Elexacaftor + tezacaftor + ivacaftor (&) ivacaftor for cystic fibrosis: analysis of utilisation

Drug utilisation sub-committee (DUSC)

October 2025

Abstract

Purpose

To review elexacaftor, tezacaftor and ivacaftor for the treatment of cystic fibrosis as requested by DUSC at its October 2024 meeting.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Elexacaftor + tezacaftor + ivacaftor was PBS listed 1 April 2022.

Data Source / methodology

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

Key Findings

- In 2024, there were 3,126 patients supplied 30,208 prescriptions of cystic fibrosis transmembrane conductance regulator (CFTR) modulators, including 307 initiating patients.
- There were 27,089 prescriptions of the combination medicine elexacaftor, tezacaftor and ivacaftor (ELX/TEZ/IVA) supplied to 2,890 patients, including 209 initiating patients.
- Between PBS listing on 1 April 2022 and 30 June 2025, 3,209 patients were supplied ELX/TEZ/IVA, including 1,320 (41%) patients who initiated on and have only been supplied ELX/TEZ/IVA.
- The mean age of patients supplied CFTR modulators in 2024 was 24 years, and the median age was 21 years. The mean age of patients supplied ELX/TEZ/IVA in 2024 was 24 years, and the median age was 21 years.

Purpose of analysis

To review elexacaftor, tezacaftor and ivacaftor for the treatment of cystic fibrosis as requested by DUSC at its October 2024 meeting.

Background

Clinical situation

Cystic fibrosis is a genetic disorder caused by an abnormal gene that is inherited from both biological parents.[1] The cystic fibrosis transmembrane conductance regulator (CFTR) gene is responsible for salt transport across different tissues in the body. In cystic fibrosis, the protein made by the abnormal CFTR gene is absent or dysfunctional, resulting in reduced salt transport and decreased water movement, which causes thick mucus to accumulate in the lungs and intestinal tract.[1,2] This mucus clogs the lungs causing them to be vulnerable to bacterial infection, and chronic infection leads to bronchiectasis, respiratory failure, and death.[3]

Treatment for cystic fibrosis generally involves:

- Intensive daily physiotherapy to clear the lungs
- Enzyme replacement capsules with food to aid digestion
- Antibiotic therapy to treat lung infections
- Aerosol mist inhalations via a nebuliser to help open the airways
- Salt and vitamin supplements
- A nutritious diet that's also high in calories, high salt and high fat
- Exercise – important to help clear the airways and build core strength.[4]

CFTR modulators have been listed on the PBS since 2014. The CFTR modulators currently listed on the PBS are:

- ivacaftor;
- lumacaftor and ivacaftor (LUM/IVA);
- tezacaftor and ivacaftor (TEZ/IVA); and
- elexacaftor, tezacaftor and ivacaftor (ELX/TEZ/IVA).

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[1] Endres TM, Konstan MW. What Is Cystic Fibrosis? JAMA. 2022;327(2):191. doi:10.1001/jama.2021.23280 https://jamanetwork.com/journals/jama/fullarticle/2787906, Accessed 29 October 2024

[2] Price CE, O'Toole GA. The Gut-Lung Axis in Cystic Fibrosis. J Bacteriol. 2021 Sep 23;203(20):e0031121. doi: 10.1128/JB.00311-21. Epub 2021 Aug 2. PMID: 34339302; PMCID: PMC8459759. https://pmc.ncbi.nlm.nih.gov/articles/PMC8459759/#B2 Accessed 29 October 2024

[3] Chmiel, J.F., Davis, P.B. State of the Art: Why do the lungs of patients with cystic fibrosis become infected and why can't they clear the infection?. Respir Res 4, 8 (2003). https://doi.org/10.1186/1465-9921-4-8 Accessed 29 October 2024

[4] Cystic Fibrosis Australia, https://www.cysticfibrosis.org.au/treatment/ Accessed 29 October 2024

Pharmacology

CFTR modulators work to increase the amount of protein at the cell surface. ELX/TEZ/IVA includes two types of tablets or granules, one contains elexacaftor, tezacaftor and ivacaftor (morning dose) and the other contains ivacaftor (evening dose).

Therapeutic Goods Administration (TGA) approved indications

Table 1: TGA indications for CFTR modulators

Drug name (Brand name)	TGA indication
Ivacaftor (Kalydeco)	Indicated for the treatment of cystic fibrosis in patients aged 1 month and older who have at least one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.
LUM/IVA (Orkambi)	Indicated for the treatment of cystic fibrosis in patients aged 1 year and older who are homozygous for the F508del mutation in the CFTR gene.
TEZ/IVA (Symdeko)	Indicated for the treatment of patients with cystic fibrosis aged 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.
ELX/TEZ/IVA (Trikafta)	Indicated for the treatment of cystic fibrosis in patients aged 2 years and older who have at least one mutation in the CFTR gene that is responsive based on clinical or in vitro evidence.

Dosage and administration

The dosage of all CFTR modulators depends on the weight of the patient. The weight based dosing of ELX/TEZ/IVA is presented below.

Table 2: Dosage and administration of elexacaftor + tezacaftor + ivacaftor

Age	Weight	Morning dose	Evening dose
2 to < 6 years	<14 kg	One sachet of elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg granules	One sachet of ivacaftor 59.5 mg granules
2 to < 6 years	≥14 kg	One sachet of elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg granules	One sachet of ivacaftor 75 mg granules
6 to <12 years	<30 kg	Two elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg tablets	One ivacaftor 75 mg tablet
6 to <12 years	≥30 kg	Two elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg tablets	One ivacaftor 150 mg tablet
≥12 years	-	Two elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg tablets	One ivacaftor 150 mg tablet

Source: Trikafta (elexacaftor + tezacaftor + ivacaftor) Australian Approved Product Information.[5]

[5] Trikafta (elexacaftor + tezacaftor + ivacaftor) Australian Approved Product Information. St Leonards, NSW: Vertex Pharmaceuticals (Australia) Pty Ltd. Approved 24 March 2021, updated 8 May 2025. Available from https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2021-PI-01350-1&d=20241114172310101

The Product Information (PI) includes recommended dosage adjustments for hepatic impairment and for concomitant use of moderate CYP3A inhibitors (e.g., fluconazole, erythromycin, verapamil) or strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, and clarithromycin).

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

PBS listing details (as at July 2025)

Table 3: PBS listing of ELX/TEZ/IVA

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
S100 HSD Private					
12938Y	elexacaftor 100 mg + tezacaftor 50 mg + ivacaftor 75 mg tablet [56] (&) ivacaftor 150 mg tablet [28], 84 (PI, CMI)	1	5	$20,355.13	Trikafta, Vertex Pharmaceuticals (Australia) Pty. Ltd.
13266F	elexacaftor 50 mg + tezacaftor 25 mg + ivacaftor 37.5 mg tablet [56] (&) ivacaftor 75 mg tablet [28], 84	1	5	$20,355.13	
14279M	elexacaftor 80 mg + tezacaftor 40 mg + ivacaftor 60 mg granules [28] (&) ivacaftor 59.5 mg granules [28], 56	1	5	$20,355.13	
14280N	elexacaftor 100 mg + tezacaftor 50 mg + ivacaftor 75 mg granules [28] (&) ivacaftor 75 mg granules [28], 56	1	5	$20,355.13	
S100 HSD Public					
12936W	elexacaftor 100 mg + tezacaftor 50 mg + ivacaftor 75 mg tablet [56] (&) ivacaftor 150 mg tablet [28], 84	1	5	$20,306.25	
13276R	elexacaftor 50 mg + tezacaftor 25 mg + ivacaftor 37.5 mg tablet [56] (&) ivacaftor 75 mg tablet [28], 84	1	5	$20,306.25	
14227T	elexacaftor 80 mg + tezacaftor 40 mg + ivacaftor 60 mg granules [28] (&) ivacaftor 59.5 mg granules [28], 56	1	5	$20,306.25	
14228W	elexacaftor 100 mg + tezacaftor 50 mg + ivacaftor 75 mg granules [28] (&) ivacaftor 75 mg granules [28], 56	1	5	$20,306.25	

Source: the PBS website. Special Pricing Arrangements apply.

Restriction

The PBS restriction for initial treatment of ELX/TEZ/IVA states:

Treatment criteria:

Must be treated by a specialist respiratory physician with expertise in cystic fibrosis or in consultation with a specialist respiratory physician with expertise in cystic fibrosis if attendance is not possible due to geographic isolation, AND

Must be treated in a centre with expertise in cystic fibrosis or in consultation with a centre with expertise in cystic fibrosis if attendance is not possible due to geographic isolation.

Clinical criteria:

Patient must have at least one mutation in the CFTR gene that is considered responsive to elexacaftor/tezacaftor/ivacaftor potentiation based on clinical and/or in vitro assay data, AND

The treatment must be given concomitantly with standard therapy for this condition, AND

Patient must have either chronic sinopulmonary disease or gastrointestinal and nutritional abnormalities, prior to initiating treatment with this drug.

