

Crizotinib and entrectinib are PBS listed for stage IIIB (locally advanced) or stage IV (metastatic) NSCLC. Criteria for treatment include the requirements for monotherapy, non-squamous type NSCLC or NOS NSCLC, WHO performance status of 2 or less, evidence of ROS1 gene arrangement in tumour material of 15% or greater positive cells by FISH testing and intolerance to ROS1 receptor TKI necessitating permanent treatment withdrawal.

As shown in Figure 11 and 12 below, prior to 2021Q4, crizotinib accounted for a greater proportion of utilisation in the ROS1 inhibitor market. From 2021Q4 onwards, a greater number of patients were treated with entrectinib compared to crizotinib.

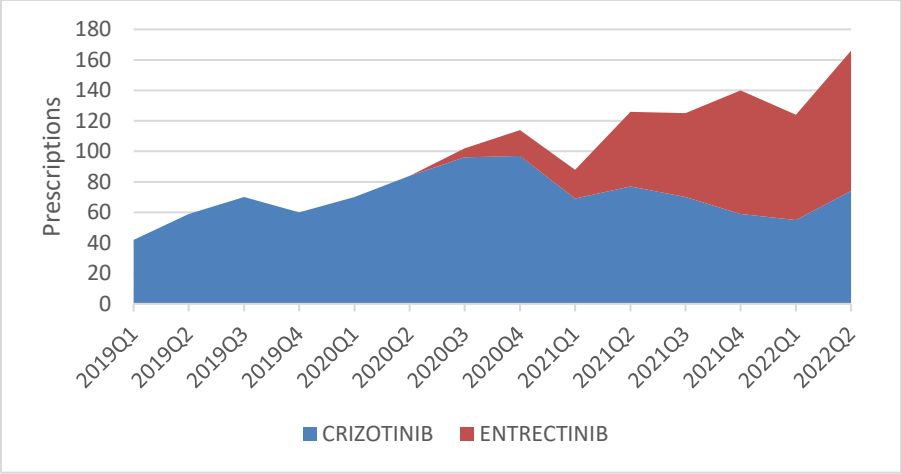

Figure 11: Number of prescriptions supplied for ROS1 inhibitors by supply quarter

