Daratumumab for newly diagnosed systemic light chain amyloidosis

Drug utilisation sub-committee (DUSC)

October 2025

Abstract

Purpose

To review the utilisation of daratumumab for newly diagnosed systemic light-chain AL amyloidosis as requested by DUSC at its June 2025 meeting.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Daratumumab was listed for the treatment of newly diagnosed systemic light chain amyloidosis on 1 January 2023.

Data Source / methodology

Data extracted from the PBS and Date of Death database maintained by Department of Health, Disability and Ageing, processed by Services Australia were used for the analyses.

Key Findings

- In 2023, 294 patients were supplied 3,270 prescriptions for the treatment of AL amyloidosis.
- In 2024, 443 patients were supplied 4,881 prescriptions for the treatment of AL amyloidosis.
- The median age of patients initiating treatment with daratumumab for the treatment of AL amyloidosis was 70 years.
- Utilisation was different from estimated with a greater number of patients initiating than estimated, and a lower number of prescriptions supplied than estimated.

Purpose of analysis

To review the utilisation of daratumumab for newly diagnosed systemic light chain amyloidosis as requested by DUSC at its June 2025 meeting.

Background

Clinical situation

Systemic light-chain AL amyloidosis AL (herein referred to AL amyloidosis) is a type of blood disorder where abnormal blood cells make excessive amounts of abnormal proteins that deposit in various organs. Organs involved usually include the kidneys, heart, gastrointestinal tract, liver and nervous system. Up to 70% of newly diagnosed patients present with cardiac involvement at diagnosis. Cardiac complications account for most deaths in this population. AL amyloidosis is among the more common and more severe forms of amyloidosis. It has been estimated that 49% of patients with amyloidosis have the AL amyloid sub-type.[1]

Daratumumab is currently the only PBS-listed medicine for the treatment of AL amyloidosis.

Pharmacology

Daratumumab is an IgG1κ human monoclonal antibody (mAb) that binds to the CD38 protein expressed on the surface of cells in a variety of haematological malignancies, including clonal plasma cells in multiple myeloma and AL amyloidosis, as well as other cell types and tissues. [2]

Therapeutic Goods Administration (TGA) approved indications

Daratumumab is indicated for the treatment of patients:

- with newly diagnosed multiple myeloma:
  - who are eligible for autologous stem cell transplant. For use in combination with bortezomib, thalidomide, and dexamethasone.
  - who are ineligible for autologous stem cell transplant. For use in combination with:
    - bortezomib, melphalan and prednisone, or
    - lenalidomide and dexamethasone.
- with relapsed or refractory multiple myeloma who have received:
  - at least one prior therapy. For use in combination with:
    - bortezomib and dexamethasone, or
    - lenalidomide and dexamethasone, or

[1] Wisniowski B, McLeod D, Adams R, Harvey Y, Armes J, Papadimos D, Brown I, McGuire L, Mollee P. The epidemiology of amyloidosis in Australia. Amyloid. 2019;26(sup1):132-133. doi: 10.1080/13506129.2019.1582481.

[2] Darzalex SC (dartumumab). Australian Approved Product Information. Macquarie Park: Janssen-Cilag Pty Ltd. Approved 8 September 2020, updated 29 November 2024. Available from < https://www.tga.gov.au/product-information-pi.>

        - carfilzomib and dexamethasone, or
        - pomalidomide and dexamethasone (after at least one prior therapy including lenalidomide and a proteasome inhibitor (PI)).
    - at least three prior lines of therapy including a PI and an immunomodulatory agent or who are refractory to both a PI and an immunomodulatory agent. For use as monotherapy.
- with AL amyloidosis for use in combination with bortezomib, cyclophosphamide and dexamethasone.

Dosage and administration

The recommended dose is 1800 mg administered subcutaneously in the abdomen, over approximately 3-5 minutes, according to the following dosing schedule:

Table 1: Daratumumab dosing schedule for AL amyloidosis

Weeks	Schedule
Weeks 1 to 8	Weekly (total of 8 doses)
Weeks 9 to 24[a]	Every two weeks (total of 8 doses)
Weeks 25 onwards until disease progression[b]	Every 4 weeks

[a] First dose of the every-2-week dosing schedule is given at Week 9.
[b]First dose of the every-4-week dosing schedule is given at Week 25.

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

PBS listing details (as at August 2025)

Daratumumab for newly diagnosed systemic light chain amyloidosis is listed under the General Schedule and Section 100 – Efficient Funding of Chemotherapy (CT).