Population criteria (different strengths are listed as separate PBS item codes for the following population criteria):

Patient must be 2 to 5 years of age.

Patient must be aged between 2 and 11 years inclusive.

Patient must be at least 6 years of age.

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

Date of listing on PBS

Table 4: Date of PBS listing of CFTR modulators

Medicine	Listed on the PBS
Ivacaftor	1 December 2014
LUM/IVA	1 October 2018
TEZ/IVA	1 December 2019
ELX/TEZ/IVA	1 April 2022

Changes to listing

Table 5: Changes to PBS listings of CFTR modulators

Drug name	Date	Change
Ivacaftor	1 December 2014	PBS listed for patients with G551D mutation in the CFTR gene on at least 1 allele who are 6 years of age or older.
Ivacaftor	1 May 2017	Restriction extended to patients 2 years of age or older.

Drug name	Date	Change
LUM/IVA	1 October 2018	PBS listed for patients homozygous for the F508del mutation in the CFTR gene who are 6 years of age or older.
Ivacaftor	1 August 2019	Sachets PBS listed for patients aged 12 months of age or older.
LUM/IVA	1 December 2019	Sachets PBS listed for patients aged 2 years of age or older.
TEZ/IVA	1 December 2019	PBS listed for patients homozygous for the F508del mutation or one residual function (RF) mutation who are 12 years of age or older.
ELX/TEZ/IVA	1 April 2022	PBS listed for patients with at least one F508del mutation in the CFTR gene who are 12 years of age or older.
ELX/TEZ/IVA	1 May 2023	Restriction extended to patients aged 6 years of age or older.
LUM/IVA	1 January 2024	Restriction extended to patients aged 1 year of age or older.
Ivacaftor	1 June 2024	Restriction extended to patients with non-gating mutations and patients aged 4 months or older.
ELX/TEZ/IVA	1 August 2024	Restriction extended to patients aged 2 years of age or older.
ELX/TEZ/IVA	1 July 2025	Restriction extended to patients who have at least one mutation in the CFTR gene that is responsive to ELX/TEZ/IVA based on clinical and/or in vitro assay data.

Note: as data were extracted to the end of June 2025, the extension of ELX/TEZ/IVA to patients who have at least one mutation in the CFTR gene was not reflected in the data.

Current PBS listing details are available from the PBS website.

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

Table 6: PBAC considerations of ELX/TEZ/IVA

PBAC meeting	Submission purpose	Recommendation
March 2021	The submission requested a Section 100, Authority Required listing for ELX/TEZ/IVA for the treatment of cystic fibrosis patients aged 12 years and older who have at least one F508del mutation in the CFTR gene (F/any).	Deferred
May 2021	The submission requested a Section 100, Authority Required listing for ELX/TEZ/IVA for the treatment of cystic fibrosis patients aged 12 years and older who have at least one F508del mutation in the CFTR gene (F/any), including a separate subgroup of patients, those with a F/R117H genotype, which had previously been included in the F/not yet characterised subgroup.	Deferred
July 2021	The submission requested a Section 100, Authority Required listing for ELX/TEZ/IVA for the treatment of cystic fibrosis patients aged 12 years and older who have at least one F508del mutation in the CFTR (F/any).	Recommended ELX/TEZ/IVA for the treatment of cystic fibrosis patients aged 12 years and older who have one F508del mutation and one minimal

PBAC meeting	Submission purpose	Recommendation
		function mutation in the CFTR gene (F/MF population). Did not make a recommendation for listing for the broader population of cystic fibrosis patients aged 12 years and older who have at least one F508del mutation in the CFTR gene (F/any population).
December 2021	The early re-entry resubmission sought listing of ELX/TEZ/IVA for the treatment of cystic fibrosis patients aged 12 years and older who have at least one F508del mutation in the CFTR (F/any population).	Recommended
November 2022	The submission requested a Section 100 (Highly Specialised Drugs Program) Authority Required listing for ELX/TEZ/IVA for the treatment of cystic fibrosis in patients who are aged 6 to 11 years CFTR gene (F/any).	Recommended
March 2023	The sponsor requested reconsideration of the financial estimates that were recommended at the November 2022 meeting.	The PBAC revised its previous advice regarding the recommendation of ELZ/TEZ/IVA for the treatment of cystic fibrosis in patients who are aged 6 to 11 years and who have at least one F508del mutation on the CFTR gene.
March 2024	The Category 2 submission requested the listing of two granule formulations of ELX/TEZ/IVA for the treatment of cystic fibrosis in patients who have at least one F508del mutation in the CFTR gene (referred to as the F/any population) to include patients aged 2 to 5 years.	Recommended
March 2025	The Category 2 submission requested an extension to the current listing of ELX/TEZ/IVA for the treatment of cystic fibrosis in patients who have at least one mutation in the CFTR gene that is responsive to ELX/TEZ/IVA based on clinical and/or in vitro assay data.	Recommended

<u>March 2021, May 2021, and July 2021</u>

At its May 2021 meeting, the PBAC noted that the submission's proposed treated patient numbers had not significantly changed compared with the March 2021 submission's proposed estimates. The PBAC recalled that it had considered the estimated number of treated patients to be overestimated and had advised that a method based on agreed

estimates for the current listings of IVA, LUM/IVA and TEZ/IVA would be an appropriate approach to estimating the size of the total treated population with ELX/TEZ/IVA.

The PBAC considered the proposal to reallocate 80% of the remaining patients classified as F/not yet characterised in the Australian Cystic Fibrosis Data Registry (ACFDR) registry to the F/MF population and 20% to the F/RF population was reasonable in the absence of any other data to support the likely subsequent characterisation.

The PBAC maintained that estimates for the F/F, F/RF and F/G groups should be based on previously agreed estimates for the listing of the available CFTR modulators on the PBS. While the PBAC acknowledged that previously agreed estimates for IVA, LUM/IVA and TEZ/IVA were based on full time equivalent patients rather than the total eligible patient pool, the PBAC was not minded to change its advice in relation to the estimated patient numbers for these patient populations noting that the current utilisation of LUM/IVA and TEZ/IVA has been lower than estimated at the time of listing. The PBAC acknowledged the use of non PBS-funded CFTR modulator therapies in clinical trials, but considered it unreasonable to assume that there will be no future participation of Australian CF patients in trials of disease-modifying therapies. The PBAC therefore considered that using an epidemiological approach was likely to overestimate uptake and that increasing the estimated treated population for these groups already eligible for CFTR modulator treatment was not sufficiently justified.

The PBAC considered that it may be reasonable for the eligible patients from those populations that are currently ineligible for PBS-listed CFTR modulator therapy (i.e. F/MF and F/R117H groups), to be estimated using an epidemiological approach with reference to the ACFDR current patient numbers. The PBAC accepted the following proposed eligible patient numbers and uptake rates for these groups, noting however that that the discontinuation rates applied in the submission (0.99% in F/MF and 0.76% for F/R117H) were extremely optimistic and likely to be higher.

This submission was deferred. Overall, the PBAC considered that the revised proposal was not aligned with the PBAC's March 2021 advice as it requested significant deviations with regard to the pricing and financial estimates. However, it deferred completion of its consideration to allow the sponsor to provide further information.

In July 2021, the PBAC recommended the listing of ELX/TEZ/IVA for the F/MF population only, who at the time did not have access to a CFTR modulator treatment through the PBS.

For further details refer to the Public Summary Document from the March 2021 PBAC Meeting with May 2021 Addendum and July 2021 Addendum.

December 2021

At its December 2021 meeting, the PBAC noted that the estimated patient numbers proposed in the resubmission were not aligned with the previous PBAC advice, which was that the F/F, F/RF and F/G groups should be based on previously agreed estimates for the listing of the available CFTR modulators on the PBS.

Instead, the resubmission proposed patient estimates that were largely unchanged from previous submissions in that the treated population was based on ACFDR data, and inconsistent with previous PBAC advice that for the populations for which there was a PBS-listed CFTR-modulator available, previously agreed patient numbers for these listings would be appropriate to inform the estimated utilisation.

The approach remained similar to the May 2021 proposal, however the resubmission made adjustments to uptake rates to the some of the populations and proposed alternate discontinuation rates for the treatment naïve populations.

In March 2021, and again in May 2021, the PBAC advised that estimates for the F/F, F/RF and F/G groups should be based on previously agreed estimates for the listing of the available CFTR modulators on the PBS. The PBAC has previously considered it may be reasonable for the eligible patients from those populations that are currently ineligible for PBS-listed CFTR modulator therapy (i.e. F/MF and F/R117H groups), to be estimated using an epidemiological approach with reference to the ACFDR current patient numbers.