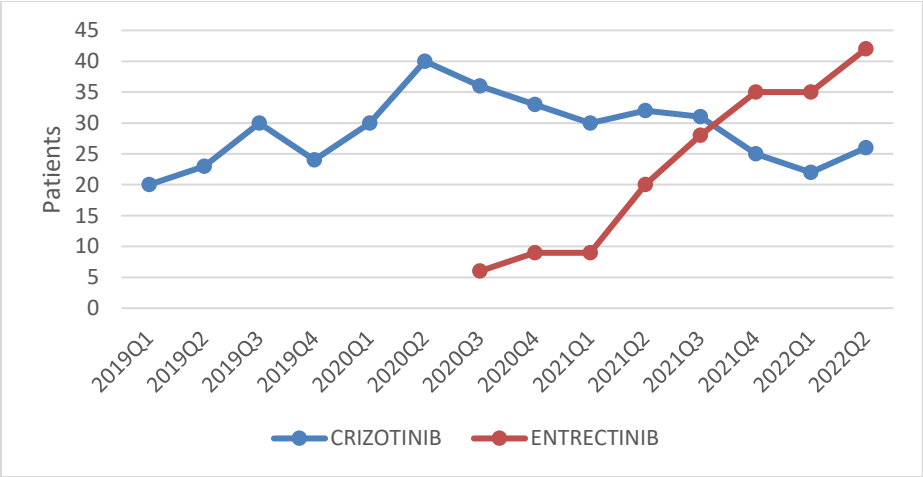

Figure 12: Number of patients treated with ROS1 inhibitors by supply quarter

Utilisation by relevant sub-populations/regions or patient level analysis

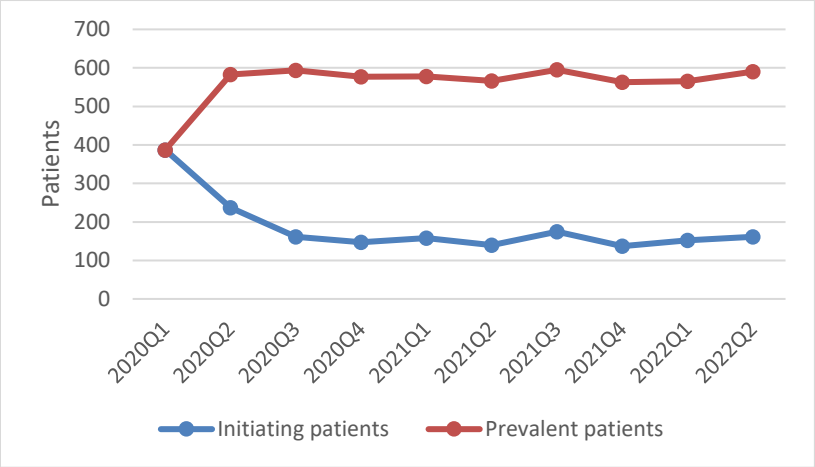

Figure 13: Number of initiating and prevalent durvalumab patients by supply quarter

Figure 13 shows the number of initiating and prevalent durvalumab patients. From 2020Q3 onwards, the number of initiating and prevalent patients have remained relatively stable, with approximately 150 initiating patients and 580 prevalent patients per supply quarter.

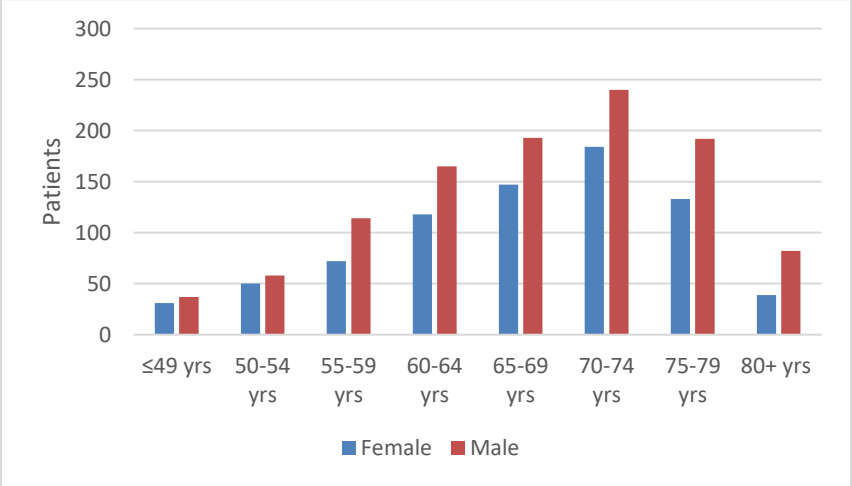

Figure 14: Age and gender distribution of initiating durvalumab patients

Figure 14 shows the age and gender distribution of patients initiating treatment with durvalumab. The most common age group for both female and male was 70-74 years. Overall, the mean and median age was 67 and 69 years, respectively. The age range of patients was between 36 to 93 years old.

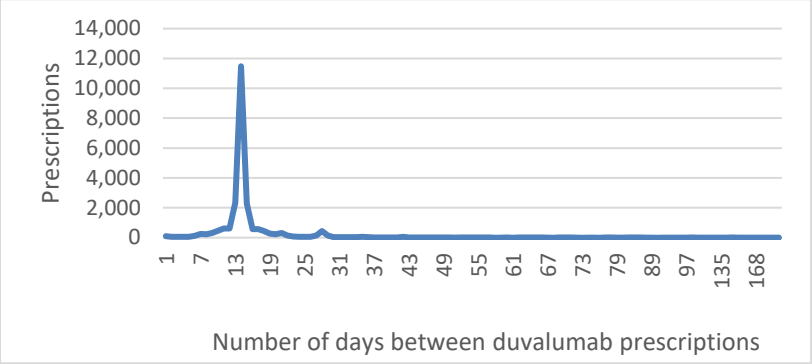

Figure 15: Time to resupply durvalumab prescriptions

From Figure 15, the most common resupply time between durvalumab prescriptions was 14 days. This is consistent with the recommended dosage interval in the Product Information, which recommended a dosage of 10 mg/kg infused every two weeks.

