Analysis of dupilumab for uncontrolled severe asthma

Drug utilisation sub-committee (DUSC)

February 2024

Abstract

Purpose

To review the utilisation of dupilumab for uncontrolled severe asthma, as requested by DUSC at its September 2023 meeting.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Dupilumab was PBS listed for uncontrolled severe asthma on 1 April 2021.

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

- A total of 41,557 prescriptions of dupilumab for uncontrolled severe asthma have been supplied to 4,446 patients since listing. In 2022, 17,292 prescriptions were supplied to 2,669 patients.
- Of the 4,446 patients who initiated dupilumab, dupilumab was the first biologic medicine supplied to 2,983 (67%) patients for severe asthma, and 1,463 patients were switched to dupilumab from either omalizumab, mepolizumab or benralizumab.
- The age group with the highest proportion of initiating patients was the 60 to 64 year old group. There were negligible cases of patients aged younger than 12 who initiated dupilumab for severe asthma.
- Respiratory and Sleep Medicine specialist prescribers accounted for 67% of the supplied prescriptions of dupilumab, and Dermatology or Immunology and Allergy specialist prescribers accounted for 21% of the supplied prescriptions.
- All of the 4,446 patients supplied dupilumab under a PBS item code for severe asthma were previously supplied inhaled corticosteroids through the PBS.

Purpose of analysis

To review the utilisation of dupilumab for uncontrolled severe asthma, as requested by DUSC at its September 2023 meeting.

Background

Clinical situation

Asthma is a heterogeneous disease characterised by chronic airway inflammation, which can lead to obstruction. The disease is characterised by respiratory wheeze, shortness of breath, chest tightness and cough that vary over time in intensity, together with variable airflow limitation which may become persistent.[1]

The target population for dupilumab is 'severe refractory' asthma, where the disease remains uncontrolled despite adherence to high-dose inhaled corticosteroids (ICS) in combination with a second controller such as a long-acting beta agonist, and/or systemic corticosteroids, or whose asthma control deteriorates when these treatments are stepped down.[1]

There are four biologic medicines listed on the PBS for the treatment of severe asthma. Omalizumab was the first biologic medicine listed on the PBS for uncontrolled severe allergic asthma. PBS eligibility criteria were developed based predominantly on relevant omalizumab clinical trials presented to the PBAC and stakeholder consultation. The PBS restrictions for mepolizumab and benralizumab for the treatment of eosinophilic asthma were developed for consistency with the omalizumab PBS listing.

Pharmacology

Dupilumab is a fully human monoclonal antibody directed against the interleukin (IL)-4 receptor α subunit (IL-4Rα) of IL-4 heterodimeric type I and type II receptors that mediate IL-4/IL-13 signalling through this pathway. Blockade of these receptors broadly suppresses type 2 inflammation associated with atopic/allergic diseases, including atopic dermatitis and asthma.[2]

[1] Dupilumab (asthma) Pharmaceutical Benefits Advisory Committee Public Summary Document, November 2020, https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2020-11/files/dupilumab-asthma-psd-nov-2020.pdf

[2] Li Z, Radin A, Li M, Hamilton JD, Kajiwara M, Davis JD, et al. Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of Dupilumab in Healthy Adult Subjects. Clin Pharmacol Drug Dev. 2020 Aug;9(6):742-755. doi: 10.1002/cpdd.798. Epub 2020 Apr 29. PMID: 32348036; PMCID: PMC7496261

Therapeutic Goods Administration (TGA) approved indications

Asthma

- Dupilumab is indicated as add on maintenance treatment in patients aged 6 years and older with moderate to severe asthma with type 2 inflammation that is inadequately controlled despite therapy with other medicinal products for maintenance treatment.

Atopic dermatitis

- Dupilumab is TGA approved for the treatment of moderate to severe atopic dermatitis in patients aged 6 months and older who are candidates for chronic systemic therapy.

Chronic rhinosinusitis with nasal polyposis

- Dupilumab is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis.

Prurigo Nodularis

- Dupilumab is indicated for the treatment of moderate-to-severe prurigo nodularis (PN) in adults who are candidates for systemic therapy.

Dosage and administration

The recommended dose of dupilumab for adults and adolescents (12 years of age and older) with moderate to severe asthma with type 2 inflammation is:

- Initial dose of 400 mg by subcutaneous injection (two 200 mg injections consecutively in different injection sites) followed by 200 mg given every other week.

Patients with oral corticosteroids-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid severe chronic rhinosinusitis with nasal polyposis for which dupilumab is indicated;

- Initial dose of 600 mg by subcutaneous injection (two 300 mg injections consecutively in different injection sites) followed by 300 mg given every other week.

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 1 November 2023)

Table 1: PBS listing of dupilumab for atopic dermatitis

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
Listings under s100 HSD Public					
12293B	dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	2	8	$1609.86	Dupixent, sanofi-aventis Australia Pty Ltd
12302L	dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	2	5	$1609.86	
12309W	dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	2	8	$1609.86	
12318H	dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	2	5	$1609.86	
Listings under s100 HSD Private					
12310X	dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	2	8	$1658.23	Dupixent, sanofi-aventis Australia Pty Ltd
12294C	dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	2	5	$1658.23	
12313C	dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	2	8	$1658.23	
12316F	dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	2	5	$1658.23	

Source: the PBS website. A Special Pricing Arrangement applies.

Restriction

Dupilumab is PBS listed for uncontrolled severe asthma.

Treatment criteria:

Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.

Clinical criteria:

Patient must be under the care of the same physician for at least 6 months; OR

Patient must have been diagnosed by a multidisciplinary severe asthma clinic team, AND

Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; OR

Patient must have had a break in treatment from the most recently approved PBS-subsidised biological medicine for severe asthma, AND

Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or (iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days; OR

Patient must have a diagnosis of asthma from at least two physicians experienced in the management of patients with severe asthma, AND

Patient must have a duration of asthma of at least 1 year, AND

200 mg/1.14 mL injection:

- Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months; OR
- Patient must have blood eosinophil count greater than or equal to 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months; OR
- Patient must have total serum human immunoglobulin E greater than or equal to 30 IU/mL with past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE in the last 12 months,

300 mg/2 mL injection:

- Patient must have been receiving regular maintenance oral corticosteroids (OCS) in the last 6 months with a stable daily OCS dose of 5 to 35 mg/day of prednisolone or equivalent over the 4 weeks prior to treatment initiation, AND
- Patient must have blood eosinophil count greater than or equal to 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months; OR
- Patient must have total serum human immunoglobulin E (IgE) greater than or equal to 30 IU/mL with past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE, that is no more than 1 year old, AND

Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND

Patient must not receive more than 32 weeks of treatment under this restriction, AND

The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma.

Population criteria:

Patient must be aged 12 years or older.

Optimised asthma therapy includes:

(i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated; AND

(ii) treatment with oral corticosteroids as outlined in the clinical criteria.

Recommencement of treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy

Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; OR

Patient must have had a break in treatment from the most recently approved PBS-subsidised biological medicine for severe asthma.

A treatment break in PBS-subsidised biological medicine therapy of at least 12 months must be observed in a patient who has either failed to achieve or sustain a response to treatment with 4 biological medicines within the same treatment cycle.

The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine was administered until the date of the first application for recommencement of treatment with a biological medicine under the new treatment cycle.

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

Date of listing on PBS

Dupilumab was PBS listed for uncontrolled severe asthma 1 April 2021.