Table 2: PBS listing of daratumumab for AL amyloidosis

Item code	Name, form & strength, pack size	Max. qty.	Rpts	DPMQ	Brand name and manufacturer
13199Q	daratumumab 1.8 g/15 mL injection, 15 mL vial	1	5	$7,173.21	Darzalex SC® Janssen-Cilag Pty Ltd
13202W	daratumumab 1.8 g/15 mL injection, 15 mL vial	1	15	$7,173.21	Darzalex SC® Janssen-Cilag Pty Ltd
13201T	daratumumab 1.8 g/15 mL injection, 15 mL vial	1	15	$7,010.28	Darzalex SC® Janssen-Cilag Pty Ltd
13203X	daratumumab 1.8 g/15 mL injection, 15 mL vial	1	5	$7,010.28	Darzalex SC® Janssen-Cilag Pty Ltd

Notes:

- The intravenously administered presentation of this drug is not PBS listed for this indication at the request of the sponsor.
- Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
- No increase in the maximum quantity or number of units may be authorised.
- No increase in the maximum number of repeats may be authorised.
- Special Pricing Arrangements apply.

Source: the PBS website.

Restriction

Treatment phase: Initial treatment from week 0 to week 24

- Clinical criteria:
  - The condition must have histological evidence consistent with a diagnosis of systemic light-chain amyloidosis, AND
  - The condition must be untreated with drug therapy, including this drug, irrespective of whether the diagnosis has been reclassified (i.e. the diagnosis changes between multiple myeloma/amyloidosis), AND
  - Patient must have a World Health Organization (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of no higher than 2 at treatment initiation.
- Treatment criteria:
  - Must be treated by a haematologist (this does not exclude treatment via a multidisciplinary team, but the PBS authority application must be sought by the treating haematologist), AND
  - Patient must be undergoing concomitant treatment limited to each of:
    (i) bortezomib,
    (ii) cyclophosphamide,
    (iii) dexamethasone, at certain weeks of treatment as outlined in the drug's approved Product Information.

Treatment phase: Continuing treatment from week 25 onwards (administered once every four weeks)

- Clinical criteria:
  - Patient must have previously received PBS-subsidised treatment with this drug for this condition.
- Treatment criteria:
  - Must be treated by a haematologist (this does not exclude treatment via a multidisciplinary team, but the PBS authority application must be sought by the treating haematologist), AND
  - Patient must be undergoing continuing treatment that does not extend treatment duration beyond whichever comes first:

(i) disease progression,
(ii) 96 cumulative weeks from the first administered dose, once in a lifetime.

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

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

November 2021

The Category 1 submission requested a Section 100 (Highly Specialised Drug), Authority Required listing for daratumumab subcutaneous (SC), in combination with cyclophosphamide, bortezomib and dexamethasone (CyBorD) for newly diagnosed patients with systemic light-chain AL amyloidosis. The requested listing is for combination therapy for the first 24 weeks, followed by daratumumab SC as monotherapy for treatment from week 25 to a maximum of 96 weeks (24 cycles). The submission requested that patients continue to access daratumumab SC until disease progression or the development of treatment-limiting toxicity, or for a maximum of 24 cycles (i.e. a maximum of 34 injections of daratumumab SC). Listing was requested on the basis of a cost-utility analysis (CUA) of daratumumab SC + CyBorD versus the submission's main comparator, CyBorD.

The PBAC did not recommend daratumumab SC, for use in combination with CyBorD for the treatment of patients with newly diagnosed systemic light-chain AL amyloidosis. The PBAC recognised that there are no treatments on the PBS available specifically for this condition, and it considered that the addition of daratumumab SC plus CyBorD offered high added therapeutic value. However, the PBAC considered that there were uncertainties in the cost-effectiveness analysis and financial estimates, particularly due to the overlap between patients with AL amyloidosis and multiple myeloma (MM). The PBAC considered that these uncertainties could be managed through a respecified economic analysis that included more conservative assumptions, and a risk sharing arrangement (RSA).

May 2022

An early resolution resubmission sought to address the PBAC's concerns from its November 2021 meeting. The PBAC recommended the listing of daratumumab SC, for use in combination with CyBorD, for the treatment of patients with newly diagnosed systemic light-chain AL amyloidosis. The PBAC recognised that there are no treatments on the PBS available specifically for this condition, and it considered that the addition of daratumumab SC plus CyBorD offered a high added therapeutic value. The PBAC considered that the revised economic analysis, which included more conservative assumptions, and a RSA, based on reduced financial estimates which also accounted for the overlap between patients with AL amyloidosis and MM, were acceptable.

For further details refer to the Public Summary Document from the November 2021 and May 2022 PBAC meetings.

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 2023 up to and including 30 June 2025.

This data was used to determine the number of incident and prevalent patients, number of prescriptions supplied and to analyse prescriber type and patient demographics such as age and gender distribution. Initiating and prevalent patients were counted by quarter and by calendar year of supply. An initiating patient was defined based on their first date of supply of daratumumab.

Date of death data were linked to the PBS claims data based on the unique de-identified patient identifier. This was used to determine the proportion of patients who ceased daratumumab treatment due to death. At the time of the review, date of death data was available up to 18 February 2025. A Kaplan-Meier curve was generated to present treatment duration. A cohort of initiating patients were selected from 1 July 2023 to account for the wash out period of grandfathered patients, up to and including 31 December 2023. These patients were followed until 18 February 2025, with patients censored if they were considered to be continuing treatment.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data.[3] The publicly available Services Australia Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included.