Table 7: Estimated length of treatment from Kaplan Meier analysis in patients who initiated durvalumab treatment from 1 June 2020 to 30 November 2020 and followed up to 30 June 2022

Number of patients	Censored	Median (weeks)	Mean (weeks)	Standard error	95% confidence interval (weeks)	
					Lower limit	Upper limit
318	0	47.14	37.06	1.14	34.83	39.30

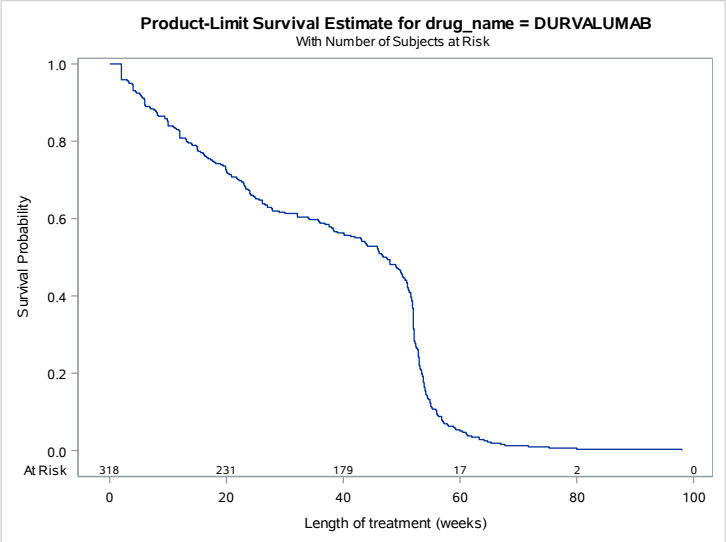

Figure 16: Treatment duration for patients who initiated durvalumab treatment for NSCLC between 1 June 2020 to 30 November 2020 and followed up to 30 June 2022

As shown in Table 7 and Figure 16 above, patients who initiated durvalumab treatment between 1 June 2020 to 30 November 2020, the mean and median length of treatment was 37.06 and 47.14 weeks, respectively. At the analysis end date of 30 June 2022, nil patients were censored and considered to be continuing treatment. Of the 318 patients who

initiated treatment with durvalumab, 19 patients died. Between the date of last supply of durvalumab and date of death, there was a median of 33 days and a mean of 50 days.

Table 8: Estimated length of treatment from Kaplan Meier analysis in patients who initiated durvalumab treatment from 1 June 2020 to 30 November 2020 and followed up to 30 June 2022, accounting for breaks

Number of patients	Censored	Median (weeks)	Mean (weeks)	Standard error	95% confidence interval (weeks)	
					Lower limit	Upper limit
318	0	43.36	34.64	1.05	32.56	36.71

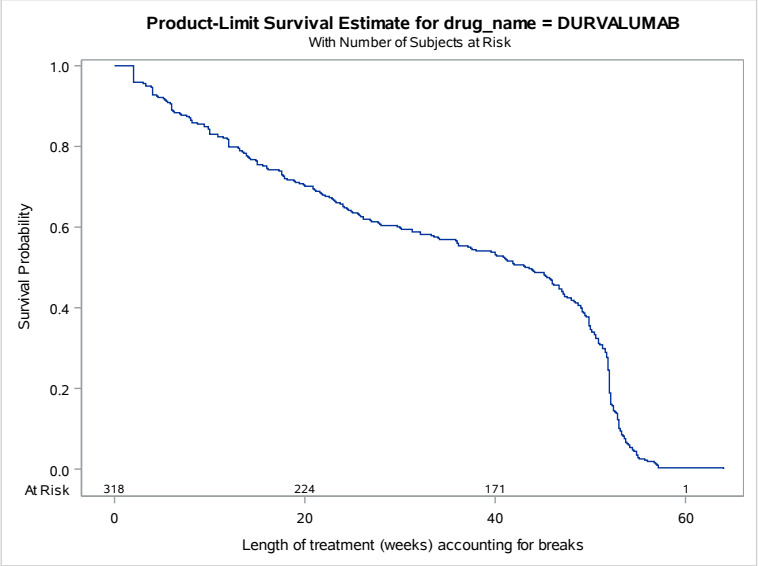

Figure 17: Treatment duration for patients who initiated durvalumab treatment for NSCLC between 1 June 2020 to 30 November 2020 and followed up to 30 June 2022, accounting for breaks

As shown in Table 8 and Figure 17, accounting for breaks in treatment reduced the estimated mean length of treatment from 37.06 to 34.64 weeks and the median length of treatment from 47.14 to 43.36 weeks.