Changes to listing

Table 2: Changes to the PBS listings for severe asthma

Date	Change to the PBS
July 2011	Omalizumab listed for severe allergic asthma
August 2014	Omalizumab pre-filled syringe added
December 2016	Omalizumab listing for uncontrolled severe allergic asthma extended to patients aged 6 to 12 years old
January 2017	Mepolizumab listed for uncontrolled severe eosinophilic asthma
December 2018	Benralizumab listed for uncontrolled severe eosinophilic asthma
April 2021	Dupilumab listed for uncontrolled severe eosinophilic or allergic asthma
July 2021	Listing for the four asthma biologics changed to be listed for uncontrolled severe asthma

Current PBS listing details are available from the PBS website.

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

At the November 2020 meeting the PBAC recommended dupilumab for uncontrolled severe asthma. The submission requested listing on the basis of a cost-minimisation analysis versus three comparators: benralizumab, mepolizumab and omalizumab. The submission took a market share approach to estimate the extent of use and financial implications associated with the listing of dupilumab.

The submission assumed that the growth of the asthma biologic market from April 2020 until the end of Year 6 of dupilumab listing (2026) would not be affected by the availability of dupilumab, as the proposed restriction criteria ensured that patients eligible for treatment with dupilumab would also currently qualify for treatment with benralizumab, mepolizumab or omalizumab. The 10% PBS sample data indicated that, despite the similar PBS restrictions of benralizumab to those of mepolizumab, the reimbursement of benralizumab accelerated the growth of the asthma biologic market, which meant that the availability of additional treatment option attracted new patients who otherwise would not receive asthma biologics. The PBAC considered this might also occur following the listing of dupilumab, especially in the allergic asthma population, for whom only one treatment (omalizumab) was available, and dupilumab therapy was associated with a more straightforward posology with no need for post-injection monitoring of anaphylaxis events. In its Pre-Sub-Committee Response, the sponsor argued that at the time of listing dupilumab, benralizumab will have been listed for 2 years, and claimed that it reasonably expected that all biologic naïve patients suitable for IL-5 therapy would have initiated therapy.

For further details refer to the Public Summary Document from the November 2020 PBAC meeting.

Previous reviews by the DUSC

DUSC previously reviewed omalizumab for the treatment of uncontrolled severe allergic asthma at its June 2014 meeting. The review found that the utilisation of omalizumab over the first 24 months of listing was lower than estimated.

- 258 patients received an authority approval for omalizumab in the second year of listing, including 156 new patients. This is fewer total and new patients than predicted.
- Over 80% of patients who received an initial authority approval received a continuing authority approval.
- An average 3.76 vials was approved per prescription over the first two years of listing, which was approximately 20% more than predicted.

For details of the DUSC consideration of omalizumab for the treatment of uncontrolled severe allergic asthma refer to the Public Release Document from the June 2014 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 for biologic medicines (dupilumab, omalizumab, benralizumab and mepolizumab) from 1 January 2017 up to and including 30 September 2023. Prescription data were extracted for inhaled corticosteroids from 1 January 2016 up to and including 30 September 2023. These data were extracted on 27 November 2023.

Authorities data were extracted from the Authorities database, and matched to the prescription data to determine whether a prescription was supplied for severe uncontrolled asthma or another indication. These matched data were used to analyse the consistency of utilisation by indication, and to analyse the data quality of PBS item codes the prescription was intended to treat.

Treatment duration was analysed using the Kaplan-Meier method. A patient was assumed to be continuing on treatment and censored if they were supplied a prescription within three times the median time to resupply prior to 30 September 2023 (i.e. 3×28 days). Three times the median time to resupply was used to test for breaks between supplies of dupilumab.

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]

Analyses were completed using SAS.

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

Results

Analysis of drug utilisation

Data quality

Table 3 shows prescriptions for medicines for severe asthma by the restriction determined from the PBS item code, and the indication determined from the authority code.

Table 3: Use of medicines for severe asthma by item code restriction and authority code restriction

Drug name	Restriction from item code	Indication from authority code	Prescriptions	Percent of total
BENRALIZUMAB	Asthma	Asthma	63,359	99%
BENRALIZUMAB	Asthma	Other	522	1%
BENRALIZUMAB	Asthma	Total	63,881	
DUPILUMAB	Asthma	Asthma	33,535	81%
DUPILUMAB	Asthma	Other	8,022	19%
DUPILUMAB	Asthma	Total	41,557	
DUPILUMAB	Other	Asthma	4,600	2%
DUPILUMAB	Other	Other	258,834	98%
DUPILUMAB	Other	Total	263,434	
MEPOLIZUMAB	Asthma	Asthma	113,995	99%
MEPOLIZUMAB	Asthma	Other	702	1%
MEPOLIZUMAB	Asthma	Total	114,697	
MEPOLIZUMAB	Other	Asthma	285	17%
MEPOLIZUMAB	Other	Other	1,402	83%
MEPOLIZUMAB	Other	Total	1,687	
OMALIZUMAB	Asthma	Asthma	124,870	92%
OMALIZUMAB	Asthma	Other	10,372	8%
OMALIZUMAB	Asthma	Total	135,242	
OMALIZUMAB	Other	Asthma	4,026	3%
OMALIZUMAB	Other	Other	152,307	97%
OMALIZUMAB	Other	Total	156,333	

Table 3 suggests that the alignment of PBS item code and authority code for severe asthma is above 90% for omalizumab, mepolizumab and benralizumab. Of the 41,557 prescriptions of dupilumab supplied under PBS item codes for severe asthma, 33,535 (81%) were supplied with an authority code for severe asthma. However, of the 4,446 patients supplied dupilumab for severe asthma, all 4,446 had been supplied previous inhaled corticosteroids. Therefore prescriptions supplied under PBS item codes were used for subsequent analyses of use.