As per its previous May 2021 proposal, the resubmission maintained that there are F/F, F/RF, F/G and 20% of patients not yet characterised (who would later be characterised as F/RF), who are not captured within the existing Deed calculations. The additional patients were estimated using ACFDR data, participation in Vertex compassionate access scheme and clinical trials.

The PBAC maintained that the proposed discontinuation rates based on the trial data were very optimistic. Taking into account that actual rates of discontinuation for LUM/IVA and TEZ/IVA were higher than estimated at time of listing (based on trial and extension study discontinuation rates), the PBAC considered that discontinuation rates based on applying the same proportional difference between the actual and estimated figures be applied to the ELX/TEZ/IVA studies – this would result in discontinuation rates of 2.6% at Year 1 and 7.3% at Year 2. The PBAC considered that the eligible patient estimates outlined in the resubmission could be accepted, in the context that: they represented the upper range of likely use based on the total eligible patients derived from the ACFDR numbers; and the sponsor had proposed a unit level rebate to achieve the cost-effective price, as opposed to an arrangement that relied on the estimates being realised in order to achieve a cost-effective price per patient (as for LUM/IVA and TEZ/IVA).

For further details refer to the Public Summary Document from the December 2021 PBAC meeting.

November 2022

The November 2022 submission used two approaches to estimate the number of eligible patients: (1) the number of patients who are currently eligible for PBS listed CFTR modulators were estimated from the subsidisation caps in existing Deeds and (2) the number of patients who are not currently eligible for PBS listed CFTRs were estimated from epidemiological data.

The PBAC considered the methodology for estimating the number of patients likely to be treated with ELX/TEZ/IVA was reasonable; however, the patient numbers were overestimated due to a number of optimistic assumptions which were not well supported. The PBAC advised a number of assumptions, including the discontinuation rates and uptake/switch rates, should be amended to be consistent with what was accepted for the ≥12 year population. The PBAC further advised it would be appropriate to assume 90% compliance consistent with that used in the economic model.

As part of the post-PBAC process, the sponsor provided a pricing proposal that was not consistent with the PSD as it did not change the assumptions applied to the financial estimates as advised. As the listing was unable to be progressed with financial estimates that were not consistent with the PSD, the sponsor requested consideration by the PBAC at its March 2023 meeting. The sponsor stated it did not consider the assumptions applied were overly optimistic and provided additional information to support the assumptions applied in the financial estimates.

The PBAC noted the financial estimates proposed by the sponsor assumed an overall uptake of 96% in eligible patients in Year 1, compared to approximately 80% in Year 1 if the uptake rates advised by the PBAC in November 2022 were applied.

The PBAC noted the experience in overseas' markets where ELX/TEZ/IVA is reimbursed in patients aged 6 to 11 years and the high and rapid uptake in the 12 years and older population in Australia since PBS listing in April 2022. The PBAC considered that the experience of CF clinics gained in treating the population of patients 12 years and older would facilitate rapid initiation of patients aged 6 to 11 years.

The PBAC noted some additional clinical data in patients aged 6 to 11 years was provided to support the use of the discontinuation rates applied in the financial estimates (1.4% in Year 1, 4.2% in Year 2).

The PBAC considered that, overall, based on the additional information provided by the sponsor, it was reasonable for the assumptions informing the financial estimates for the population aged 6 to 11 years to be different to those informing the population aged 12 years and over as it was likely uptake would be higher and more rapid than initially predicted for the older age group.

For further details refer to the Public Summary Document from the November 2022 PBAC Meeting with March 2023 Addendum.

March 2024

The submission presented an epidemiological approach to the financial estimates of ELX/TEZ/IVA in F/any patients aged 2 to 5 years who have at least one F508del mutation in the CFTR gene. The approach used in developing the estimates was similar to that presented to the PBAC at the November 2022 meeting for the PBS listing of ELX/TEZ/IVA in the ≥6 years population. Eligible populations were estimated separately according to three groups: those eligible for use under the existing Deeds including F/F and F/G patients; those ineligible for use under the existing Deeds including F/MF, F/RF, and F/R117H patients; and

those eligible for use under the existing Deeds but not currently on treatment i.e., CFTR naïve F/F patients and grandfathering patients.

For further details refer to the Public Summary Document from the March 2024 PBAC Meeting.

Previous reviews by the DUSC

Previous DUSC reviews of medicines for cystic fibrosis include:

- Dornase alfa and mannitol October 2014.
- Tobramycin October 2014.
- Ivacaftor February 2018.

For details of the DUSC consideration of previous DUSC reviews for cystic fibrosis medicines refer to the Public Release Document.

Methods

Data extracted from the PBS claims database maintained by the Department of Health, Disability and Ageing and processed by Services Australia were used for the analyses. Prescription data were extracted on 7 July 2025 from the date the first CFTR was listed on the PBS, 1 December 2014, up to and including 30 June 2025 for the main analyses, and on 6 August 2025 to 31 July 2025 for one predicted versus actual analysis.

Date of death data were linked to the PBS claims data using the unique patient identifier. Date of death data were last updated 19 February 2025.

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.[6] The publicly available Services Australia Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included.

These data were used to determine the number of initiating and prevalent patients, number of prescriptions supplied, and to analyse patient demographics such as age and gender. Initiating and prevalent patients were counted by calendar year. Prevalent patients were defined as the number of patients who received at least one supply of any CFTR modulator in the given calendar year. Initiating patients were defined as the number of patients who received their first supply of a CFTR modulator. Patient age at initiation was determined by the age of the patient at the first supply of a CFTR modulator. For age and gender analyses of treated patients, the age of the patient at their first supply during the time period was used, to ensure patients were not counted in more than one age group.

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

An analysis of sequence of medicine use was conducted for ELX/TEZ/IVA patients, using data from the listing of the first CFTR in 2014. This was presented excluding and including 'switchbacks' to previous medicines.

Treatment duration was analysed using the Kaplan-Meier method. A patient was censored if they were supplied a prescription within three times the median time to resupply (29 days) prior to 30 June 2025 (i.e. 3×29 days).

Analyses were undertaken in SAS.

Results

Analysis of drug utilisation

Overall utilisation

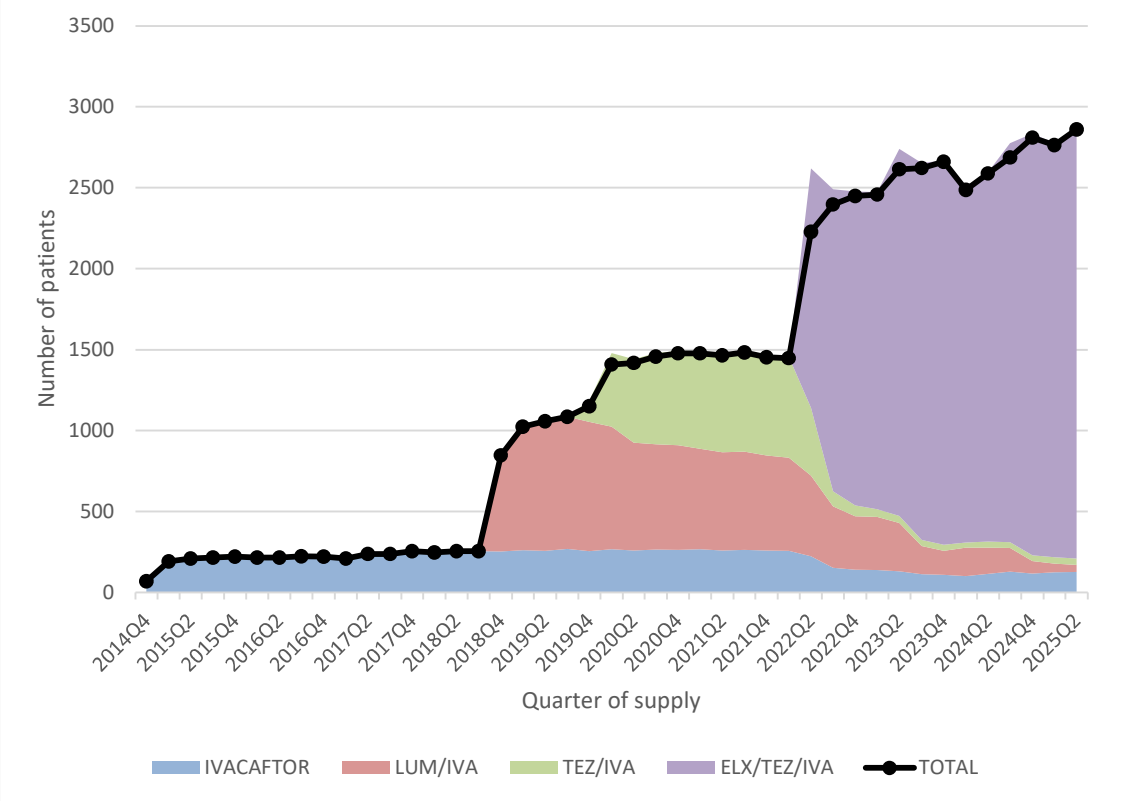

Figure 1: Number of treated patients by drug

Figure 1 shows the number of treated patients by the quarter of supply. The overall total is lower than suggested by the counts by drug because it shows the number of unique patients. In quarters when new drugs were listed and patients switched from one therapy to another, these patients were counted twice for each drug.

