2022 Illuminate Orphan Drug Report

Orphan Drugs in Australia

•••

January, 2022

illuminate

Health Consulting Pty Ltd

Overview – Orphan drugs in Australia

- ➔ The orphan drug landscape
- ➔ Methods for data collection and analysis
- ➔ Current trends in orphan drug designation and funding
- ➔ Summary and conclusions

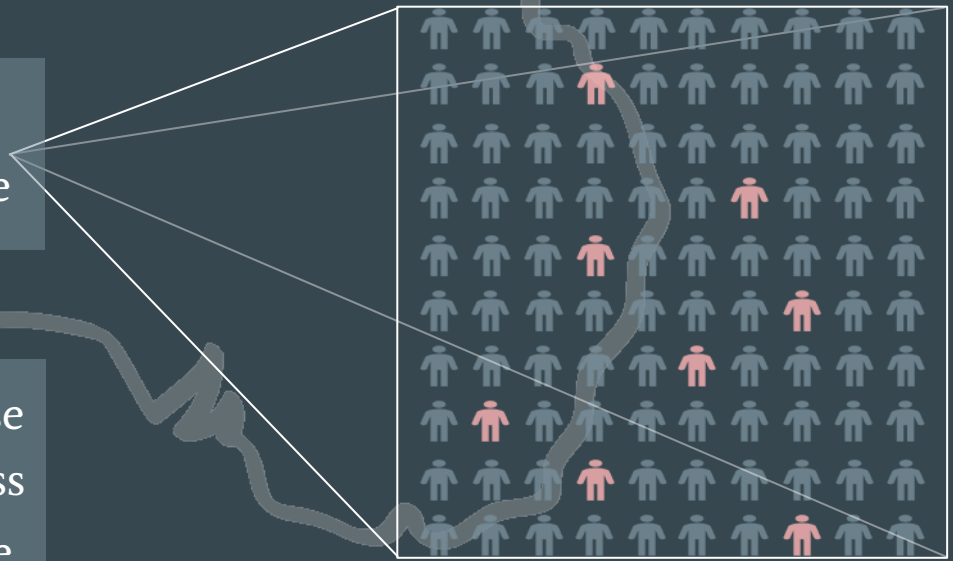
The orphan drug landscape

The Australian Orphan Drugs Program, launched in 1997, was designed to encourage research and marketing of therapies to treat rare diseases.

Rare diseases are life-threatening or chronically debilitating conditions that affect a small percentage of the population

Approximately **2 Million (8%)** Australians live with a rare disease

In Australia a rare disease is defined as affecting less than **5 in 10,000** people



For a drug to receive an Orphan designation, it is submitted for assessment and approval by the Therapeutic Goods Administration (TGA)

Orphan drug designation may be granted for:

- A previously unregistered medicine.
- An already registered medicine with a new orphan indication, a new dosage form, or a major variation application that meets all relevant criteria.

On the 1st July 2017 amendments to the Therapeutic Goods Regulations 1990 came into effect[1]

Resulting changes to the Orphan Drugs Program included:

- The rare disease threshold was increased from affecting 2,000 or fewer people to affecting <5 in 10,000 people.
- Stipulation that the disease/condition needs to be life-threatening or seriously debilitating.
- Time limited orphan designation status (lapses after 6 months).
- Changes to designation pathway options and other eligibility criteria.

If a medicine meets the eligibility criteria for Orphan drug designation and is granted approval by the TGA, the fees for registration are waived.

- As of December 2021 the TGA registration fee for a new chemical entity is AUD$251,900, and an extension of indication is AUD$149,600.[2]
- An Orphan drug designation does not guarantee TGA registration and the drug will still need to undergo assessment and approval.
- Orphan designation will remain in place for 6 months after which the designation will lapse if no registration application is made and the sponsor will have to submit for orphan designation again or apply for an extension.

Eligibility criteria

Orphan drug eligibility criteria		
Application type	**Standard orphan drug**	**New dosage form medicine**
1. One indication	The application is for only one indication of the medicine	
2. Serious Condition	The indication is the treatment, prevention or diagnosis of a life-threatening or seriously debilitating condition in a particular class of patients (the relevant patient class)	The indication is the treatment, prevention or diagnosis of a life-threatening or seriously debilitating condition
3. Medical Plausibility	It is not medically plausible that the medicine could effectively treat, prevent or diagnose the condition in another class of patients that is not covered by the relevant patient class	-

Eligibility criteria cont.