Overall utilisation of biologic medicines for severe asthma

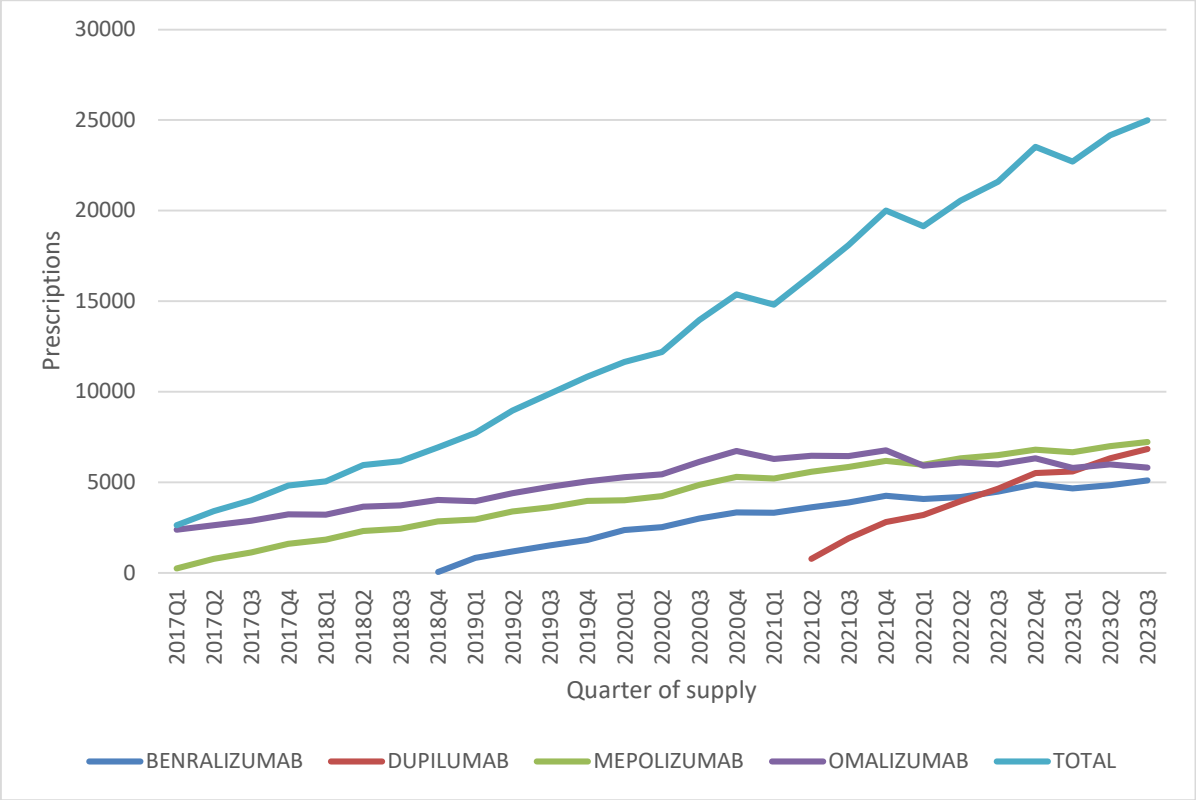

Figure 1: Prescriptions of biologic medicines for severe asthma by drug

Note: Use by drug for severe asthma using PBS item code

Figure 1 shows the number of supplied prescriptions of biologic medicines for severe asthma over time. The gradient of the total curve appears to have increased over time, suggesting use has increased over time. It appears that seasonal effects have affected the use over time, with more prescriptions supplied in quarter 4 of 2020, 2021 and 2022 and fewer in quarter 1 of 2021, 2022 and 2023.

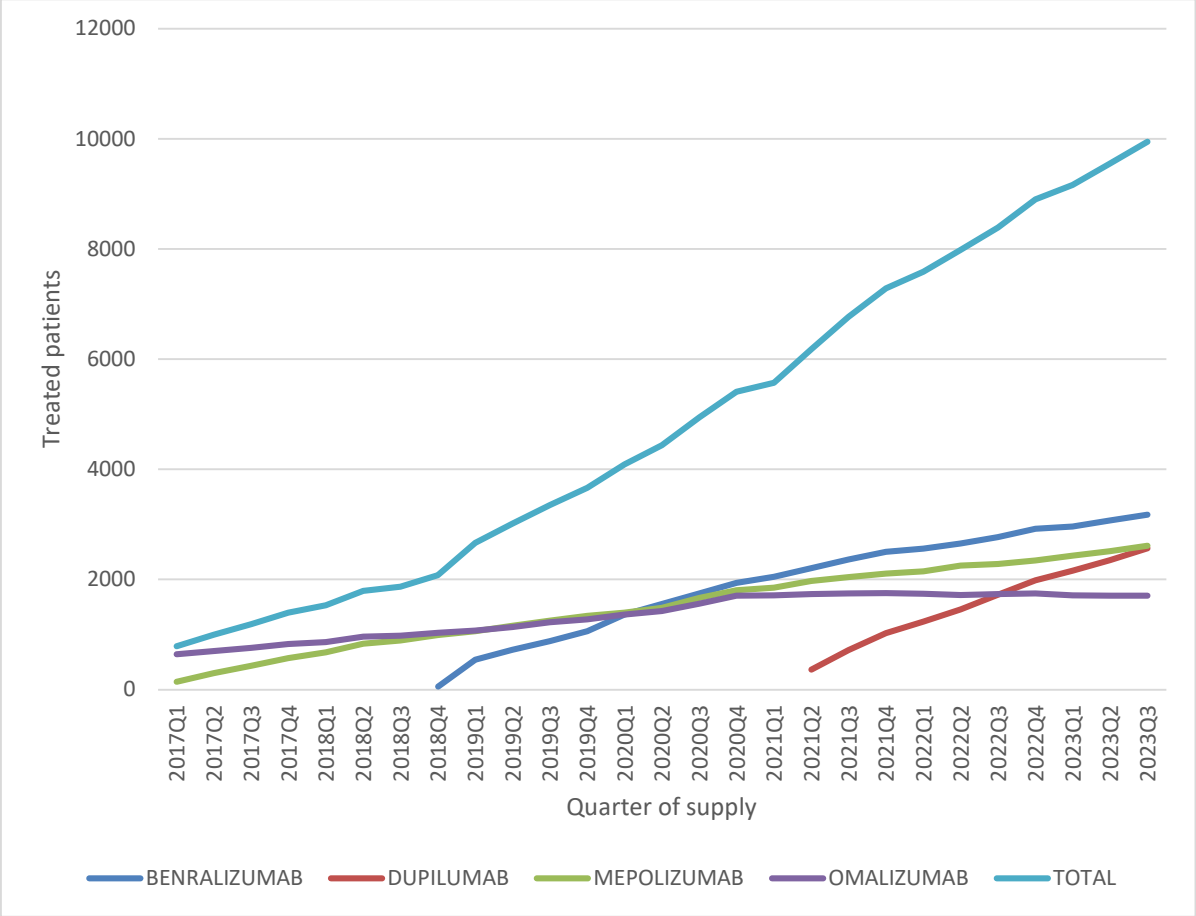

Figure 2: Patients supplied biologic medicines for severe asthma by drug

Note: Use by drug for severe asthma using PBS item code

Figure 2 shows the number of patients supplied biologic medicines for severe asthma over time. The gradient of the line that represents the total number of treated patients appears to have increased with the listing of benralizumab, however does not appear to have increased with the listing of dupilumab.

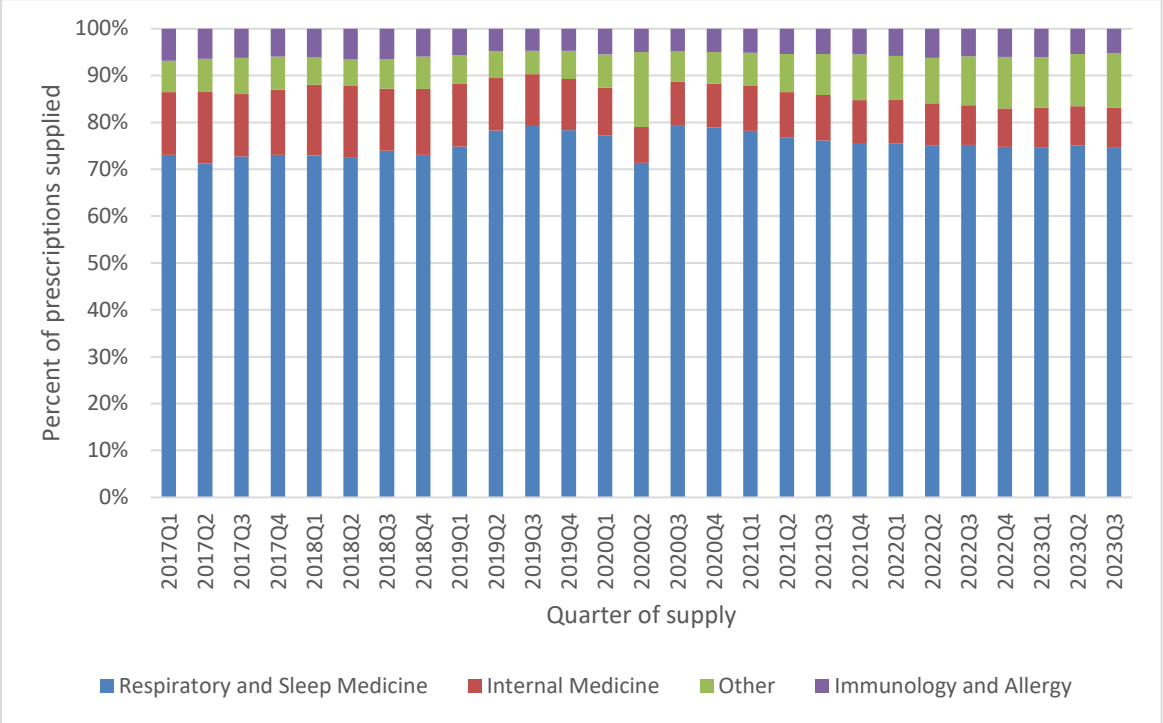

Figure 3: Prescriber type for biologic medicines for severe asthma as percent of overall prescriptions supplied