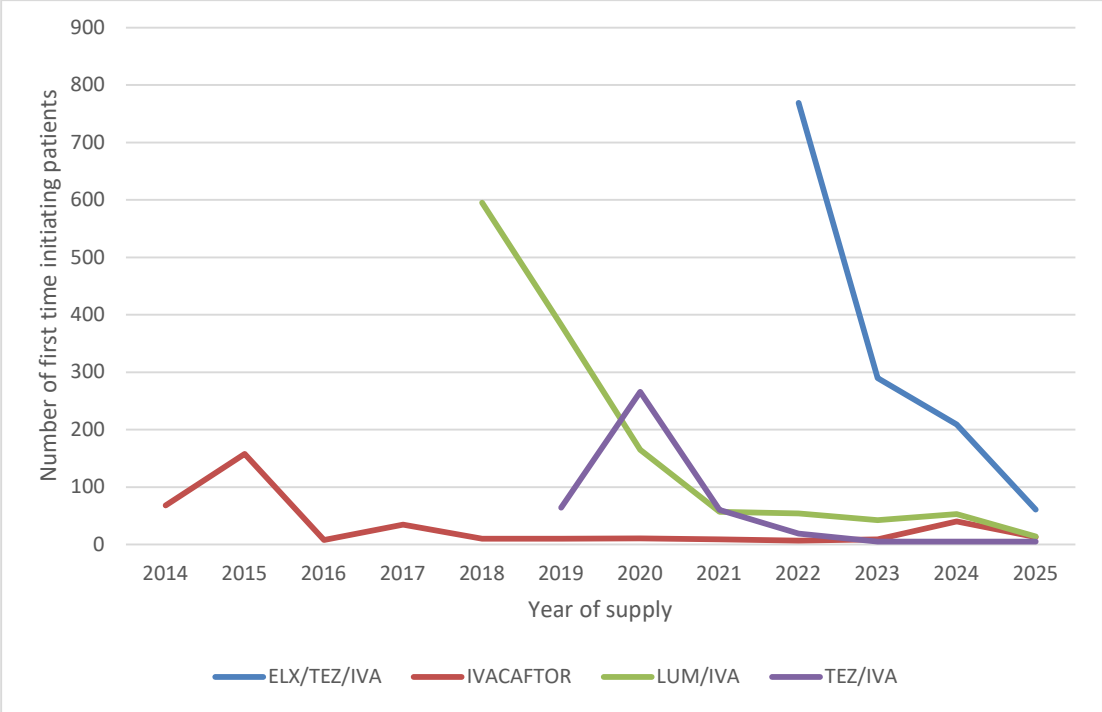

Figure 2: Number of first time initiating patients over time by drug

Note: Patient counts smaller than 5 are shown as 5 to reduce the risk of patient re-identification.

Since its listing in 2022, the majority of first time initiating patients have commenced CFTR treatment with ELX/TEZ/IVA. There was a small increase in the number of patients initiating on ivacaftor and LUM/IVA in 2024, likely because of the extensions to listing to patients aged 1 year of age or older (LUM/IVA) and to patients with non-gating mutations and patients aged 4 months or older (ivacaftor) on 1 January 2024 and 1 June 2024 respectively.

The majority of supplied prescriptions since the second quarter of 2022 have been for ELX/TEZ/IVA (Figure 3). In 2024, 27,089 of the 30,208 supplied CFTR prescriptions were for ELX/TEZ/IVA. It appears that most patients who were supplied ivacaftor or TEZ/IVA prior to the listing of ELX/TEZ/IVA switched immediately, however some patients continued on LUM/IVA after the listing of ELX/TEZ/IVA.

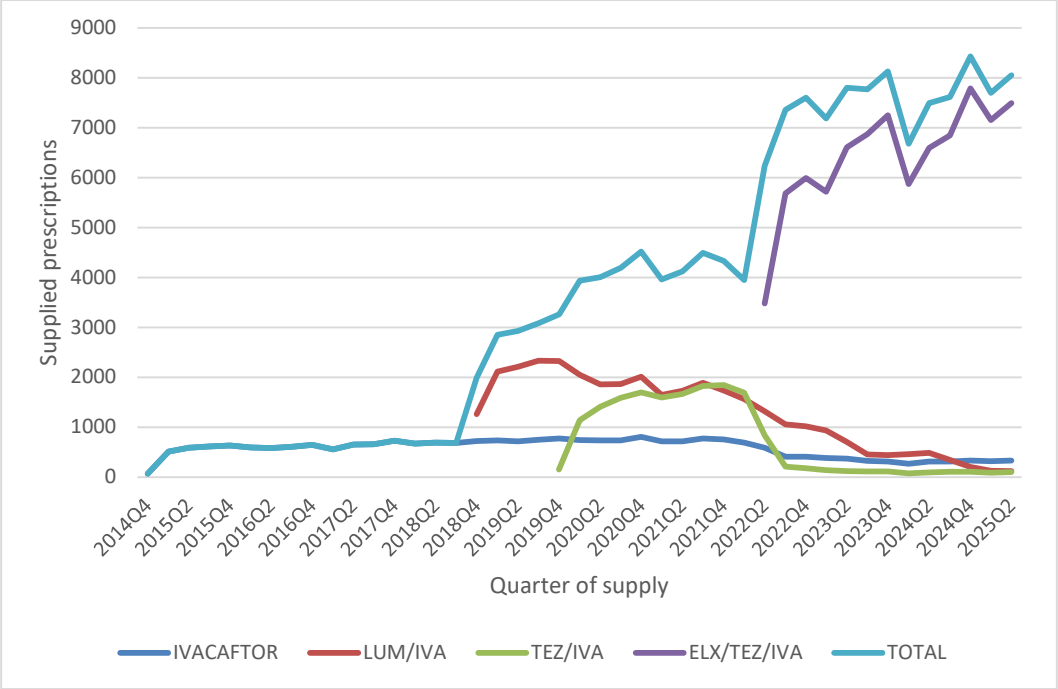

Figure 3: Number of supplied prescriptions over time by drug

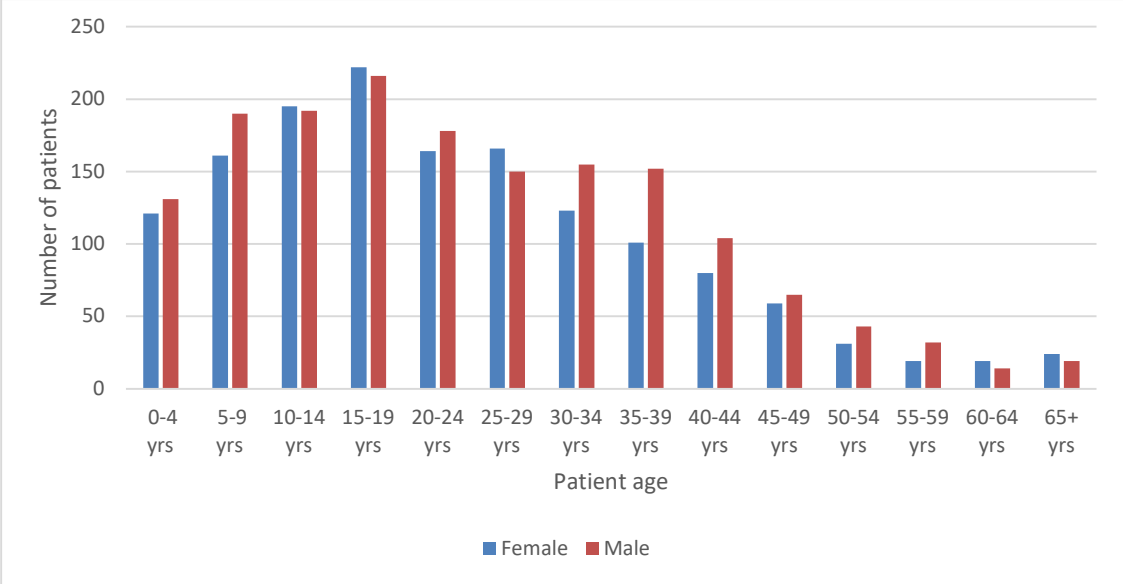

Figure 4: Age of patients treated in 2024

The mean age of patients supplied CFTR modulators in 2024 was 24 years, and the median age was 21 years. The mean age of patients supplied ELX/TEZ/IVA in 2024 was also 24 years, and the median age was 21 years.