[3] 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

Figures 1 and 2 show the increase in the number of patients treated and the number of prescriptions supplied since listing. Approximately 63 patients initiated treatment with daratumumab per quarter.

Table 3: Utilisation of daratumumab for AL amyloidosis by calendar year

	2023	2024	2025
Initiating patients	294	225	110
Prevalent patients	294	443	406
Prescriptions supplied	3,270	4,881	2,786

Note: Data for 2025 represents six months of data to 30 June 2025.

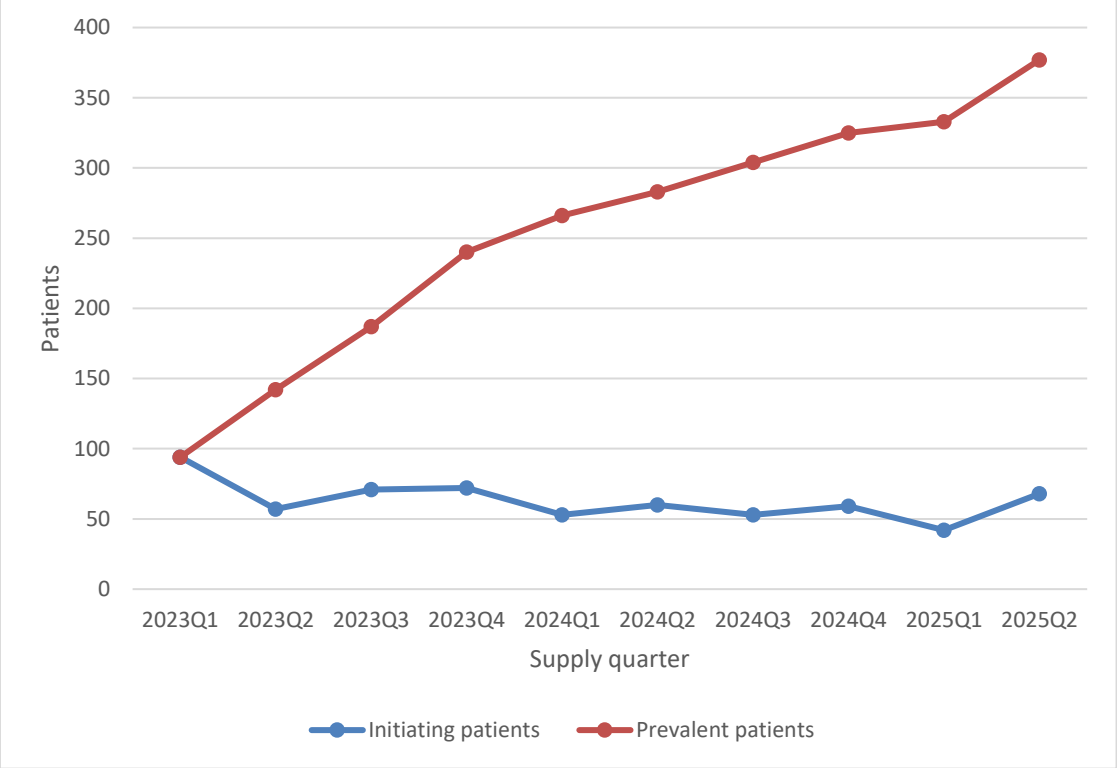

Figure 1: Initiating and prevalent patients treated with daratumumab for AL amyloidosis by supply quarter