Figure 3 shows the prescriber type for supplied prescriptions of biologics for severe asthma since 2017. It appears there was an increase in the number of prescriptions written by other specialists in the second quarter of 2020, likely because patients had issues accessing specialists due to the start of the COVID-19 pandemic.

Table 4 shows the sequence of medicines patients have been supplied since 2017. Where a patient is supplied a medicine before and after a second medicine, this medicine is only recorded once.

Of the 4,446 patients who have been supplied dupilumab, 2,983 (67%) of these patients initiated therapy on dupilumab, and 1,463 patients were switched to dupilumab from either omalizumab, mepolizumab or benralizumab. Of the 2,983 patients who initiated therapy on dupilumab, 2,898 (97%) have not been supplied another biologic medicine for severe asthma. Of the 15,238 patients who have been supplied a medicine for severe asthma, 48 (0.32%) have been supplied all four medicines.

Table 4: Medicine sequence

Sequence	Patient count	Percent
OMALIZUMAB	3,546	23%
BENRALIZUMAB	3,233	21%
MEPOLIZUMAB	2,963	19%
DUPILUMAB	2,898	19%
MEPOLIZUMAB > BENRALIZUMAB	442	3%
OMALIZUMAB > DUPILUMAB	418	3%
BENRALIZUMAB > DUPILUMAB	371	2%
MEPOLIZUMAB > DUPILUMAB	282	2%
OMALIZUMAB > BENRALIZUMAB	229	2%
BENRALIZUMAB > MEPOLIZUMAB	155	1%
OMALIZUMAB > MEPOLIZUMAB	126	1%
MEPOLIZUMAB > BENRALIZUMAB > DUPILUMAB	94	1%
OMALIZUMAB > BENRALIZUMAB > DUPILUMAB	91	1%
DUPILUMAB > BENRALIZUMAB	38	0.2%
OMALIZUMAB > MEPOLIZUMAB > DUPILUMAB	36	0.2%
BENRALIZUMAB > MEPOLIZUMAB > DUPILUMAB	31	0.2%
BENRALIZUMAB > OMALIZUMAB	25	0.2%
OMALIZUMAB > MEPOLIZUMAB > BENRALIZUMAB	25	0.2%
DUPILUMAB > MEPOLIZUMAB	24	0.2%
MEPOLIZUMAB > OMALIZUMAB > DUPILUMAB	23	0.2%
MEPOLIZUMAB > OMALIZUMAB	23	0.2%
OMALIZUMAB > MEPOLIZUMAB > BENRALIZUMAB > DUPILUMAB	22	0.1%
MEPOLIZUMAB > DUPILUMAB > BENRALIZUMAB	18	0.1%
OMALIZUMAB > DUPILUMAB > BENRALIZUMAB	17	0.1%
BENRALIZUMAB > OMALIZUMAB > DUPILUMAB	16	0.1%
OMALIZUMAB > BENRALIZUMAB > MEPOLIZUMAB	13	0.1%
BENRALIZUMAB > DUPILUMAB > MEPOLIZUMAB	12	0.1%
DUPILUMAB > OMALIZUMAB	12	0.1%
OTHER	55	0.4%
TOTAL	15,238	

The PBS restrictions for biologic medicines for severe asthma state that a patient who has either failed to achieve or sustain a response to treatment with four biological medicines within the same treatment cycle may recommence treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy of at least 12 months. Prior to the PBS listing of dupilumab, the PBS restrictions stated, “A patient who wishes to trial a second or subsequent new treatment cycle, following a break in PBS-subsidised therapy of at least 6 months (in patients where omalizumab is the only appropriate treatment option for uncontrolled severe allergic asthma) or 12 months (in patients who have failed to achieve or ceased to sustain a response to treatment 3 times within a treatment cycle), must re-qualify through an Initial 1 restriction.” Since 2017, 696 (5%) of the treated patients

have had a break of 12 months or longer and recommenced treatment, and 2,006 (13%) have had a break of 6 months or longer and recommenced treatment.

Table 5: Six and 12 month breaks

6 month break	12 month break	Patient count	Percent
No	No	13,232	87%
Yes	No	1,310	9%
Yes	Yes	696	5%
Total		15,238	

Table 6: Age of patients at initiation of medicine and therapy

	Number	Mean	25th Percentile	Median	75th Percentile	Quartile Range
Age at initiation of medicine (including patients switching from a previous biologic)						
Benralizumab	4,880	58	49	61	70	21
Dupilumab	4,446	50	35	53	66	31
Mepolizumab	4,338	58	49	60	70	21
Omalizumab	4,671	50	37	53	65	28
Age at initiation of therapy (excluding patients switching from a previous biologic)						
Benralizumab	3,849	58	49	61	70	21
Dupilumab	2,983	47	30	49	64	34
Mepolizumab	3,867	59	49	60	70	21
Omalizumab	4,538	50	37	52.5	65	28
Overall age at therapy initiation	15,237	54	42	57	68	26

Table 6 shows the mean and median of the age of patients at initiation of medicine, which includes patients switching from a previous biologic, and therapy, which excludes patients switching from a previous biologic. Overall, the mean age of patients initiating therapy was 54, and the median was 57. Patients who initiated therapy on dupilumab were younger than the overall population, with a mean of 47 and a median of 49. When patients who had received a prior biologic for asthma were included, the age of dupilumab patients increased to a mean of 50 and a median of 53. The mean and median age of patients initiating therapy on omalizumab was younger than those initiating benralizumab or mepolizumab, likely because omalizumab is the only one of the four asthma biologics PBS listed for patients aged younger than 12.