In 2024, 209 (68%) of the 307 initiating patients were supplied ELX/TEZ/IVA on the initiating prescription. Of the remaining patients, 58% (59 of 102) were under the age of 2 and therefore not eligible for ELX/TEZ/IVA. It is likely that the majority of the remaining patients who initiated ivacaftor in 2024 became eligible for it on 1 June 2024 when the PBS restriction was extended to patients with non-gating mutations.

Table 7: Age of initiating patients in 2024

	0-1 yrs	2-5 yrs	6-11 yrs	12+ yrs	Total
ELX/TEZ/IVA		104	29	76	209
IVACAFTOR	11	<5	<5	24	40
LUM/IVA	48	5			53
TEZ/IVA				5	5
Total	59	110-113	30-33	105	307

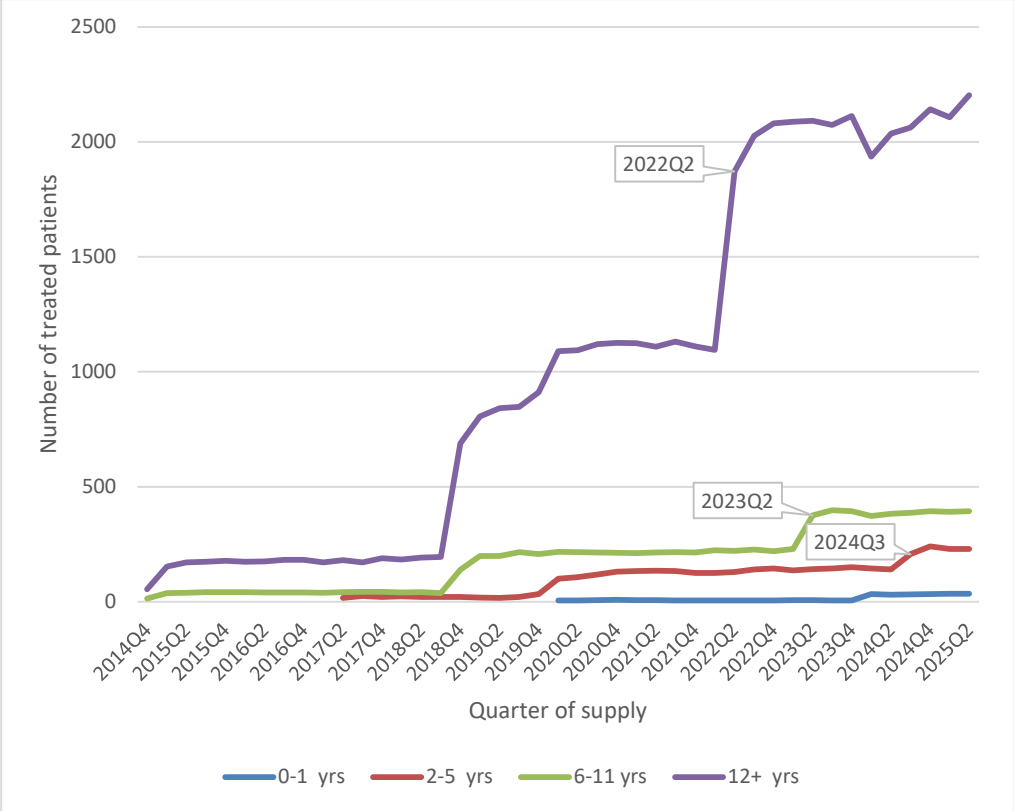

Figure 5: Age of treated patients over time for all CFTRs

Figure 5 shows the number of patients supplied all CFTRs over time, grouped by age eligibility. There was a clear increase in the number of patients aged 12 years and older when ELX/TEZ/IVA listed in the second quarter of 2022, and smaller increases in the number of patients in the 6-11 year group and 2-5 year group when it was listed for these age groups in the second quarter of 2023 and the third quarter of 2024 respectively. These

patients may have been supplied ELX/TEZ/IVA through a clinical trial or compassionate access scheme prior to its listing on the PBS. Appropriately, zero prescriptions of ELX/TEZ/IVA were supplied to patients aged 2 to 5 years old or 6 to 11 years old prior to its PBS listing for these age groups.

Table 8: Medicine sequence for ELX/TEZ/IVA patients excluding switchbacks

Sequence	Patient count
ELX/TEZ/IVA	1,320
LUM/IVA > ELX/TEZ/IVA	830
LUM/IVA > TEZ/IVA > ELX/TEZ/IVA	448
TEZ/IVA > ELX/TEZ/IVA	369
IVACAFTOR > ELX/TEZ/IVA	227
ELX/TEZ/IVA > IVACAFTOR	7
OTHER	8

Table 8 shows the CFTR medicine sequence for patients who were supplied ELX/TEZ/IVA, excluding switchbacks to previous medicines. Table 9 shows the CFTR medicine sequence for patients who were supplied ELX/TEZ/IVA, including switchbacks to previous medicines. Of the patients who were supplied ELX/TEZ/IVA, 41% (1,320/3209) were only supplied ELX/TEZ/IVA.

Table 9: Medicine sequence for ELX/TEZ/IVA patients including switchbacks

Sequence	Patient count
ELX/TEZ/IVA	1,320
LUM/IVA > ELX/TEZ/IVA	783
LUM/IVA > TEZ/IVA > ELX/TEZ/IVA	408
TEZ/IVA > ELX/TEZ/IVA	355
IVACAFTOR > ELX/TEZ/IVA	207
LUM/IVA > ELX/TEZ/IVA > LUM/IVA > ELX/TEZ/IVA	28
LUM/IVA > TEZ/IVA > LUM/IVA > ELX/TEZ/IVA	16
LUM/IVA > ELX/TEZ/IVA > LUM/IVA	16
IVACAFTOR > ELX/TEZ/IVA > IVACAFTOR	10
LUM/IVA > TEZ/IVA > ELX/TEZ/IVA > TEZ/IVA > ELX/TEZ/IVA	8
LUM/IVA > TEZ/IVA > LUM/IVA > TEZ/IVA > ELX/TEZ/IVA	7
TEZ/IVA > ELX/TEZ/IVA > TEZ/IVA	7
IVACAFTOR > ELX/TEZ/IVA > IVACAFTOR > ELX/TEZ/IVA	6
ELX/TEZ/IVA > IVACAFTOR	6
TEZ/IVA > ELX/TEZ/IVA > TEZ/IVA > ELX/TEZ/IVA	6
OTHER	26

Patients not supplied ELX/TEZ/IVA

Of the 271 patients who were never supplied ELX/TEZ/IVA, 188 were supplied another CFTR between 1 July 2024 and 30 June 2025 inclusive. Figure 6 below shows the age and gender breakdown for these patients using the patient's age at the first supplied prescription during this 12 month period. Of these patients, 20% (38) were younger than 2. The mean age of these patients was 25.3 and the median age was 24 years old. As the PBS restriction for ELX/TEZ/IVA was extended to patients who have at least one mutation in the CFTR gene that is responsive to ELX/TEZ/IVA based on clinical and/or in vitro assay data on 1 July 2025, the number of older patients supplied CFTRs other than ELX/TEZ/IVA may decrease in the future.

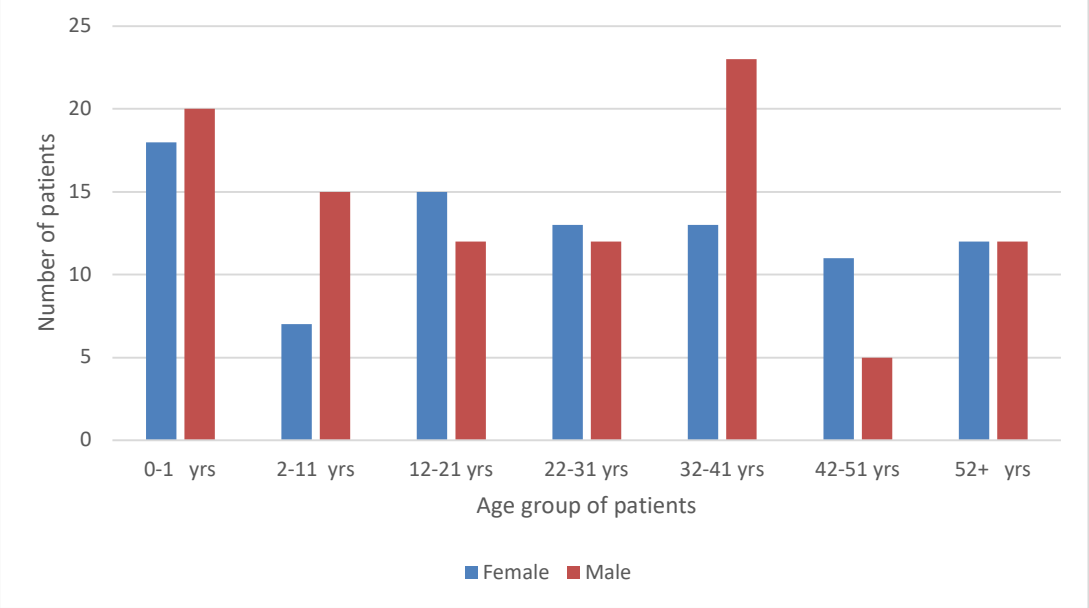

Figure 6: Age and gender of patients not supplied ELX/TEZ/IVA July 2024 to June 2025

Of the 188 patients who were supplied a CFTR other than ELX/TEZ/IVA between 1 July 2024 and 30 June 2025, all 188 patients were only supplied one drug. The mean number of supplies in this 12 month period was 8.2, and the median was 9. Approximately 35% of these patients were supplied a CFTR for the first time during this time period (Table 10).