Changes in the use of other drugs

Table 9: Sequence analysis between immunotherapies for NSCLC since PBS listing of durvalumab (March 2020 to June 2022)

Sequence	Percent
PEMBROLIZUMAB	60.7%
DURVALUMAB	13.0%
NIVOLUMAB	12.3%
ATEZOLIZUMAB	7.3%
ATEZOLIZUMAB+BEVACIZUMAB	3.9%
NIVOLUMAB+IPILIMUMAB	1.2%
BEVACIZUMAB	0.6%
DURVALUMAB>PEMBROLIZUMAB	0.3%
DURVALUMAB>NIVOLUMAB	0.1%
IPILIMUMAB	0.1%
NIVOLUMAB>PEMBROLIZUMAB	0.1%
DURVALUMAB>NIVOLUMAB+IPILIMUMAB	<0.1%
ATEZOLIZUMAB+BEVACIZUMAB>PEMBROLIZUMAB	<0.1%
PEMBROLIZUMAB>DURVALUMAB	<0.1%
PEMBROLIZUMAB>ATEZOLIZUMAB	<0.1%
Other sequences	0.3%

In Table 9 above, 99.1% of patients who were treated with an immunotherapy for NSCLC did not switch to another immunotherapy between March 2020 and June 2022. Less than one percent of patients who were treated with durvalumab switched to another immunotherapy during this period.

Analysis of actual versus predicted utilisation of durvalumab

Approach taken to estimate utilisation

An epidemiological approach was used to estimate durvalumab utilisation.

Table 10: Revised financial estimates for durvalumab considered at the November 2019 PBAC Meeting

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of durvalumab treated patients	[redacted]					
Number of nivolumab patients with cost offsets (70%)						
Estimated financial implications of durvalumab						
Net cost to PBS/RPBS (effective price minus co-payments)	[redacted]					
Net reduction in cost of PD-L1 medicines (at nivolumab rebate of [redacted]%)						
Net cost to PBS/RPBS (effective price)	[redacted]					
Net financial implications						
Net cost to PBS/RPBS (effective price)	[redacted]					
Net cost to MBS						
Net cost to health budget						

[redacted]

[redacted]

Table 11: Durvalumab predicted versus actual utilisation

durvalumab listing years		Year 1 March 2020 – February 2021	Year 2 March 2021 – February 2022	Year 3 March 2022- February 2023
Patients	Predicted	[redacted]		
	Actual	1,033	1,032	647
	Difference	[redacted]		
Prescriptions	Predicted			
	Actual	11,129	10,667	3,670
	Difference	[redacted]		

Note: The predicted number of treated patients in the first year of listing includes [redacted] eligible grandfather patients. Year 3 predicted numbers are for the full year, actual numbers are six months of data (March 2022 to June 2022, inclusive).

As shown in Table 11, durvalumab utilisation was [redacted] than estimated in its first three years of listing.

Based on the streamlined code for grandfather patients, there were 359 grandfather patients who were treated with durvalumab. This was [redacted]% of the estimated number of [redacted] grandfather patients and [redacted]% of the estimated number of [redacted] eligible grandfather patients.

Table 12: Durvalumab predicted versus actual dosing

	Predicted	Actual	Difference
Average dose per patient	[redacted] mg	758 mg	[redacted]
Average treatment duration	[redacted] weeks	34.64 weeks	
Average prescriptions per patient	[redacted]	17.32	

Discussion

Utilisation of immunotherapies and targeted therapies for the treatment of NSCLC has increased over time, following the PBS listings of new therapies. Due to the different dosing regimens between drugs, the patient counts were considered more representative of utilisation compared to the number of prescriptions supplied. In 2021, NSCLC patients were most commonly treated with pembrolizumab (Table 4). Based on the targeted therapy type, the most common therapies were alectinib (ALK inhibitor), osimertinib (EGFR receptor inhibitor) and entrectinib (ROS1 inhibitor) (Figure 6, 8, 10).