Utilisation of dupilumab for severe asthma

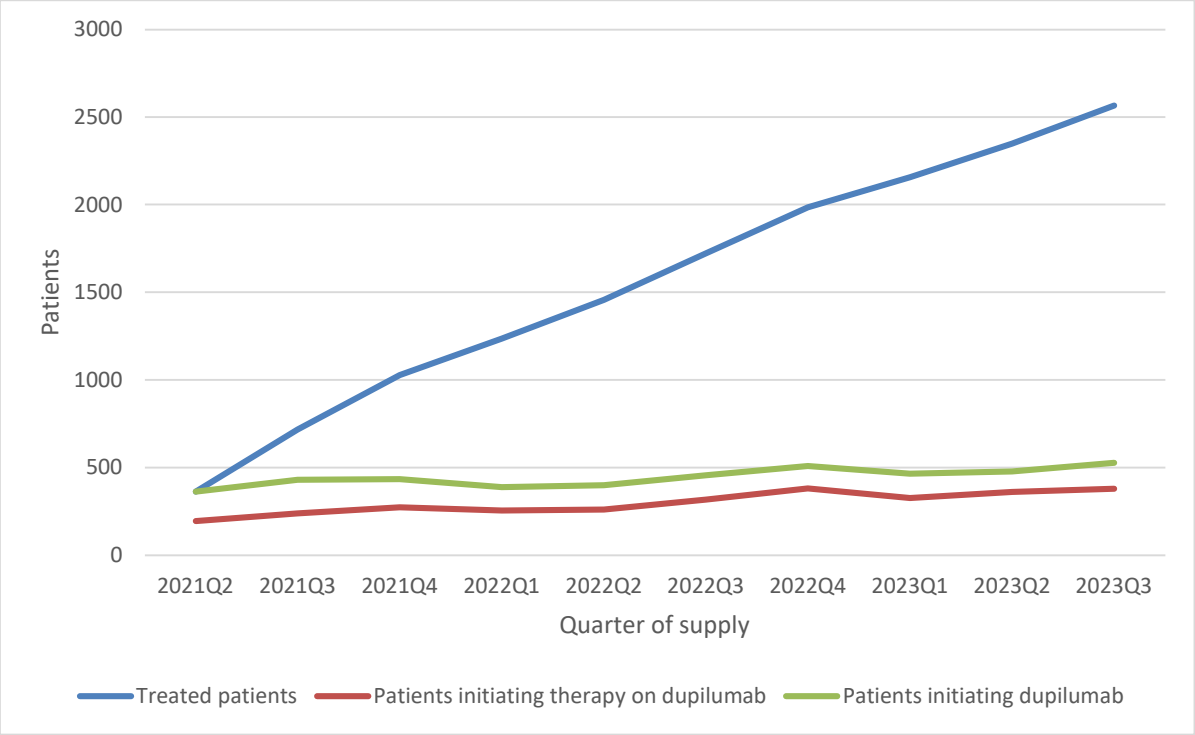

Figure 4: Patients supplied dupilumab for severe asthma

Shows the number of treated patients per month, the number initiating therapy on dupilumab (2,983 total), and the number initiating dupilumab (4,446). The difference between the latter two groups is the number of patients who initiated dupilumab after being supplied another therapy. There were more patients who initiated therapy on dupilumab (2,983) than patients who initiated dupilumab from another therapy (1,463). This likely includes patients presenting for the first time being initiated on dupilumab, and may include patients who otherwise would not have received a biologic medicine for asthma.

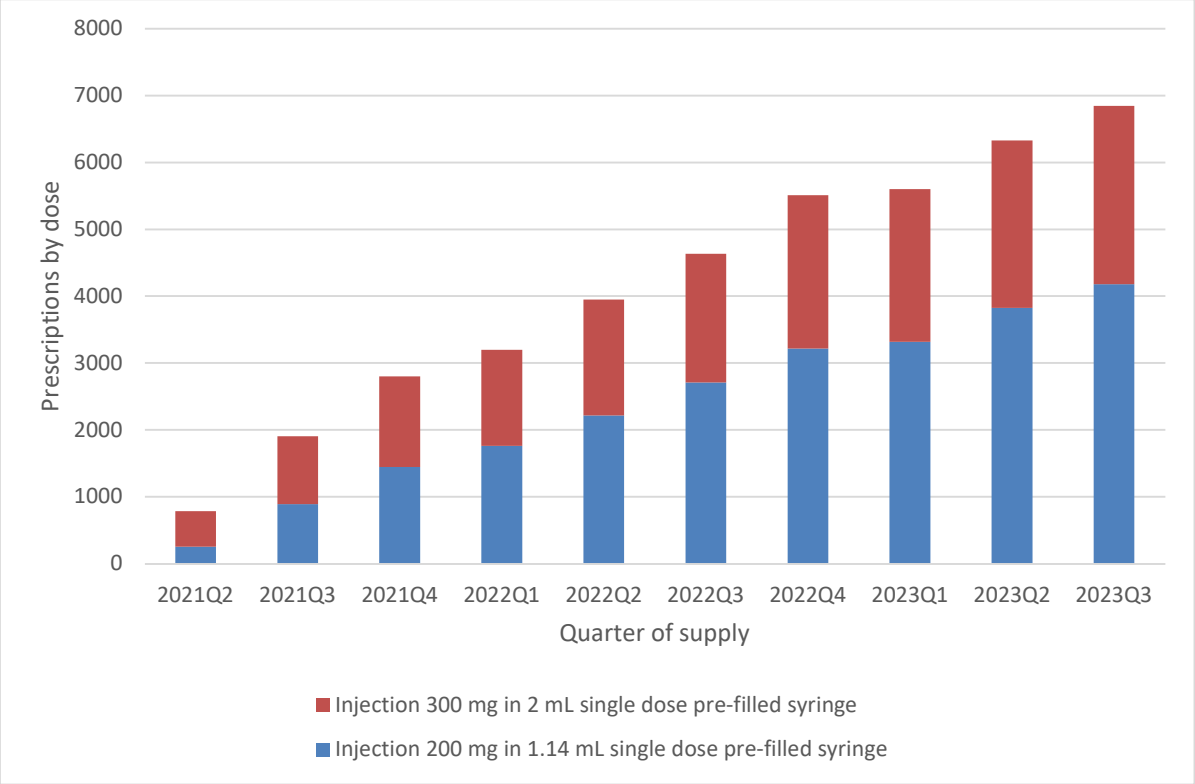

Figure 5: Dupilumab prescriptions by dose

Of the 41,557 supplied prescriptions of dupilumab for severe asthma since PBS listing, there have been 23,818 (57%) supplies of dupilumab 200 mg and 17,739 (43%) supplies of dupilumab 300 mg.