Table 10: CFTR patients not supplied ELX/TEZ/IVA July 2024 to June 2025

Drug name	Patient count	Patients whose first initiation was between July 2024 to June 2025	Percent of treated
IVACAFTOR	131	41	31%
LUMACAFTOR + IVACAFTOR	29	24	83%
TEZACAFTOR + IVACAFTOR (&) IVACAFTOR	28	<5	4% - 14%
Total	188	66-69	35% - 37%

Length of treatment

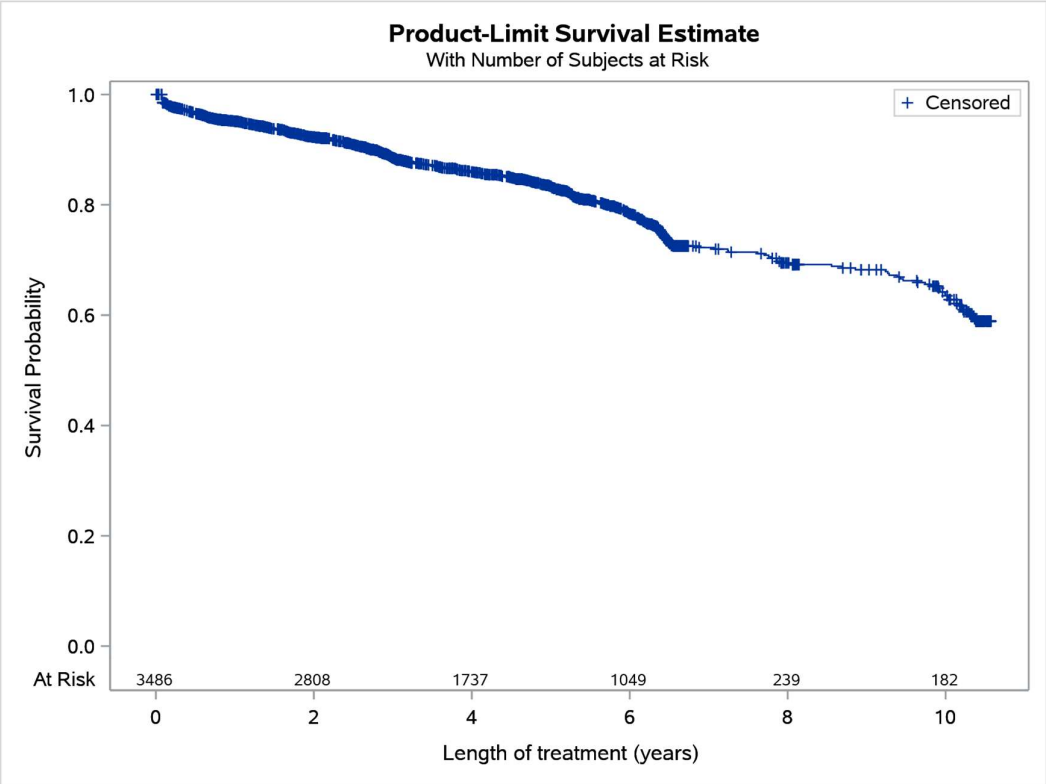

Figure 7: Kaplan Meier estimate of length of treatment

Table 11: Kaplan Meier length of treatment quartile estimates in years for all CFTR modulators

Percent	Point estimate	95% Confidence Interval		
		Transform	Lower	Upper
75	.	LOGLOG	.	.
50	.	LOGLOG	.	.
25	6.4000	LOGLOG	6.1890	6.5123

Table 12: Kaplan Meier mean length of treatment estimate in years for all CFTR modulators

Mean	Standard error
8.3868	0.0700

For the estimates of length of overall treatment by initial drug, the mean survival time and its standard error were underestimated because the largest observation was censored (the patient had not stopped treatment at the end of the data collection period) and the

estimation was restricted to the largest event time. A median length of treatment was not reached for any drug.

Of the 3,486 patients who had initiated CFTR modulators, 40 patients (1.15%) had a date of death recorded in the date of death data, including 6 patients who died in 2024.

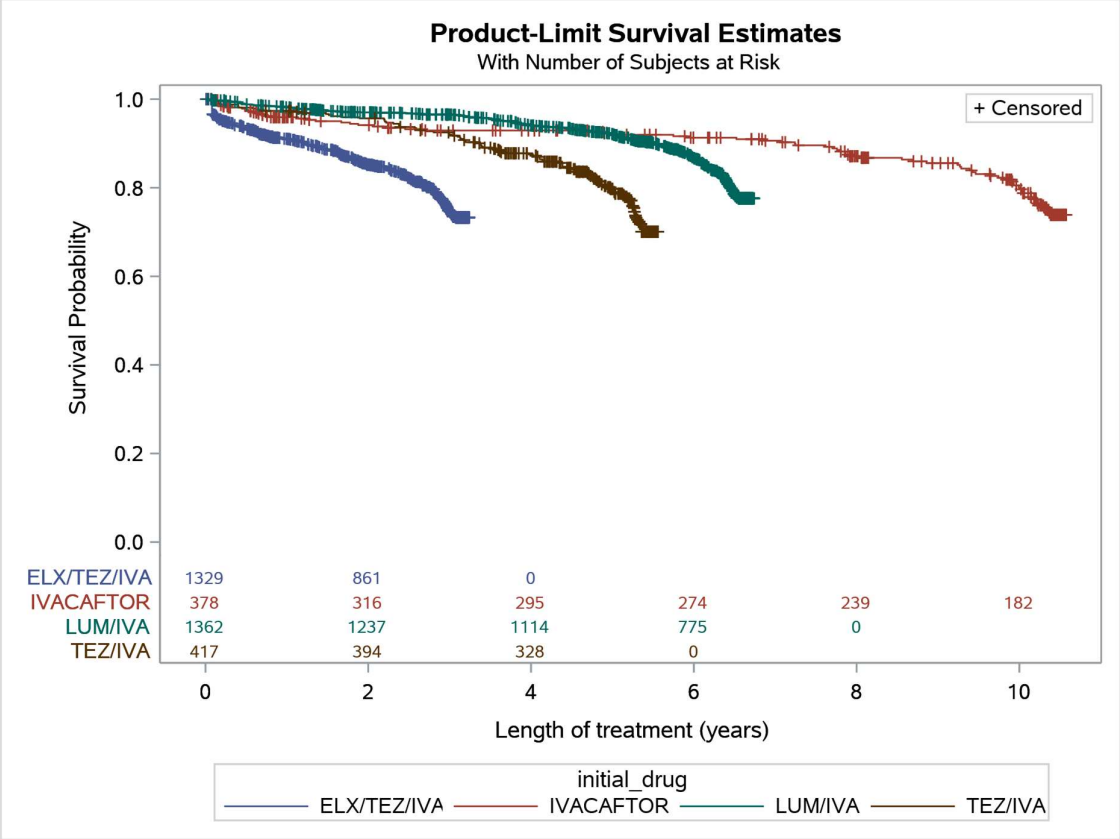

Figure 8: Kaplan Meier estimate of length of treatment by initial drug

Table 13: Kaplan Meier median and mean length of treatment estimate in years by drug

	Estimated mean	Standard error
ELX/TEZ/IVA	2.6929	0.0241
IVACAFTOR	9.4327	0.1352
LUM/IVA	6.1681	0.0318
TEZ/IVA	4.8938	0.0554

Analysis of actual versus predicted utilisation

Patients aged 12 years and older

Approach taken to estimate utilisation

In May 2021, the PBAC considered that it may be reasonable for the eligible F/MF patients, who do not currently have access to a CFTR-modulator treatment through the PBS, to be estimated using an epidemiological approach with reference to the ACFDR current patient numbers. The PBAC previously accepted the following proposed eligible patient numbers and uptake rates for these groups, however recommended that discontinuation rates consistent with those applied to the PBS listing of LUM/IVA should apply. Departmental analysis of the discontinuation rate of LUM/IVA and TEZ/IVA over the first two years of listing of each product indicated higher rates of discontinuation at Year 1 and 2 than estimated at time of listing (13.4% and 11.8% in Year 1 and 25.4% and 26.4% in Year 2 for LUM/IVA and TEZ/IVA respectively).