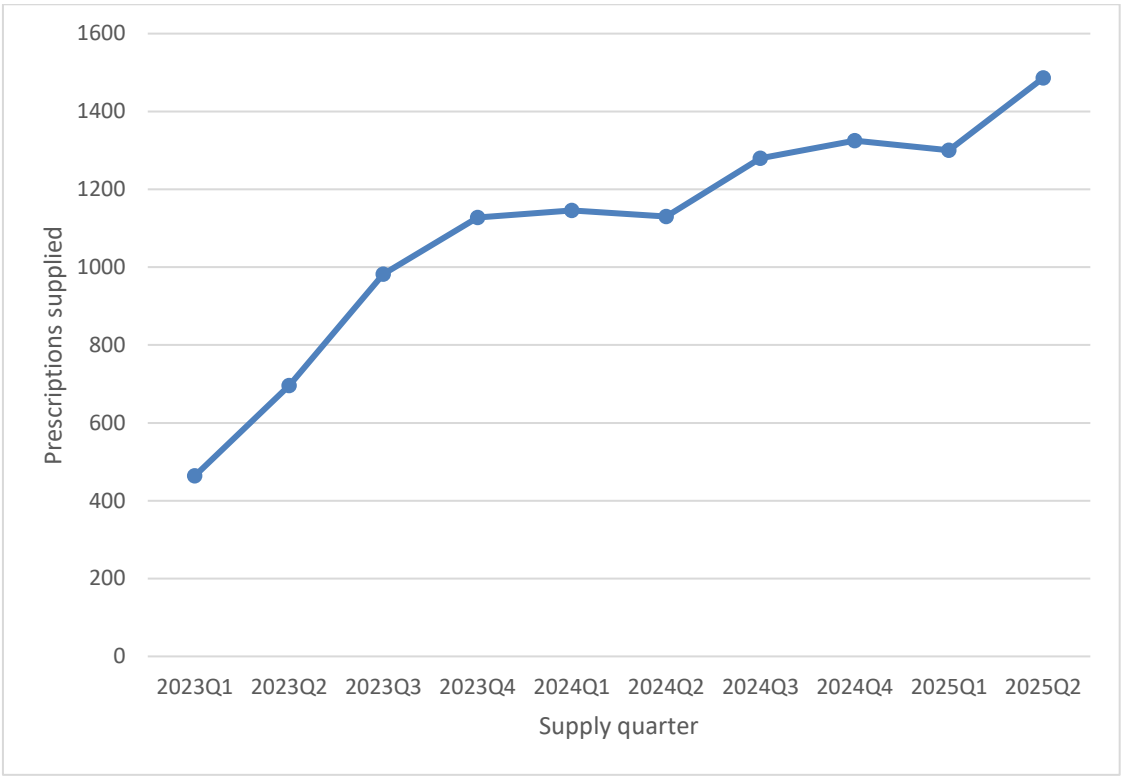

Figure 2: Daratumumab prescriptions for AL amyloidosis supplied by quarter

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

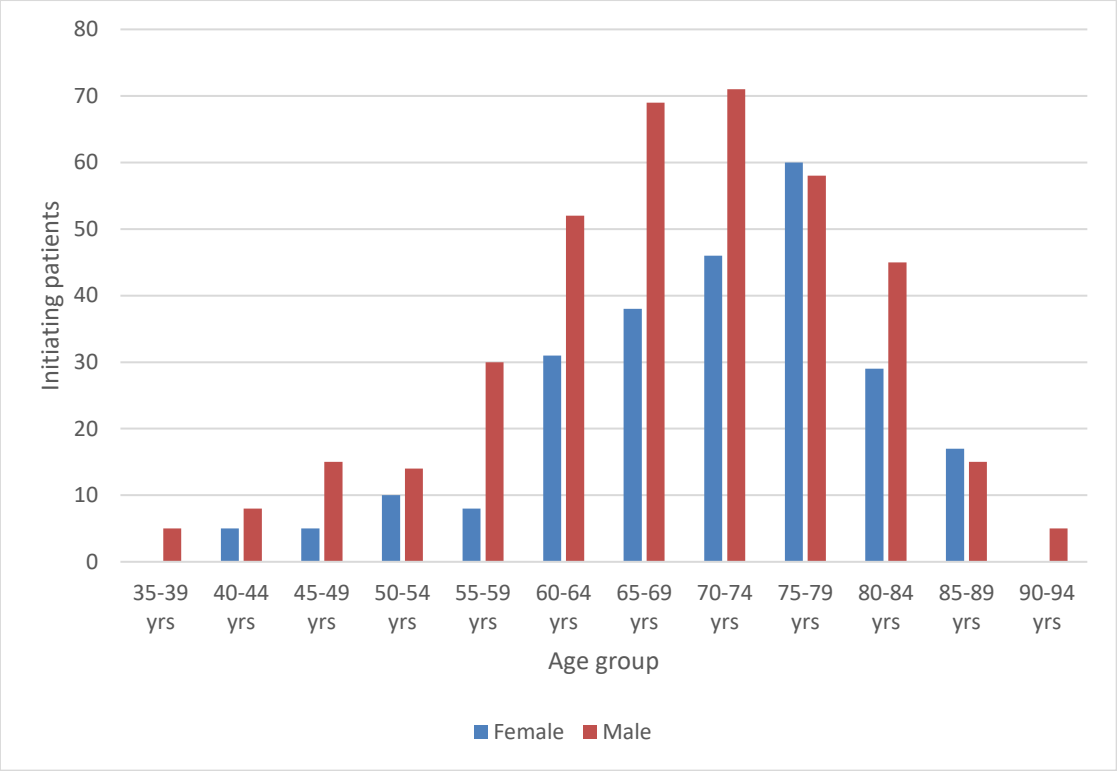

Figure 3: Age and gender distribution of initiating patients

Note: Patients with an unknown age amounted to less than one percent. Patient counts of less than five were redefined as five to reduce the risk of patient identification.