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

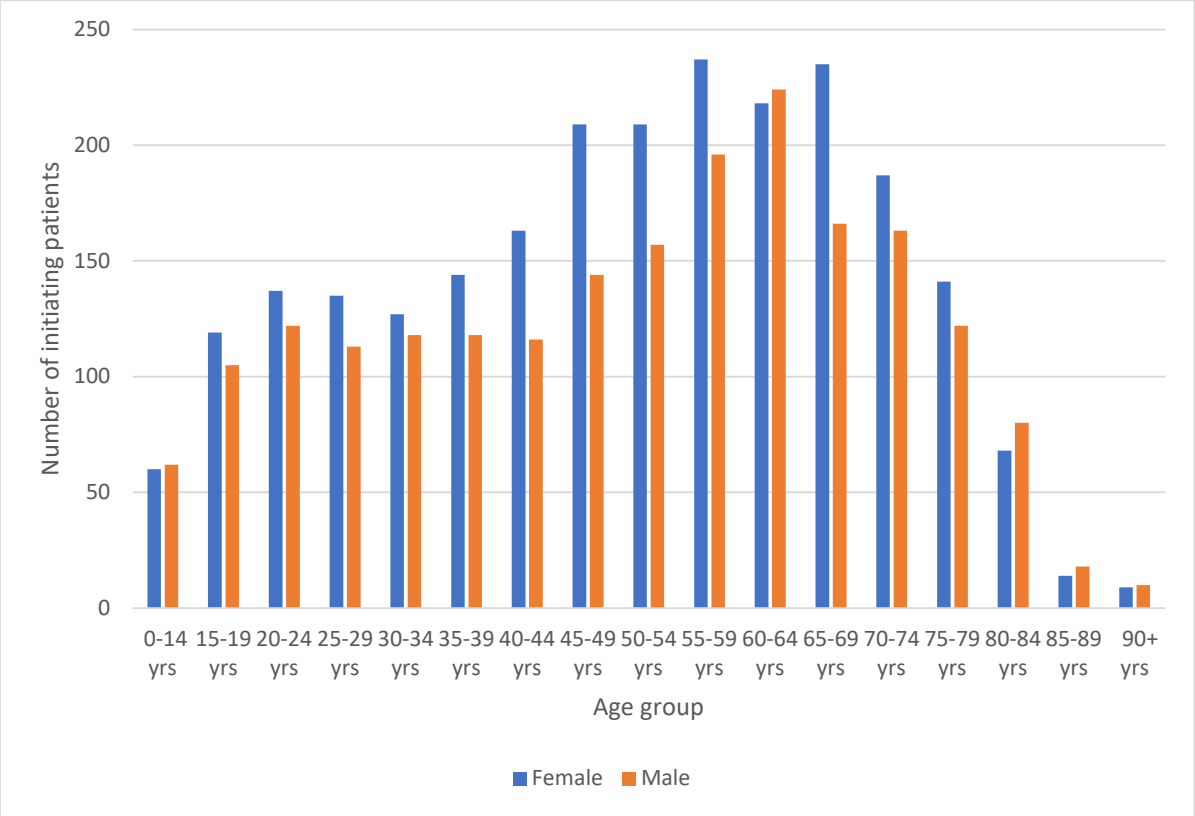

Figure 6: Age and gender of initiating patients for dupilumab

Figure 6 shows the age and gender of initiating patients of dupilumab for severe asthma. The mean age at initiation was 50 years old, and the median was 53 years old. The group with the highest number of patients is those aged 60 to 64 years old, although there were also over 400 patients in the 55 to 59 year old and 65 to 69 year old groups. Of the 4,446 patients who initiated dupilumab, 29% (1,276) were aged 55 to 69 years old and 59% (2,608) were aged 45 to 79 years old. More female than male patients initiated in nearly every age group, with the exception of the 0 to 14 and 60 to 64 age range, and patients aged 80 years or older. Less than 5 patients under the age of 12 initiated dupilumab for severe asthma and these patients are grouped in the 0 to 14 age range.

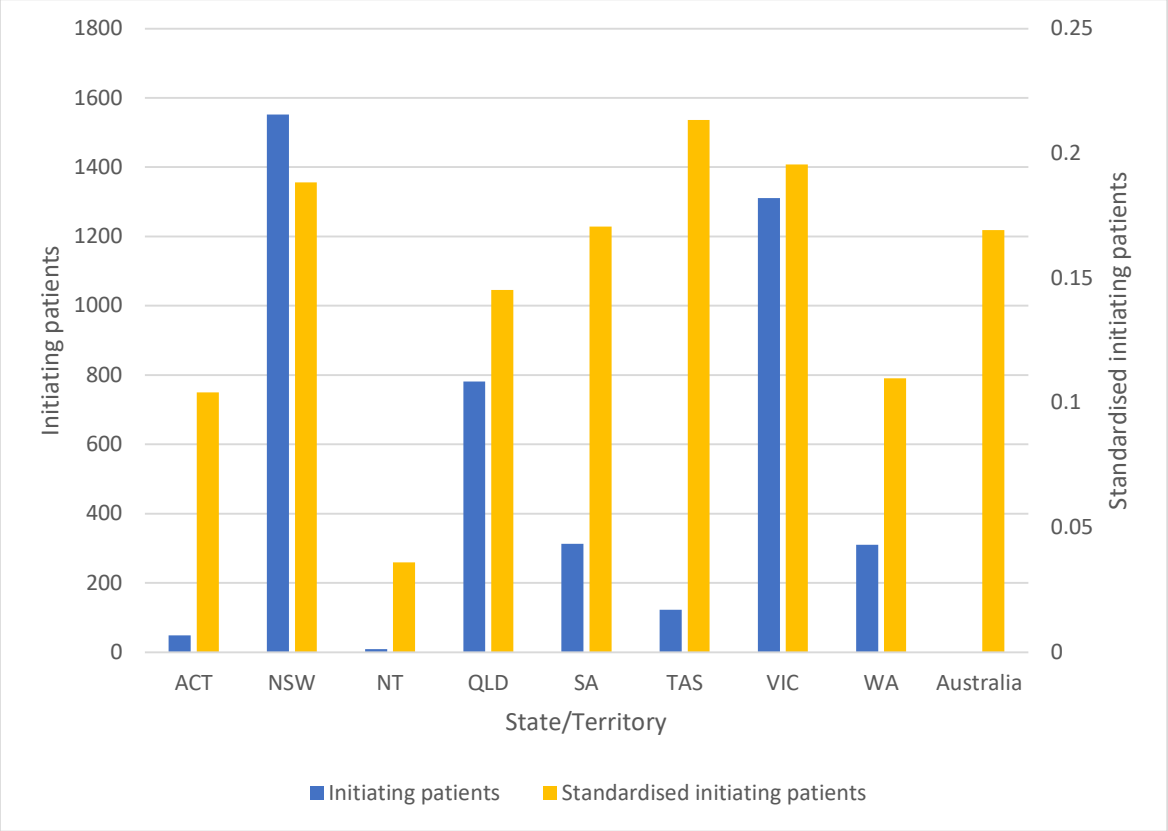

Figure 7: Number of initiating patients and standardised initiating patients by State
Note: Number of initiators for Australia (4,446) is not shown

Figure 7 counts every patient once for the State or Territory that the patient initiated in, using the patient's postcode. The State in Australia with the highest number of initiating patients was NSW, and the standardised data shows that the standardised number of initiating patients was highest in Tasmania, with Victoria and South Australia also above the national average. Northern Territory had the lowest number of initiating patients and the lowest standardised number of initiating patients.

Table 7: Prescriber type for initiating patients and prescriptions for dupilumab

Major Specialty Name	Initiating patients	Percent of total	Prescriptions	Percent of total
Respiratory and Sleep Medicine	2,260	51%	27,652	67%
Dermatology	1,282	29%	5,693	14%
Immunology and Allergy	290	7%	2,855	7%
Internal Medicine	210	5%	2,326	6%
Not found	117	3%	619	1%
GP	114	3%	787	2%
Pathology	65	1%	356	1%
Paediatric Medicine	54	1%	630	2%
ENT	21	0.5%	253	1%
Intensive Care	14	0.3%	182	0.4%
Medical Oncology	10	0.2%	139	0.3%
Other	9	0.2%	65	0.2%
Total	4,446		41,557	

Prescriber type is shown above for initiating patients and all supplied prescriptions. Respiratory and sleep medicine specialists accounted for 51% of supplies to patients initiating dupilumab either as the first or subsequent treatment, and 67% of supplied prescriptions.