Overall utilisation of durvalumab was [redacted] than estimated. At its November 2018 meeting, the PBAC considered that if durvalumab was PBS listed, "there would only be a modest increase in the overall number of patients treated for NSCLC, provided sequential treatment with different PD-(L)1 therapies was precluded" (paragraph 7.13, durvalumab Public Summary Document, November 2018 meeting). Between 2020 and 2021, there was only a 6% increase in the overall number of patients treated for NSCLC (Table 4), and only a 0.3% increase in the number of NSCLC patients treated with immunotherapies (Table 6). In Table 9, following the PBS listing of durvalumab, 99.1% of NSCLC patients treated with immunotherapies did not switch to a different immunotherapy.

The Kaplan-Meier analysis of the patient cohort treated with durvalumab demonstrated that the median treatment duration was 10.84 months (43.36 weeks). None of these patients (initiated treatment between 1 June to 30 November 2020) were considered to be continuing treatment with durvalumab up to 24 months (30 June 2022) following initiation. These findings were consistent with durvalumab's restriction which states that, "treatment must not exceed 12 months for this condition under the initial and continuing restriction combined."

At its March 2022 meeting, the PBAC recommended the listing of the durvalumab 1500 mg Q4W regimen for the treatment of NSCLC. The PBAC recommended amending the existing of durvalumab (increasing the maximum amount from 1200 mg to 1500 mg, reducing the number of repeats from 8 to 4, and removal of administrative advice preventing the increase in the maximum number of repeats that may be authorised). It is noted that these changes were implemented in August 2022, however as the data analysis period ended in June 2022, the impact of these changes were not included as part of the review.

DUSC consideration

DUSC noted the utilisation of NSCLC therapies over time. DUSC considered the overall NSCLC market to be stable and noted that over time, utilisation of immunotherapies have been declining, whilst utilisation of targeted therapies have been increasing.

DUSC noted pembrolizumab was the most common NSCLC immunotherapy. DUSC considered its high level of utilisation compared to other immunotherapies may have been due to clinician preference and clinical inertia. DUSC noted the differences in treatment regimen between immunotherapies and commented that patients may be less likely to be

treated with combination therapies due to their toxicity. Additionally, DUSC commented on the lack of data demonstrating a greater level of clinical effectiveness associated with pembrolizumab compared to other NSCLC immunotherapies. DUSC noted epidermal growth factor receptor (EGFR) inhibitors were the most commonly used targeted therapy. DUSC noted osimertinib was the most common EGFR inhibitor used and noted the growth in utilisation following its extension to listing from second line to the first line setting.

DUSC noted utilisation of durvalumab for the treatment of Stage III NSCLC was [redacted] than estimated. DUSC commented that its [redacted] than expected utilisation may be due to recent evidence of the benefits of targeted therapy in Stage III NSCLC patients. Additionally, DUSC considered the added risk of toxicity following chemotherapy and patients being restricted to only ever being treated with one immunotherapy as other reasons these patients would be less likely to be treated with immunotherapy.

DUSC noted that durvalumab patients were adhering to the two weekly dosing regimen and noted the average treatment duration and average prescriptions per patient was slightly lower than estimated. DUSC commented that these findings did not correspond with the predicted versus actual analysis of the number of durvalumab prescriptions supplied and considered that the final estimates did not apply a half-cycle correction to adjust for the date of PBS listing.

DUSC actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Apotex Pty Ltd: The sponsor has no comment.

AstraZeneca Pty Ltd: The sponsor has no comment.

Boehringer Ingelheim Pty Ltd: The sponsor has no comment.

Bristol-Myers Squibb Australia Pty Ltd: The sponsor has no comment.

Cipla Australia Pty Ltd: The sponsor has no comment.

Merck Sharp & Dohme (Australia) Pty Ltd: The sponsor has no comment.

Novartis Pharmaceuticals Australia Pty Limited: The sponsor has no comment.