Figure 3 shows the age and gender distribution of initiating daratumumab patients. Across the majority of age groups, a greater proportion of males initiated treatment compared to females. The most common age group that initiated treatment was between 70-79 years with a median age of 70 years. For females the median age of initiation was 71 years old whereas for males the median age of initiation was 69 years old.

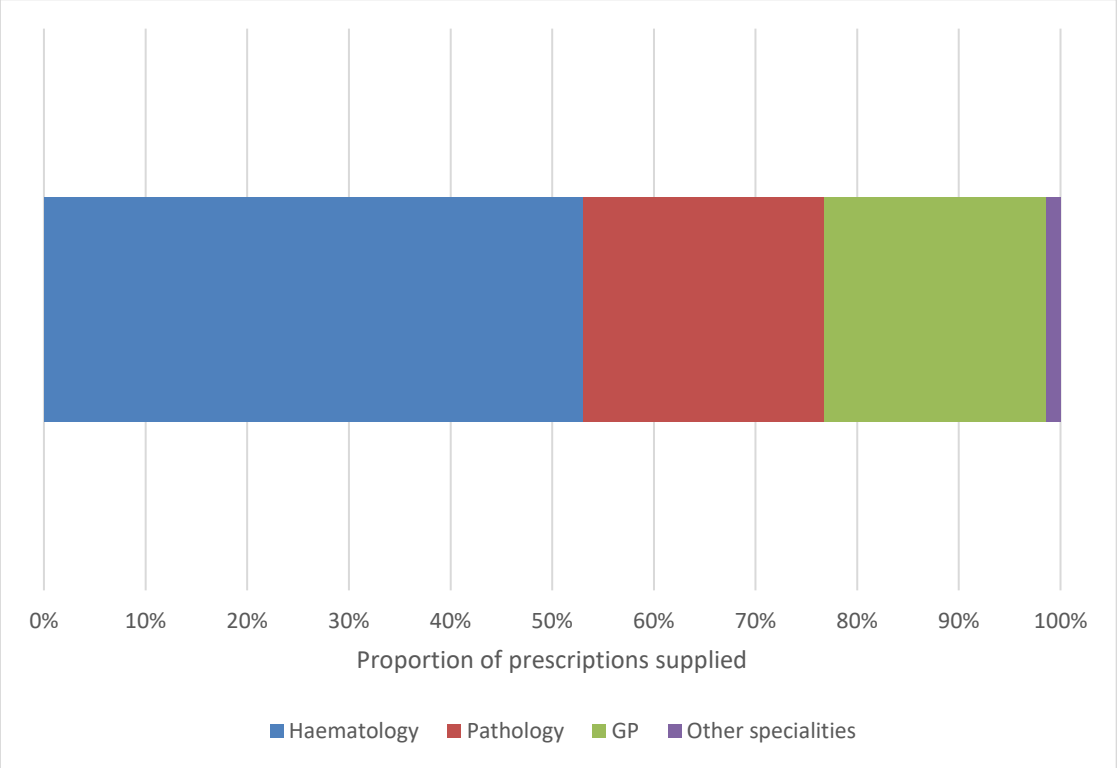

Figure 4: Prescriptions supplied by prescriber type

Figure 4 shows the proportion of prescriptions supplied by prescriber type. Haematologists accounted for the majority of prescribing and accounted for 53% of prescriptions supplied.