Duration and number of treatments

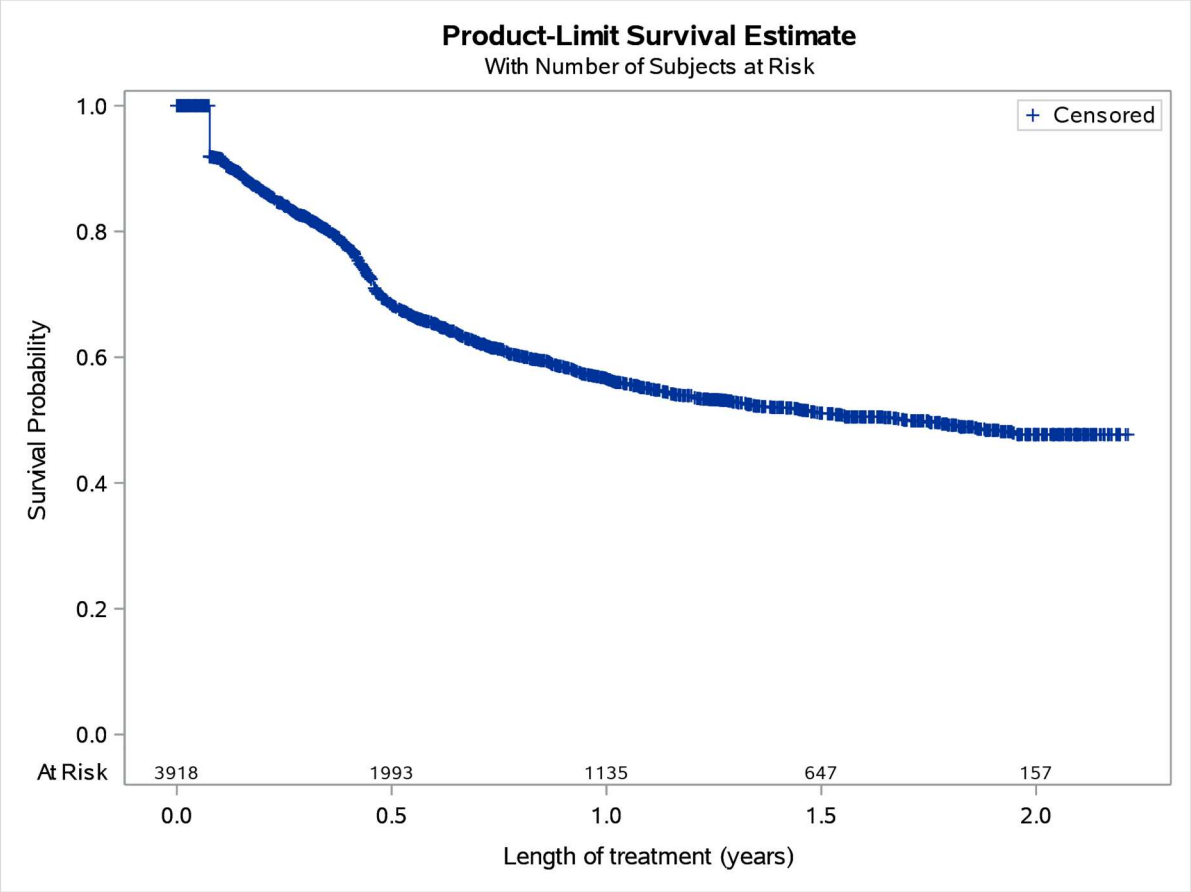

Figure 8: Length of time on treatment

Of the 4,446 patients who were supplied dupilumab under an item code for severe asthma, 57% (2,534) were supplied a prescription within 84 days (3 × median resupply of 28 days) of the last date of extracted data (30 September 2023) and were considered to be continuing treatment.

Of these 4,446 patients, 16% (690) were considered to have had a break in therapy as there was more than 84 days between supplies of dupilumab at least once during their course of treatment, and 84% (3,756) did not. There were 2,048 patients (46%) who did not have a break and were considered to be continuing treatment.

The median length of time on treatment was estimated to be 1.2 years with a lower 95% confidence interval of 1.1 and an upper 95% confidence interval of 1.4. Using data to the end of September 2023, the mean length of treatment was estimated to be 1.2 years with a standard error of 0.01 years.

Analysis of expenditure

Table 8: Expenditure by quarter and year of supply

Supply quarter	Benefit paid
2021Q2	$1,257,436
2021Q3	$3,065,464
2021Q4	$4,554,275
2021 total	**$8,877,175**
2022Q1	$5,191,610
2022Q2	$6,421,296
2022Q3	$7,545,259
2022Q4	$8,971,901
2022 total	**$28,130,066**
2023Q1	$9,123,178
2023Q2	$10,320,808
2023Q3	$11,192,259
2023 total	**$30,636,246**
Total since listing	**$67,643,487**

Note: 2023 includes January to September 2023
Based on the published list price.
Benefits are based on the date of supply, there may be small differences between publicly available Medicare Australia date of processing data.

The total benefit paid for dupilumab for severe asthma since PBS listing to the end of June 2023 is $67.6 million, based on published prices. A special pricing arrangement is in place.

Approach taken to estimate utilisation

The submission used a market share approach to estimate the extent of use and financial implications associated with the listing of dupilumab, and stated that the listing of dupilumab was not expected to increase the size of the asthma biologic market more than would otherwise be expected. The submission used a 10% sample from July 2011 to March 2020 to estimate the predicted market growth, and to estimate the market share by product.

The predicted market share with and without dupilumab is summarised in Table 9. The submission assumed the predicted uptake of dupilumab and predicted the utilisation of the 200 mg versus 300 mg doses would be 60% and 40% respectively.

Table 9: Predicted market share with and without dupilumab

	Apr-19 to Mar-20	Apr-20 to Mar-21	Apr-21 to Mar-22	Apr-22 to Mar-23	Apr-23 to Mar-24	Apr-24 to Mar-25	Apr-25 to Mar-26	Apr-27 to Mar-28
Market Share (no dupilumab)								
Benralizumab MS								
Mepolizumab MS								
Omalizumab MS								
Market Share (with dupilumab)								
Benralizumab MS								
Mepolizumab MS								
Omalizumab MS								
Dupilumab MS								

Analysis of actual versus predicted utilisation

The table below shows the prescriptions supplied for severe asthma since 2021, compared to the estimated number of prescriptions in the final estimates for dupilumab. It appears that the market grew further than was predicted, as the total number of supplied prescriptions was 35% higher than estimated. The use of each medicine was underestimated, and the use of dupilumab was the furthest underestimated, as there were 17,292 prescriptions supplied in 2022 compared to an estimated 7,924. The numbers presented for 2023 includes nine months of data and use is approximately equal to the estimated number of prescriptions, therefore use in 2023 will also be higher than estimated. Overall it appears the market is larger than predicted and the uptake of dupilumab within the market has been higher than predicted.

Table 10: Predicted versus actual prescriptions by year

		2021	2022	2023
Benralizumab	Predicted	[redacted]	[redacted]	[redacted]
	Actual	15,050	17,639	14,599
	Difference	[redacted]	[redacted]	[redacted]
Mepolizumab	Predicted	[redacted]	[redacted]	[redacted]
	Actual	22,818	25,577	20,875
	Difference	[redacted]	[redacted]	[redacted]
Omalizumab	Predicted	[redacted]	[redacted]	[redacted]
	Actual	25,955	24,291	17,590
	Difference	[redacted]	[redacted]	[redacted]
Dupilumab	Predicted	[redacted]	[redacted]	[redacted]
	Actual	5,491	17,292	18,774
	Difference	[redacted]	[redacted]	[redacted]
Total market	Predicted	[redacted]	[redacted]	[redacted]
	Actual	69,314	84,799	71,838
	Difference	[redacted]	[redacted]	[redacted]

Note: 2023 includes nine months of data to the end of September 2023.

The numbers presented for 2023 includes nine months of data and use is approximately equal to the estimated number of prescriptions, therefore use in 2023 will also be higher than estimated. Overall it appears the market is larger than predicted and the uptake of dupilumab within the market has been higher than predicted.