Pfizer Australia Pty Ltd: The sponsor has no comment.

Roche Products Pty Ltd: The sponsor has no comment.

Sandoz Pty Ltd: The sponsor has no comment.

Takeda Pharmaceuticals Australia Pty. Ltd: The sponsor has no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health and Aged Care has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

To the extent provided by law, the Department of Health and Aged Care makes no warranties or representations as to accuracy or completeness of information contained in this report.

To the fullest extent permitted by law, neither the Department of Health and Aged Care nor any Department of Health and Aged Care employee is liable for any liability, loss, claim, damage, expense, injury or personal injury (including death), whether direct or indirect (including consequential loss and loss of profits) and however incurred (including in tort), caused or contributed to by any person's use or misuse of the information available from this report or contained on any third party website referred to in this report.

References

Alecensa (alectinib). Australian Approved Product Information. Sydney: Roche Products Pty Limited. Approved 14 March 2017, updated 7 May 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Alunbrig (brigatinib). Australian Approved Product Information. Sydney: Takeda Pharmaceuticals Australia Pty Ltd. Approved 6 March 2019, updated 3 June 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Australian Institute of Health and Welfare. Cancer data in Australia [Internet]. Canberra: Australian Institute of Health and Welfare, 2020 [cited 2020 Aug. 19]. Available from: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia

Cipla Gefitinib (gefitinib). Australian Approved Product Information. South Melbourne: Cipla Australia Pty Ltd. Approved 23 April 2020, updated 30 April 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Department of Health and Aged Care. Pharmaceutical Benefits Scheme (PBS). Bevacizumab on the PBS. Available from https://www.pbs.gov.au/info/news/2021/07/bevacizumab-on-the-pbs

Erlotinib Apotex (erlotinib). Australian Approved Product Information. Kew East: Accelagen Pty Ltd. Approved 13 August 2020. Available from < https://www.tga.gov.au/product-information-pi.>

Erlotinib Sandoz (erlotinib). Australian Approved Product Information. Macquarie Park: Sandoz Pty Ltd. Approved 2 September 2020. Available from < https://www.tga.gov.au/product-information-pi.>

Giotrif (afatinib). Australian Approved Product Information. North Ryde: Boehringer Ingelheim Pty Limited. Approved 7 November 2013, updated 17 December 2020. Available from < https://www.tga.gov.au/product-information-pi.>

Imfinzi (durvalumab). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 2 October 2018, updated 27 October 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Iressa (gefitinib). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 28 April 2003, updated 13 January 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Lorviqua (lorlatinib). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 19 November 2019, updated 22 December 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Keytruda (pembrolizumab). Australian Approved Product Information. Macquarie Park: Merck Sharp & Dome (Australia) Pty Limited. Approved 16 April 2015, updated 18 May 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Opdivo (nivolumab). Australian Approved Product Information. Mulgrave: Bristol-Myers Squibb Australia Pty Ltd. Approved 11 January 2016, updated 18 July 2022. Available from < https://www.tga.gov.au/product-information-pi.>

PBS statistics. Australian Government Services Australia. Canberra. Available from <http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>.

Rozlytrek (entrectinib). Australian Approved Product Information. Sydney: Roche Products Pty Limited. Approved 15 May 2020, updated 25 March 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Tagrisso (osimertinib). Australian Approved Product Information. Macquarie Park: AstraZeneca Pty Ltd. Approved 3 August 2016, updated 14 September 2021. Available from < https://www.tga.gov.au/product-information-pi.>

Tecentriq (atezolizumab). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 27 July 2017, updated 12 May 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Xalkori (crizotinib). Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 27 September 2013, updated 10 September 2020. Available from < https://www.tga.gov.au/product-information-pi.>

Zarogoulidis K, Zarogoulidis P, Darwiche K, et al. Treatment of non-small cell lung cancer (NSCLC). J Thorac Dis. 2013;5 Suppl 4(Suppl 4):S389-S396. doi:10.3978/j.issn.2072-1439.2013.07.10

Zykadia (ceritinib). Australian Approved Product Information. Macquarie Park: Novartis Pharmaceuticals Australia Pty Limited. Approved 31 March 2016, updated 23 March 2022. Available from < https://www.tga.gov.au/product-information-pi.>