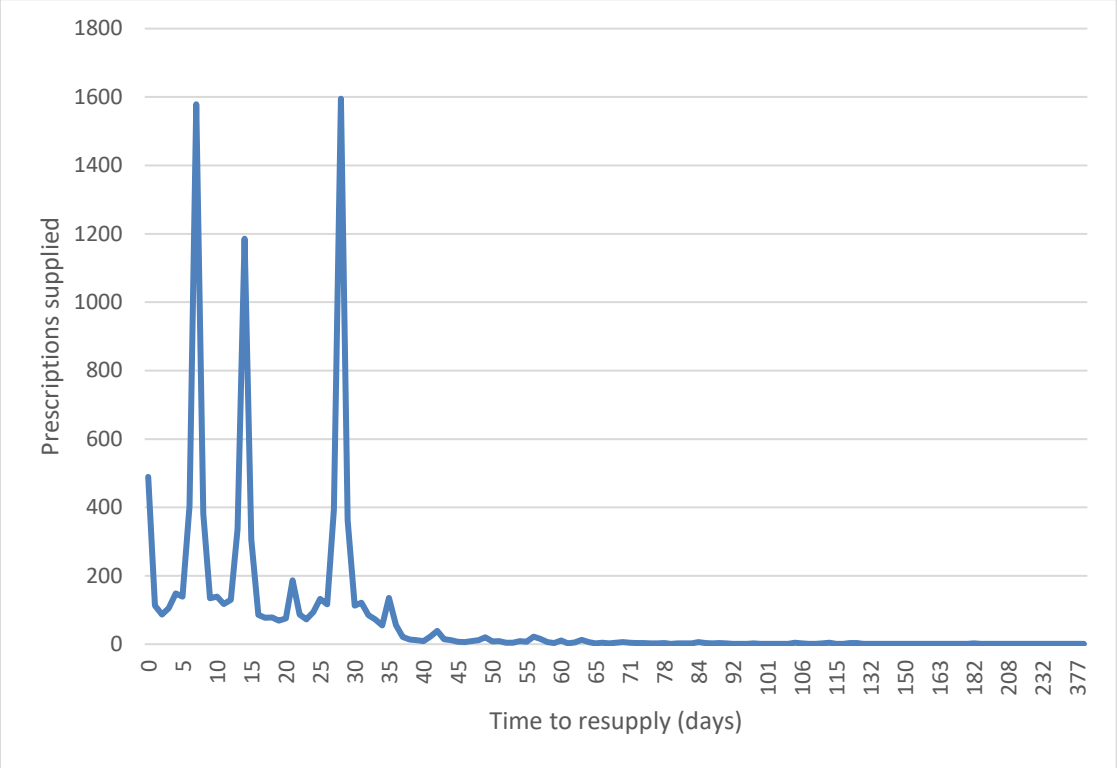

Figure 5: Time to re-supply prescriptions

Figure 5 shows the time to re supply prescriptions, with three peaks at 7, 14 and 28 days which correspond to the dosing schedule.

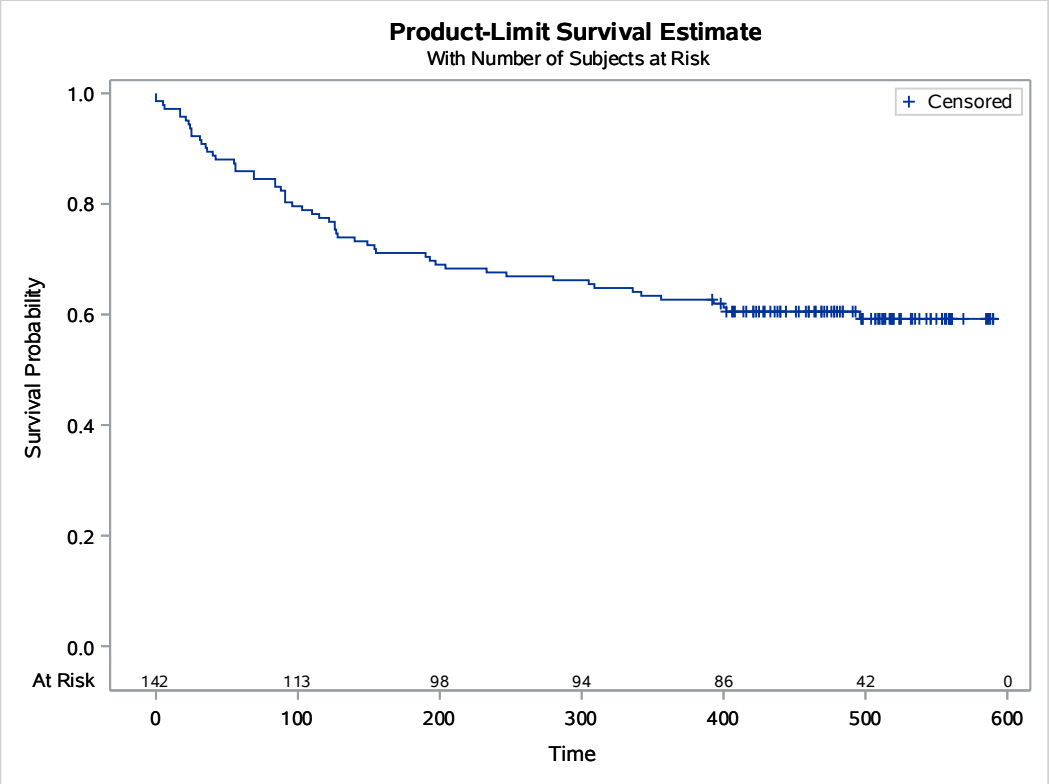

Figure 6: Treatment duration of patients who initiated daratumumab between 1 July 2023 and 31 December 2023

The median treatment duration was not reached in patients who initiated treatment between 1 July 2023 and 31 December 2023 and followed to the analysis end date (18 February 2025). Based on the date of death data up to 18 February 2025, 20% of these patients discontinued treatment due to death. Approximately 60% of patients were censored and considered to be continuing treatment at analysis end date.