Discussion

The number of prescriptions of biologic medicines supplied for severe asthma has increased over time, and its use is now affected by safety net in the first and last quarters of the year. The gradient of the line that represents the total number of treated patients appears to have increased with the listing of benralizumab, which confirms the 10% PBS sample data used by the dupilumab submission to estimate the financial impact of listing dupilumab. The rate of growth of total supplied prescriptions and treated patients per quarter do not appear to have increased following the PBS listing of dupilumab. However, the comparison of predicted versus actual utilisation shows that the use of all four medicines was underestimated, and dupilumab was the furthest underestimated.

The dupilumab submission predicted the utilisation of the 200 mg versus 300 mg doses would be 60% and 40% respectively. Since PBS listing, there have been 23,818 (57%) supplies of dupilumab 200 mg and 17,739 (43%) supplies of dupilumab 300 mg.

It appears that prescribing of biologics for asthma moved from respiratory, immunology and allergy specialists to other specialists, including GPs, in the second quarter of 2020, likely because patients had issues accessing specialists due to the start of the COVID-19 pandemic. The analysis of prescriber type for dupilumab shows that respiratory and sleep medicine specialists accounted for 51% of supplies to patients initiating dupilumab either as the first or subsequent treatment, and 67% of supplied prescriptions. Dermatology specialists were the second most common specialist, and accounted for 29% of supplies to patients initiating dupilumab either as the first or subsequent treatment, and 14% of supplied prescriptions. As PBS item code was used for these analyses, it is possible this could be due to miscoding for dermatitis, however as every included patient had a previous supply of inhaled corticosteroids, it is also possible these patients have dermatitis and asthma.

The sequence of medicine use within the class since 2017 showed that 83% (12,640) of patients supplied a biologic medicine for severe asthma were only supplied one medicine, and 0.32% (48) were supplied all four medicines. Of the 15,238 patients supplied a biologic medicine for severe asthma since 2017, 87% have not had a break of 6 months or more and restarted treatment, although this count includes patients who recently initiated dupilumab.

Of the 4,446 patients supplied dupilumab:

- 65% (2,898) were only supplied dupilumab,
- 67% (2,983) were supplied dupilumab as their first biologic for asthma, and
- 33% (1,463) were supplied another biologic medicine prior to dupilumab.

Of the 2,983 patients supplied dupilumab as the first biologic for asthma, 97% (2,898) have not been supplied any other biologics for asthma, although this count includes patients who have recently initiated. In recommending dupilumab, the PBAC noted that there may be patients who initiate dupilumab who otherwise would not have received asthma biologics, especially in the allergic asthma population, for whom only one treatment

(omalizumab) was available, and dupilumab therapy was associated with a more straightforward posology with no need for post-injection monitoring of anaphylaxis events. However, as the rate of growth does not appear to have increased, it is unclear whether the patients who have only received dupilumab would have been treated with a different asthma biologic or whether there is a patient or prescriber preference for dupilumab.

The mean age of patients who initiated dupilumab was 50 years old, and the median was 53 years old, however patients who initiated therapy on dupilumab were younger, with a mean of 47 and a median of 49. Of the 4,446 patients who initiated dupilumab, 29% (1,276) were aged 55 to 69 years old and 59% (2,608) were aged 45 to 79 years old. There was negligible use in patients aged under the age of 12, in line with the PBS restriction that states patients must be over the age of 12 to access PBS listed dupilumab.

In recommending dupilumab, the PBAC noted that therapies were costed over three years with loading dose(s) for dupilumab and benralizumab taken into account. The PBAC noted that the 3 year time frame was longer than the treatment duration in the dupilumab (24-52 weeks) and comparator (24-56 weeks) clinical trials. The PBAC recalled that it had recommended a one year time horizon in its March 2018 consideration of benralizumab as it aligned with the duration of the key trials. Using a Kaplan-Meier estimate, the median length of treatment time on treatment was estimated to be 1.2 years with a lower 95% confidence interval of 1.1 and an upper 95% confidence interval of 1.4.

DUSC consideration

The report showed the number of supplied prescriptions and patients supplied biologic medicines for severe asthma over time. The report suggested that the total number of treated patients appears to have increased with the listing of benralizumab, however does not appear to have increased with the listing of dupilumab. DUSC commented that there may have been a small increase in the number of supplied prescriptions and patients with the listing of dupilumab. DUSC agreed that seasonal effects have affected the use over time, with more prescriptions supplied in quarter 4 of 2020, 2021 and 2022 and fewer in quarter 1 of 2021, 2022 and 2023.

DUSC noted that the mean age at initiation of dupilumab was 50 years old, and the median was 53 years old. DUSC noted that more female than male patients initiated in nearly every age group, with the exception of the 0 to 14 and 60 to 64 age range, and patients aged 80 years or older. DUSC noted that the mean and median age of patients initiating therapy on omalizumab was younger than those initiating benralizumab or mepolizumab, which DUSC agreed was likely because omalizumab is the only one of the four asthma biologics PBS listed for patients aged younger than 12.

DUSC noted there was variability in the use of dupilumab across States and Territories, with NSW having the highest number of initiating patients, and the standardised number of initiating patients highest in Tasmania, with Victoria and South Australia also above the national average. Northern Territory had the lowest number of initiating patients and the

lowest standardised number of initiating patients. DUSC considered this suggested there may be a lack of equitable access across Australia.

DUSC suggested that there was a particular access issue for the Indigenous population. DUSC commented that the Remote Area Aboriginal Health Services Program, which provides free PBS medicines to patients of Aboriginal health services in remote areas under the section 100 program, is unable to supply medicines listed on the s100 Highly Specialised Drugs (HSD) program, including biologics for asthma.

DUSC noted that respiratory and sleep medicine specialists accounted for 51% of supplies to patients initiating dupilumab either as the first or subsequent treatment, and 67% of supplied prescriptions. DUSC noted that Dermatology specialists accounted for 29% of supplies to patients initiating dupilumab either as the first or subsequent treatment, and 14% of supplied prescriptions. In its Pre-Sub-Committee Response (PSCR, p3) the sponsor noted that this indicated that approximately 98% of prescriptions representing 97% of treated patients were written either by clinicians included in the PBS restrictions for severe uncontrolled asthma or by dermatologists. DUSC commented that this could be due to miscoding of dupilumab for dermatitis, but noted that 100% of patients supplied dupilumab for severe asthma were supplied previous inhaled corticosteroids. DUSC commented that the database only records one specialty for each clinician although clinicians may have dual specialties, but DUSC questioned whether clinicians would be likely to be dual certified as respiratory and dermatology specialists. DUSC agreed with the PSCR (p4) which suggested that the patients supplied dupilumab by dermatitis specialists may be affected by both asthma and dermatitis.

DUSC noted that it appeared that the number of supplied prescriptions of biologic medicines for severe asthma and the number of treated patients have not plateaued and are continuing to grow. DUSC noted that the PSCR (p5) suggested that the rate of growth may have peaked in 2022 and will more closely reflect the assumed annual rates of growth predicted in the submission from 2023 onwards. DUSC commented that dupilumab has already reached the market share it was predicted to have in 2027, and it appears dupilumab has taken market share from omalizumab. DUSC noted that the use of injectable biologics were originally estimated to have a slow uptake as patients may have been hesitant to use an injectable therapy, but that the mode of administration has not affected use as expected. DUSC commented that the length of time on treatment was also higher than predicted, and considered it is likely use will continue to grow in the coming years as more patients initiate therapy and are treated for many years.

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

Sanofi-Aventis Australia: The sponsor has no comment.

Novartis Pharmaceuticals Australia: The sponsor has no comment.

GlaxoSmithKline Australia: The sponsor has no comment.

AstraZeneca: 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.

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