Appendices

Appendix A: PBS listing of immunotherapies for NSCLC (as at August 2022)

Item code	Name, form & strength, pack size	Max amount	Rpts	DPMA	Brand name and manufacturer
Unresectable stage III NSCLC					
	durvalumab,				Imfinzi®
11915D	120 mg/2.4 mL injection, 2.4 mL vial 500 mg/10 mL injection, 10 mL vial	1500 mg	4	$12,012.07	AstraZeneca Pty Ltd
11911X	120 mg/2.4 mL injection, 2.4 mL vial 500 mg/10 mL injection, 10 mL vial	1500 mg	4	$12,220.65	
Stage IV (metastatic) NSCLC (1L)					
	atezolizumab,				Tecentriq®
11807K	1.2 g/20 mL injection, 20 mL vial	1200 mg	5	$7,189.56	Roche Products Pty Ltd
11802E	1.2 g/20 mL injection, 20 mL vial	1200 mg	7	$7,189.56	
11792P	1.2 g/20 mL injection, 20 mL vial	1200 mg	5	$7,330.62	
11801D	1.2 g/20 mL injection, 20 mL vial	1200 mg	7	$7,330.62	
12097Q	840 mg/14 mL injection, 14 mL vial	1680 mg	5	$10,030.55	
12098R	840 mg/14 mL injection, 14 mL vial	1680 mg	5	$10,211.38	
	ipilimumab,				Yervoy®
12322M	50 mg/10 mL injection, 10 mL vial	120 mg	4	$16,964.83	Bristol-Myers Squibb Australia Pty Ltd
12324P	50 mg/10 mL injection, 10 mL vial	120 mg	4	$16,964.83	
12304N	50 mg/10 mL injection, 10 mL vial	120 mg	4	$17,242.74	
12308T	50 mg/10 mL injection, 10 mL vial	120 mg	4	$17,242.74	
	nivolumab,				Opdivo®
12303M	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	360 mg	13	$7,189.57	Bristol-Myers Squibb Australia Pty Ltd
12323N	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	360 mg	13	$7,189.57	
12312B	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	360 mg	13	$7,330.64	
12315E	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	360 mg	13	$7,330.64	
	pembrolizumab				Keytruda®
11492W	100 mg/4 mL injection, 4 mL vial	200 mg	6	$7,883.26	Merck Sharp & Dohme (Australia) Pty Ltd
11494Y	100 mg/4 mL injection, 4 mL vial	200 mg	6	$7,334.57	
12119W	100 mg/4 mL injection, 4 mL vial	400 mg	3	$15,382.07	
12121Y	100 mg/4 mL injection, 4 mL vial	400 mg	3	$15,637.82	

Item code	Name, form & strength, pack size	Max amount	Rpts	DPMA	Brand name and manufacturer
Locally advanced and metastatic NSCLC (2L)					
	Atezolizumab,				Tecentriq®
11284X	1.2 g/20 mL injection, 20 mL vial	1200 mg	5	$7,189.56	Roche Products Pty Ltd
11277M	1.2 g/20 mL injection, 20 mL vial	1200 mg	7	$7,189.56	
11309F	1.2 g/20 mL injection, 20 mL vial	1200 mg	5	$7,330.62	
11297N	1.2 g/20 mL injection, 20 mL vial	1200 mg	7	$7,330.62	
11930X	840 mg/14 mL injection, 14 mL vial	1680 mg	5	$10,030.55	
11931Y	840 mg/14 mL injection, 14 mL vial	1680 mg	3	$10,030.55	
11940K	840 mg/14 mL injection, 14 mL vial	1680 mg	3	$10,211.38	
11957H	840 mg/14 mL injection, 14 mL vial	1680 mg	5	$10,211.38	
	nivolumab,				Opdivo®
11158G	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	480 mg	8	$9,557.05	Bristol-Myers Squibb Australia Pty Ltd
11153B	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	480 mg	11	$9,557.05	
11143L	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	480 mg	8	$9,731.26	
11152Y	40 mg/4 mL injection, 4 mL vial 100 mg/10 mL injection, 10 mL vial	480 mg	11	$9,731.26	

Source: the PBS website.