Analysis of expenditure

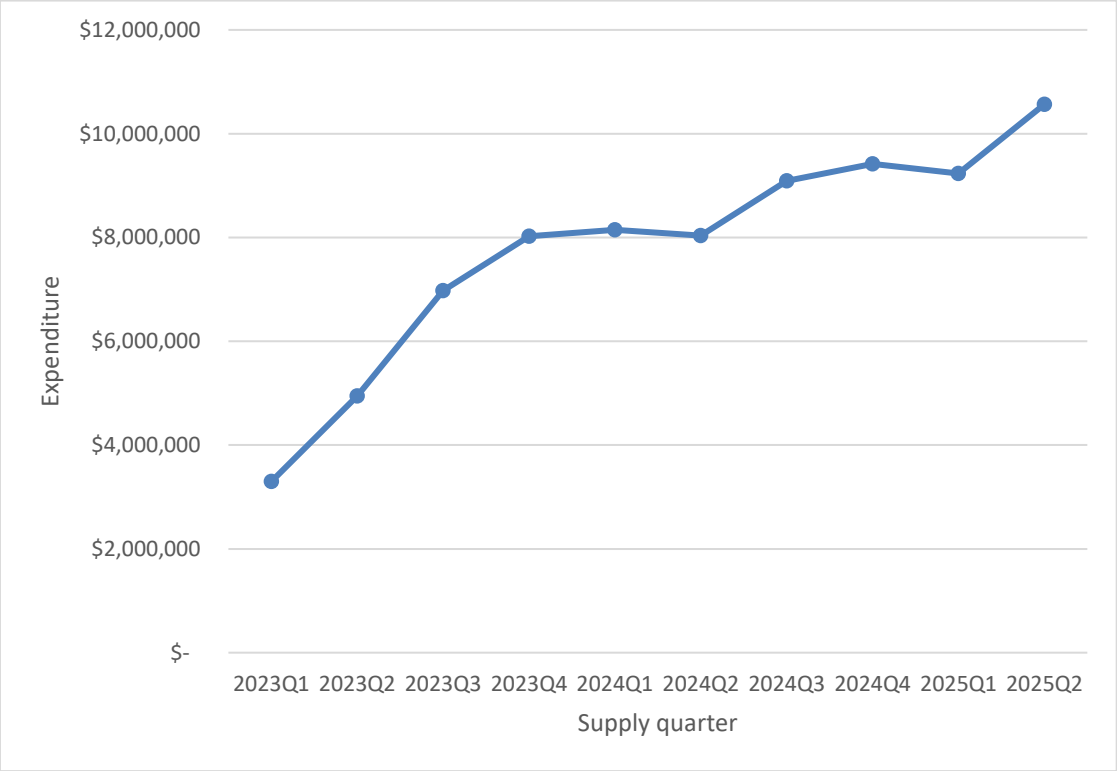

Figure 7: Expenditure based on published prices excluding patient co-payments

Similar to trends observed in the number of prescriptions supplied (Figure 2), expenditure based on published prices has increased over time.

Approach taken to estimate utilisation

DUSC (October 2021) considered the November 2021 submission. The submission used an epidemiological approach to estimate utilisation and financial implications associated with the proposed listing of daratumumab SC in combination with CyBorD.

The utilisation estimates were based on the following:

- Incidence and prevalence of systemic AL amyloidosis based on Wisniowski et al. 2019 which estimated the incidence and mortality burden of amyloidosis among Queensland residents aged ≥20 years between 1999–2013 based on case ascertainment from histopathology reports.
- The submission assumed the diagnosis rate would increase following PBS listing as it is the first therapy specifically listed on the PBS for the disease and applied a total of 15% increase in the incidence rate over the first two years of listing. The assumed increase was based on the advice of expert clinicians experienced in treating systemic AL amyloidosis in Australia.

- Based on the Australian Amyloidosis Network registry data, 75% of the newly diagnosed systemic AL amyloidosis patients would be eligible for daratumumab under the proposed PBS restriction (Eastern Cooperative Oncology Group [ECOG] Performance Status of 0-2 and without Mayo Stage IIIB cardiac disease).
- Based on a market research survey completed by 20 Australian haematologists, it was estimated that 8% of the prevalent patients would remain untreated and thus eligible for daratumumab.
- A treatment uptake rate of 95% was applied to the estimated eligible incident and prevalent patients.
- The treatment duration was modelled based on the ANDROMEDA trial time to treatment discontinuation data, consistent with the economic evaluation.

DUSC considered the estimates presented in the submission were reasonable. However, they identified the following areas of uncertainty:

- The application of a 15% increased diagnosis rate, which resulted in an increased incidence rate of 7.2% over the two years, was uncertain. It was probable that the consequence of listing would be earlier diagnosis (rather than increasing incidence) for some patients and therefore, the magnitude of any market growth remained uncertain. The pre-PBAC response clarified that the 15% relative increase (phased over the first 2 years) in incident patients was intended to reflect the patients being diagnosed more rapidly following the PBS listing of daratumumab SC due to greater awareness and an effective treatment being PBS listed. The incidence of the disease and the patient presentation to doctors were assumed to remain unchanged.
- The financial estimates were consistent with the proposed PBS restriction in that previously diagnosed untreated prevalent patients were included. However, the proportion of prevalent patients deemed untreated and therefore eligible for daratumumab SC + CyBorD was uncertain. The sponsor acknowledged that the AL amyloidosis prevalent population in the financial estimates was lower than the prevalence estimate in the United States which was based on hospitalisation claims for any type of amyloidosis, and included a larger proportion of patients aged ≥65 years compared with the population. [4]
- The submission did not adjust the estimates to account for patients with a concurrent diagnosis of MM (up to 15% of MM patients will develop symptomatic AL amyloidosis) that already have access to daratumumab via the PBS.