- F/MF: 630 patients in Year 1 increasing to 684 patients in Year 6, before uptake (90% in Year 1 increasing to 95% from Year 2 onwards) and discontinuation rates (6.8% at Year 1 and 14.9% at Year 2) are applied.
- The Department's modelling of the impact of the uptake and discontinuation rates resulted in treated patient numbers of approximately 472 patients in Year 1 increasing to 485 in Year 6.

The PBAC (July 2021) noted that the above patient numbers included reallocation of 80% of patients classified as F/not yet characterised in the ACFDR registry to the F/MF population.

The December 2021 resubmission proposed patient estimates based on ACFDR data, which was inconsistent with previous PBAC advice that for the populations for which there was a PBS-listed CFTR-modulator available, previously agreed patient numbers for these listings would be appropriate to inform the estimated utilisation.

Table 14: Financial implications of listing ELX/TEZ/IVA on the PBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
December 2021 resubmission						
Total FTE patients receiving ELX/TEZ/IVA	1,732	1,888	1,903	1,937	1,971	2,006
Total number of ELX/TEZ/IVA packs dispensed	20,324	22,161	22,332	22,736	23,145	23,559
March 2021 pre-PBAC response						
Total FTE patients receiving ELX/TEZ/IVA	1,980	2,034	2,067	2,101	2,134	2,167
May 2021 proposal						
Total FTE patients receiving ELX/TEZ/IVA	1,896	2,017	2,076	2,116	2,153	2,189
Department estimates based on May 2021 PBAC advice						
Total FTE patients receiving ELX/TEZ/IVA	1,217	1,286	1,268	1,258	1,250	1,242

The PBAC considered that the eligible patient estimates outlined in the resubmission could be accepted, in the context that: they represented the upper range of likely use based on the total eligible patients derived from the ACFDR numbers; and the sponsor had proposed a unit level rebate to achieve the cost-effective price, as opposed to an arrangement that relied on the estimates being realised in order to achieve a cost-effective price per patient (as for LUM/IVA and TEZ/IVA).

Predicted versus actual utilisation

Table 15: Predicted versus actual utilisation of ELX/TEZ/IVA for patients aged 12+

		Year 1 April 2022 to March 2023	Year 2 April 2023 to March 2024	Year 3 April 2024 to March 2025	Year 4 April 2025 to March 2026
Patients switching from other CFTR modulators	Predicted	951	996	1,015	1,034
	Actual	1,351	1,382	1,388	1,247
	Difference	+42%	+39%	+37%	+21%
Patients new to CFTR modulators	Predicted	779	962	951	965
	Actual	808	851	921	824
	Difference	+4%	-12%	-3%	-15%
Total patients	Predicted	1,730	1,959	1,966	1,999
	Actual	2,159	2,233	2,309	2,071
	Difference	+25%	+14%	+17%	+4%
Prescriptions	Predicted	20,314	22,990	23,073	23,073
	Actual	20,874	22,666	22,252	5,726
	Difference	+3%	-1%	-4%	-75%

Note: the actual figures for Year 4 represent three months of data, from April to June 2025 inclusive.

The number of treated patients aged 12 years or older was underestimated. It appears that the number of patients new to CFTR modulators was approximately accurate or overestimated, however the number of patients who switched from other CFTR modulators to ELX/TEZ/IVA was substantially underestimated. Overall, the number of treated patients was underestimated by 14 to 25 percent in the first three years of listing. The estimated number of supplied prescriptions was approximately correct, within 4%, in the first three years of listing.

Patients aged 6 to 11 years old

Approach taken to estimate utilisation

The submission used two approaches to estimate the number of eligible patients: (1) the number of patients who are currently eligible for PBS listed CFTR modulators were estimated from the subsidisation caps in existing Deeds and (2) the number of patients who are not currently eligible for PBS listed CFTRs were estimated from epidemiological data.

Table 16: Estimation of number of treated patients

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Patients included within the subsidisation caps under existing Deeds (calculated from subsidisation caps in existing Deed)						
Estimated number of F/F patients on LUM/IVA[a]	182	185	188	192	195	198
F/F patients on LUM/IVA switching to ELX/TEZ/IVA (100% switch)	182	185	188	192	195	198
Estimated number of F/G patients on IVA[b]	40	41	42	44	45	46
F/G patients on IVA switching to ELX/TEZ/IVA (100% switch)	40	41	42	44	45	46
Total treated population	222	226	230	236	240	244
Patients not currently eligible for PBS-reimbursed CFTR modulators (using epidemiological approach)						
F/MF prevalent population	164	166	169	171	174	177
Treated F/MF patients (98% uptake and applying discontinuation rates[c])	158	156	155	158	160	162
F/RF population	43	43	44	45	45	46
Treated F/RF patients (80% uptake and applying discontinuation rates[c])	34	33	33	34	34	35
F/F117H population	29	30	30	31	31	32
Treated F/R117H patients (80% uptake and applying discontinuation rates[c])	23	23	23	23	23	24
Total treated population	215	212	211	215	217	221
F/F patients not captured in the Deed calculations						
Total F/F not captured in the Deeds	82	83	83	84	85	85
Treated F/F not captured in the Deeds (98% uptake and applying discontinuation rates of 1.4% in Yr 1, 4.2% in Yr 2	80	79	78	79	79	80
Total all subpopulations treated with ELX/TEZ/IVA	517	517	519	528	537	545

At its March 2023 meeting, the PBAC noted the financial estimates proposed by the sponsor assumed an overall uptake of 96% in eligible patients in Year 1, compared to approximately 80% in Year 1 if the uptake rates advised by the PBAC in November 2022 were applied, and noted some additional clinical data in patients aged 6 to 11 years was provided to support the use of the discontinuation rates applied in the financial estimates. The PBAC considered that, overall, based on the additional information provided by the sponsor, it was reasonable for the assumptions informing the financial estimates for the population aged 6 to 11 years to be different to those informing the population aged 12 years and over as it was likely uptake would be higher and more rapid than initially predicted for the older age group.

Predicted versus actual utilisation

Table 17: Predicted versus actual utilisation of ELX/TEZ/IVA for patients aged 6-11

		Year 1 May 2023 to April 2024	Year 2 May 2024 to April 2025	Year 3 May 2025 to April 2026
Patients switching from other CFTRs	Predicted	223	227	232
	Actual	262	260	197
	Difference	+17%	+15%	-15%
Patients new to CFTRs	Predicted	293	290	290
	Actual	197	195	145
	Difference	-33%	-33%	-50%
Total patients	Predicted	517	517	522
	Actual	459	455	342
	Difference	-11%	-12%	-34%
Prescriptions	Predicted	6,404	6,417	6,472
	Actual	4,324	4,485	759
	Difference	-32%	-30%	-88%

Note: the actual figures for Year 3 represent two months of data, from May to June 2025 inclusive

In the first two years of listing of ELX/TEZ/IVA for patients aged 6 to 11 years old, the number of treated patients was underestimated. It appears that the number of patients new to CFTR modulators was overestimated by 33% in both year 1 and year 2, however the number of patients who switched from other CFTR modulators to ELX/TEZ/IVA was underestimated by 15% to 17%. Overall, the number of treated patients was overestimated by 11% to 12% in the first two years of listing.

In both of these complete years of listing, the number of supplied prescriptions was overestimated, by 30% to 32%. One reason for this may be an overestimate of the requirements of weight based dosing in these age groups.

Patients aged 2 to 5 years old

Approach taken to estimate utilisation

The submission presented an epidemiological approach to the financial estimates of ELX/TEZ/IVA in F/any patients aged 2 to 5 years who have at least one F508del mutation in the CFTR gene. The approach used in developing the estimates was similar to that presented to the PBAC at the November 2022 meeting for the PBS listing of ELX/TEZ/IVA in the ≥6 years population. Eligible populations were estimated separately according to three groups: those eligible for use under the existing Deeds including F/F and F/G patients; those ineligible for use under the existing Deeds including F/MF, F/RF, and F/R117H patients; and those eligible for use under the existing Deeds but not currently on treatment i.e., CFTR naïve F/F patients and grandfathering patients.

The submission used the same inputs, including uptake/switching rates, discontinuation, and compliance, as accepted for the 6 to 11 years submission.