Appendix B: PBS listing of targeted therapies for NSCLC (as at August 2022)

Item code	Name, form & strength, pack size	Max qty packs	Max qty units	Rpts	DPMQ	Brand name and manufacturer
EGFR inhibitors						
	afatinib,					Giotrif®
11335N	20 mg tablet, 28	1	28	3	$2,885.28	Boehringer Ingelheim Pty Ltd
11336P	20 mg tablet, 28	1	28	3	$2,885.28	
11341X	30 mg tablet, 28	1	28	3	$2,885.28	
11348G	30 mg tablet, 28	1	28	3	$2,885.28	
11347F	40 mg tablet, 28	1	28	3	$2,885.28	
11359W	40 mg tablet, 28	1	28	3	$2,885.28	
11329G	50 mg tablet, 28	1	28	3	$2,885.28	
11342Y	50 mg tablet, 28	1	28	3	$2,885.28	
	erlotinib,					Erlotinib APOTEX®
10022L	25 mg tablet, 30	1	30	3	$172.45	Apotex Pty Ltd
10028T	25 mg tablet, 30	1	30	3	$172.45	Elortinib Sandoz®
11263T	25 mg tablet, 30	1	30	3	$172.45	Sandoz Pty Ltd
10019H	100 mg tablet, 30	1	30	3	$607.15	
10020J	100 mg tablet, 30	1	30	3	$607.15	
11260P	100 mg tablet, 30	1	30	3	$607.15	
10014C	150 mg tablet, 30	1	30	3	$749.42	
10025P	150 mg tablet, 30	1	30	3	$749.42	
11259N	150 mg tablet, 30	1	30	3	$749.42	
	gefitinib,					Cipla Gefitinib®
8769M	250 mg tablet, 30	1	30	3	$926.73	Cipla Australia Pty Ltd
11264W	250 mg tablet, 30	1	30	3	$926.73	Iressa® AstraZeneca Pty Ltd
	osimertinib,					Tagrisso®
11620N	40 mg tablet, 30	1	30	5	$7,971.28	AstraZeneca Pty Ltd
12233W	40 mg tablet, 30	1	30	5	$7,971.28	
11622Q	80 mg tablet, 30	1	30	5	$7,971.28	
12232T	80 mg tablet, 30	1	30	5	$7,971.28	

Item code	Name, form & strength, pack size	Max qty packs	Max qty units	Rpts	DPMQ	Brand name and manufacturer
ALK inhibitors						
11226W	alectinib, 150 mg capsule, 4 × 56	1	224	3	$6,814.36	Alecensa® Roche Products Pty Ltd
11980M 11974F 11984R 11976H	brigatinib, 30 mg tablet, 28 90 mg tablet, 28 180 mg tablet, 28 90 mg tablet [7] (&) brigatinib 180 mg tablet [21], 1 pack	4 1 1 1	112 28 28 1	3 3 3 0	$6,814.36 $6,814.36 $6,814.38 $6,814.36	Alunbrig® Takeda Pharmaceuticals Australia Pty. Ltd
11056X	ceritinib 150 mg capsule, 3 × 50	1	150	3	$6,933.17	Zykadia® Novartis Pharmaceuticals Australia Pty Limited
10323H 10322G	crizotinib 200 mg capsule, 60 250 mg capsule, 60	1 1	60 60	3 3	$6,933.17 $6,933.17	Xalkori® Pfizer Australia Pty Ltd
12096P 12091J	lorlatinib, 25 mg tablet, 90 100 mg tablet, 30	1 1	90 30	3 3	$7,289.58 $7,289.58	Lorviqua® Pfizer Australia Pty Ltd
ROS1 inhibitors						
11589Y 11594F	crizotinib 200 mg capsule, 60 250 mg capsule, 60	1 1	60 60	3 3	$6,933.17 $6,933.17	Xalkori® Pfizer Australia Pty Ltd
12092K	entrectinib, 200 mg capsule, 90	1	90	3	$7,289.58	Rozlytrek® Roche Products Pty Ltd

Source: the PBS website.