Orphan drug eligibility criteria		
Application type	**Standard orphan drug**	**New dosage form medicine**
4. Orphan drug prevalence threshold **OR** **lack of financial viability**	At least one of the following applies: i. If the medicine is intended to treat the condition – the condition affects fewer than 5 in 10,000 individuals in Australia when the application is made; ii. If the medicine is intended to prevent or diagnose the condition the medicine, if it were included in the Register, would not be likely to be supplied to more than 5 in 10,000 individuals in Australia during each year that it is included in the Register; iii. It is not likely to be financially viable for the sponsor to market the medicine in Australia unless each fee referred to in paragraph 45(12)(c) of the Regulations were waived in relation to the medicine	It is not likely that it would be financially viable for the sponsor to market the medicine in Australia unless each fee referred to in paragraph 45(12)(c) of the Regulations were waived in relation to the medicine

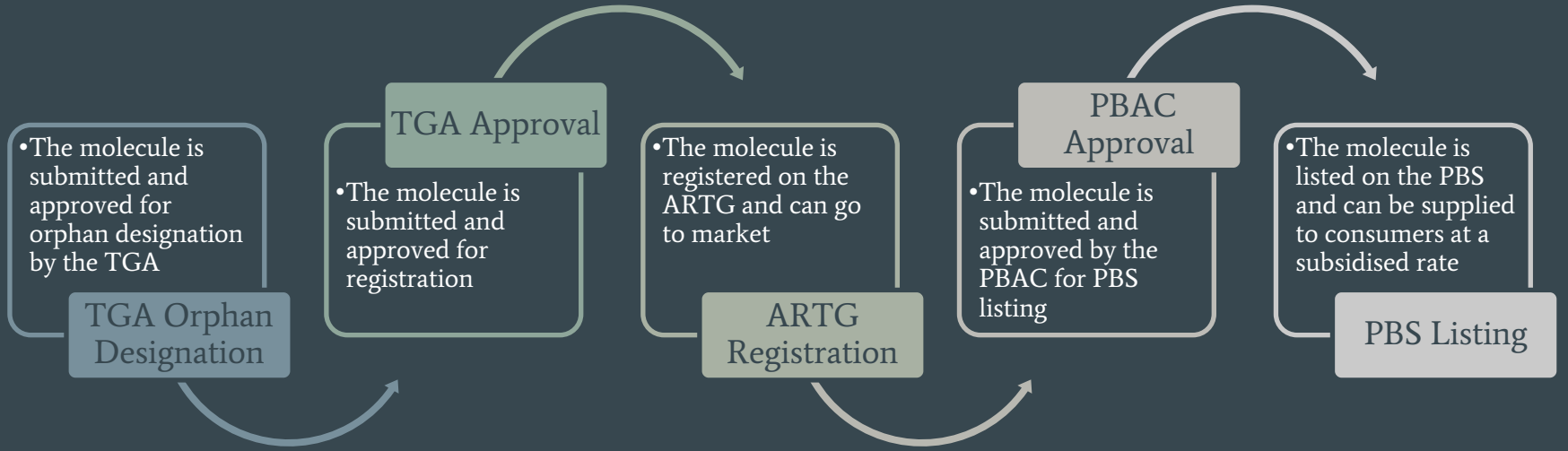
Eligibility criteria cont.

Orphan drug eligibility criteria		
Application type	**Standard orphan drug**	**New dosage form medicine**
5. Refusal to approve on grounds of safety	None of the following has refused to approve the medicine for the treatment, prevention or diagnosis of the condition for a reason relating to the medicine's safety: i. The Secretary; ii. The United States Food and Drug Administration; iii. The European Medicines Agency; iv. Health Canada; v. The Medicines and Healthcare Products Regulatory Agency of the United Kingdom;	
6. Comparison with registered therapeutic goods	i. No therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods); or ii. If one or more therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods)—the medicine provides a significant benefit in relation to the efficacy or safety of the treatment, prevention or diagnosis of the condition, or a major contribution to patient care, compared to those goods.	