DUSC did not consider the May 2022 resubmission. The resubmission applied the following changes to its utilisation estimates:

- Inclusion of Mayo Stage IIIB cardiac disease patients.
- Accounting for patients with a concurrent diagnosis of MM.

[4] Quock TP, Yan T, Chang E, Guthrie S, Broder MS. Healthcare resource utilization and costs in amyloid light-chain amyloidosis: a real-world study using US claims data. J Comp Eff Res. 2018 Jun;7(6):549-559.

Analysis of actual versus predicted utilisation

Table 4: Actual versus predicted analysis of daratumumab for AL amyloidosis

		Year 1	Year 2
		1 January 2023 – 31 December 2023	1 January 2024 – 31 December 2024
Initiating patients	Predicted	[redacted]	[redacted]
	Actual	294	225
	Difference	[redacted]	[redacted]
Prescriptions supplied	Predicted	[redacted]	[redacted]
	Actual	3,270	4,881
	Difference	[redacted]	[redacted]

As shown in Table 4, the actual number of patients initiating treatment with daratumumab was greater than estimated across both listing years. However, the actual number of prescriptions supplied was less than estimated.

Although the caps were breached as part of the RSA (Table 4), the number of prescriptions supplied was less than estimated. It is noted the subsidisation caps for the AL amyloidosis listing were set lower than the utilisation estimates (the number of prescriptions was reduced by [redacted] (paragraph 9.6 daratumumab Public Summary Document, November 2021 PBAC Meeting with May 2022 Addendum).

Discussion

Utilisation of daratumumab for AL amyloidosis has increased over time, with the number of initiating patients greater than estimated, whereas the number of prescriptions supplied was less than estimated.

The median age of patients treated with daratumumab for AL amyloidosis was 70 years, whereas patients were younger in the ANDROMEDA trial, with a median age of 65 years. As part of its Pre-Sub-Committee Response (PSCR), the sponsor stated 52.8% of patients in the trial were aged between 34-64 years. This is compared to the above analyses where this age group only accounted for 28.1% of patients treated.

At the time of PBAC's consideration, the PBAC noted that the median follow-up in ANDROMEDA was 11.4 months. The PBAC considered that the data were too immature to demonstrate a survival benefit (paragraph 7.6, daratumumab Public Summary Document November 2021 PBAC Meeting with May 2022 Addendum). A retrospective study published in 2025, found daratumumab in combination with CyBorD was associated with a superior

overall survival rate.[5] In this review, the median treatment duration was not reached due to the immaturity of the data.

DUSC consideration

DUSC noted in the first two years of listing, the number of initiating patients was greater than estimated. The Pre-Sub-Committee Response (PSCR) noted "daratumumab remains the only PBS listed option for these patients." DUSC considered the greater than estimated number of initiating patients observed was likely due to the unmet need in the population.

DUSC noted the number of prescriptions supplied was lower than estimated and considered this is likely due to patients treated in clinical practice being older and frailer compared to the trial population. DUSC noted the analysis (Figure 3) showed the median age of patients treated with daratumumab for AL amyloidosis was 70 years, whereas patients were younger in the ANDROMEDA trial, with a median age of 65 years. DUSC considered the survival rate of this population and noted most newly diagnosed patients present with cardiac involvement at diagnosis and cardiac complications account for most deaths in this population.[6]

DUSC actions

DUSC requested 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.

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[5] Yohannan B, Rees M, Gertz MA, Dispenzieri A, Kapoor P, Buadi FK, Dingli D, Leung N, Lacy MQ, Hayman SR, Gonsalves W, Kourelis T, Cook J, Binder M, Siddiqui M, Lin Y, Hwa L, Rogers MG, Hobbs M, Fonder A, Warsame R, Rajkumar SV, Kumar SK, Muchtar E. Improved survival with daratumumab-CyBorD compared with CyBorD as frontline therapy for AL amyloidosis. Blood Neoplasia. 2025 Mar 10;2(2):100092. doi: 10.1016/j.bneo.2025.100092.

[6] Wechalekar AD, Fontana M, Quarta CC, Liedtke M. AL Amyloidosis for Cardiologists: Awareness, Diagnosis, and Future Prospects: *JACC: CardioOncology* State-of-the-Art Review. JACC CardioOncol. 2022 Nov 15;4(4):427-441. doi: 10.1016/j.jaccao.2022.08.009

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

Janssen-Cilag 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, Disability and Ageing 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.

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