Predicted versus actual utilisation

Table 18: Predicted versus actual utilisation of ELX/TEZ/IVA for patients aged 2 to 5

		Year 1 August 2024 to July 2025
Patients switching from other CFTRs	Predicted	99
	Actual	165
	Difference	+67%
Patients new to CFTRs	Predicted	205
	Actual	131
	Difference	-36%
Total patients	Predicted	304
	Actual	296
	Difference	-3%
Prescriptions	Predicted	3,480
	Actual	2,520
	Difference	-28%

In the first year of listing for patients aged 2 to 5 years old, the number of treated patients was approximately correct (Table 16). The number of patients new to CFTR modulators was overestimated by 36%, however the number of patients who switched from other CFTR modulators to ELX/TEZ/IVA was underestimated by 67%. The number of supplied prescriptions was overestimated by 28%. One reason for this may be an overestimate of the requirements of weight based dosing in these age groups.

Discussion

Since PBS listing on 1 April 2022, ELX/TEZ/IVA has become the most utilised of CFTR modulators, in terms of the number of prescriptions supplied, and the number of treated and initiating patients. In 2024, 90% of the supplied prescriptions of CFTR modulators were ELX/TEZ/IVA and 88% of patients supplied a CFTR modulator were supplied ELX/TEZ/IVA.

Of the 3,486 patients who were supplied a CFTR modulator during the data collection period (to 30 June 2025), 3,209 (92%) have been supplied ELX/TEZ/IVA, including 1,320 who have only been supplied ELX/TEZ/IVA.

The majority of patients who were supplied CFTR modulators prior to its listing and have continued treatment, have switched to ELX/TEZ/IVA. Of the 1,646 patients supplied a CFTR modulator in the 12 months prior to ELX/TEZ/IVA listing (April 2021 to March 2022 inclusive), 1,610 (98%) were supplied a CFTR between April 2022 and March 2023. Of these 1,610 patients, 1,153 (70%) were supplied ELX/TEZ/IVA.

The majority of new patients are being initiated on ELX/TEZ/IVA. In 2024, 68% of the 307 patients who initiated were supplied ELX/TEZ/IVA on the initiating prescription. It is likely that the majority of patients who did not initiate on ELX/TEZ/IVA were ineligible for ELX/TEZ/IVA.

Of the patients who did not switch to ELX/TEZ/IVA during the data collection period, prior to 1 July 2025, 20% were aged younger than two. The trends in switching in older age groups suggest many of these patients likely switched to ELX/TEZ/IVA once it was PBS listed for patients aged younger than two, on 1 July 2025. Some of the patients older than two years who have not switched or initiated on another CFTR modulator may have a non-gating mutation and only currently be eligible for ivacaftor, or may not have switched for other unknown reasons.

Although the median duration of treatment could not be estimated, the duration of treatment for these medicines is likely to be long. The mortality of patients treated with CFTR modulators in Australia is relatively low. Of the patients supplied CFTR modulators during the data collection period, 1.15% (40 of 3,486) had a date of death recorded in the date of death data.

As the mean age of patients supplied CFTR modulators in 2024 was 24 years, and as PBS restrictions are expanded to younger populations, younger patients are initiating therapy. Until newer therapies are listed for cystic fibrosis, it is likely that a growing number of patients will remain on CFTR modulators, particularly ELX/TEZ/IVA, over the long term.

DUSC consideration

DUSC noted the graph of the number of treated patients by drug and quarter of supply showed that most patients who were supplied ivacaftor or TEZ/IVA prior to the listing of ELX/TEZ/IVA switched immediately, however some patients continued on LUM/IVA after the listing of ELX/TEZ/IVA. Similarly, DUSC noted that since its listing in 2022, the majority of first time initiating patients have commenced CFTR treatment with ELX/TEZ/IVA. DUSC commented that the different age groups were able to access the different medicines at different times, and noted the corresponding increases in patients of different age groups when ELX/TEZ/IVA was listed for these age groups. DUSC commented that the use of ELX/TEZ/IVA now dominates the market of CFTR modulators.

DUSC commented that the uptake of ELX/TEZ/IVA was high and immediate, and commented CF patients and families are a motivated patient population, and that clinics and patients were aware that ELX/TEZ/IVA would be available through the PBS prior to its listing. DUSC commented that the rapid uptake should inform future estimated uptake rates, particularly in other rare conditions with motivated and engaged patient populations.

DUSC noted the mean age of patients supplied CFTR modulators in 2024 was 24 years, and the median age was 21 years. DUSC commented that although the most commonly treated age group was 15-19, there were there 509 patients aged 40 years or older who were supplied CFTR modulators in 2024. DUSC noted there have been reports of patients with atypical presentations of CF, such as gastrointestinal disease and infertility, who were born before the introduction of newborn screening for CF, diagnosed as adults.[7]

DUSC noted the analysis of the 188 patients who were never supplied ELX/TEZ/IVA and who were supplied a CFTR modulator other than ELX/TEZ/IVA between 1 July 2024 and 30 June 2025 inclusive. DUSC agreed that the 20% of those patients who were younger than 2 were likely not eligible for ELX/TEZ/IVA during this time period, and agreed eligible older patients would have likely switched to ELX/TEZ/IVA when its PBS listing was extended to patients who have at least one mutation in the CFTR gene that is responsive to ELX/TEZ/IVA based on clinical and/or in vitro assay data on 1 July 2025. DUSC questioned whether there was a group of patients not supplied ELX/TEZ/IVA due to adverse effects, and noted the consumer comments mentioned that there is a very small cohort of patients who are not responding to this drug combination.

DUSC noted the predicted versus actual review of patients aged 12 and older showed the patient numbers were underestimated, but the number of prescriptions was approximately correct in the first three years of listing. DUSC noted the predicted versus actual reviews of patients aged 2 to 5 years and 6 to 11 years old showed the number of patients was approximately correct, but the number of prescriptions were overestimated. DUSC agreed these differences were likely due an overestimate of the requirements of weight based dosing in these age groups. DUSC commented that untreated patients were likely to be underweight, and that as patients become older and healthier their weight will increase as they grow, and their required doses are therefore likely to increase.

DUSC noted the treatment duration presented in the report but commented that as the overall median treatment duration had not been reached, it cannot reliably be determined from the data available. DUSC noted a publication which estimated survival statistics from the Australian Cystic Fibrosis Data Registry (ACFDR) data. The estimated median survival increased from 48.9 years (95% CI: 44.7–53.5) for people with CF born in 2005–2009, to 56.3 years (95% CI: 51.2–60.4) for those born in 2016–2020.[8] DUSC commented that life expectancy has increased substantially and agreed that until newer therapies are listed for cystic fibrosis, it is likely that a growing number of patients will remain on CFTR modulators, particularly ELX/TEZ/IVA, over the long term.

DUSC noted consumer comments regarding the report, which highlighted the overwhelmingly positive impact ELX/TEZ/IVA has had for patients. The comments noted the improved quality of life patients are experiencing, through fewer hospital visits and being

[7] Lin, A., Wong, K., Visser, S.K., et al., Diagnosis of cystic fibrosis in adults: Australian Cystic Fibrosis Data Registry data, 2000–2019. Med J Aust, 218: 138-139 (2023). https://doi.org/10.5694/mja2.51797

[8] Ruseckaite, R., Salimi, F., Earnest, A. et al. Survival of people with cystic fibrosis in Australia. Sci Rep 12, 19748 (2022). https://doi.org/10.1038/s41598-022-24374-4

able to contribute to society in ways they were previously not expecting to, such as studying at university, working and paying taxes, and raising children.

The comments noted some side effects, such as behavioural problems that returned to normal after the medication was ceased, weight gain due to the necessary high fat diet, and survivor's guilt as they are doing well after watching siblings or friends pass away. The comments also noted an increase in fertility and that women have become pregnant after being told they were infertile.

DUSC noted that data from Australia suggest the number of pregnancies among CF patients has doubled, with 88 pregnancies recorded in the ACFDR in 2023 compared to 42 in 2020.[9] DUSC noted some of the research surrounding women continuing therapy while pregnant, and that one study conducted using the French health insurance data warehouse found 99.3% of pregnancies included in the study with exposure to CFTR modulators resulted in livebirths, and that the rate of small for gestational age (<10th percentile) was significantly lower in pregnancies exposed to CFTR modulators compared to unexposed (6.8% vs. 16 %; $p < 0.01$).[10]

DUSC commented that overall, the PBS listing of CFTR modulators, particularly ELX/TEZ/IVA, have improved the management and care of patients with CF, and improved the life expectancy and quality of life for patients.

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.

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[9] https://www.cysticfibrosis.org.au/cf-data-registry/

[10] Chouchana, L., Collier, M., Martin, C. el al. CFTR modulators and pregnancy outcomes: Early findings from a nationwide cohort study, Journal of Cystic Fibrosis, Volume 24, Issue 3, 2025, Pages 469-475, ISSN 1569-1993, https://doi.org/10.1016/j.jcf.2025.03.002.

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.

Sponsor comments

Vertex Pharmaceuticals (Australia) Pty. Ltd.
Vertex welcomes the DUSC findings and remains committed to continuing to serially innovate to further improve the lives of people living with Cystic Fibrosis.

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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