From 1st July 2019, orphan drugs are exempt from an evaluation fee for the first submission to the Pharmaceutical Benefits Advisory Committee (PBAC)[3]

- An application for submission services must be made concurrently with the corresponding TGA registration application or within 12 months of the designated orphan drug being registered on the Australian Register of Therapeutic Goods (ARTG).
- Previously, an exemption applied to all applications for medicines that had an active orphan drug designation. This no longer applies.
- Normally, submission fees can be upwards of AUD$200,000[3]

General pathway from Orphan Designation to PBS



The Australian Orphan Drugs Program has been active for 25 years yet little information on the trends in Orphan drug designation and subsidisation have been published.

Objective: The aim of this study was to report on the recent trends in orphan drug designation and subsidisation by evaluating TGA designations and PBAC submissions between 2016-2021

Methods for data collection and analysis

Methods – Data collection

- Orphan drug designation notices between the start of 2016 to the end of 2021 were downloaded from the TGA website in December 2021

- Information included:
  - Molecule name
  - Sponsor
  - Therapeutic area
  - Indication
  - Orphan designation effective date

- PBAC submission details, meeting dates and PBS listing dates were also downloaded using the Illuminate Health Consulting proprietary database illuminate RED

- All data were imported into Microsoft Excel for analysis

Methods – Data Analysis

- To determine whether orphan drugs were considered by the PBAC, molecules that were assigned an orphan indication by the TGA were compared to the same molecules with the same indication in the illuminate RED database. If the Orphan designation date preceded the PBAC meeting date, the molecule was considered an orphan drug and was included in the analysis.

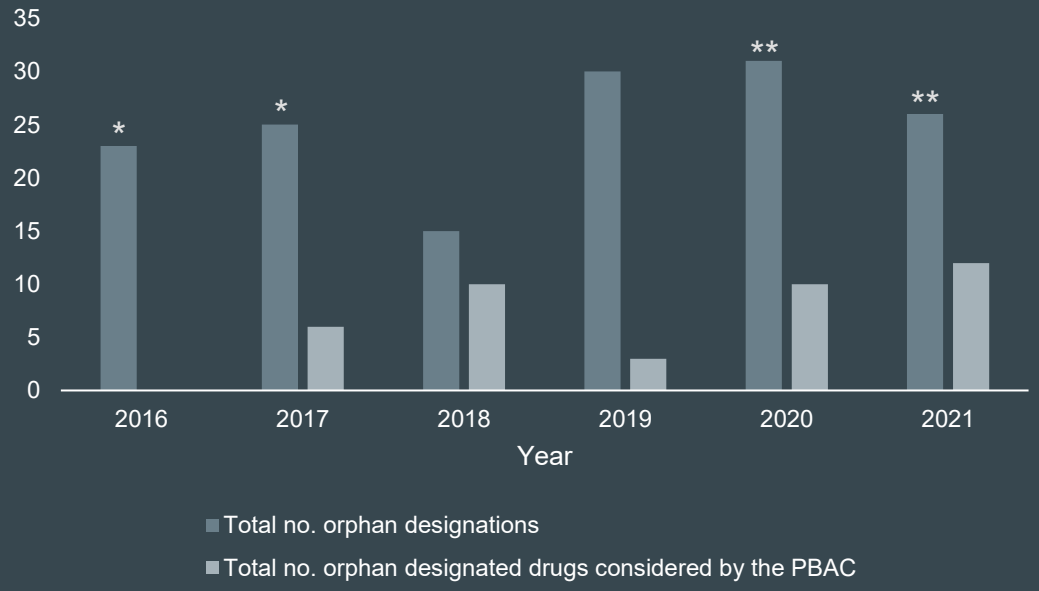
- In cases where the indication was the same as the orphan designation but the PBAC meeting preceded the orphan designation date, the molecule was excluded.

- Out of 150 orphan designation approvals (including multiple approvals for single molecules) between 2016-2021, 41 molecules were considered by the PBAC and were included in the analysis.

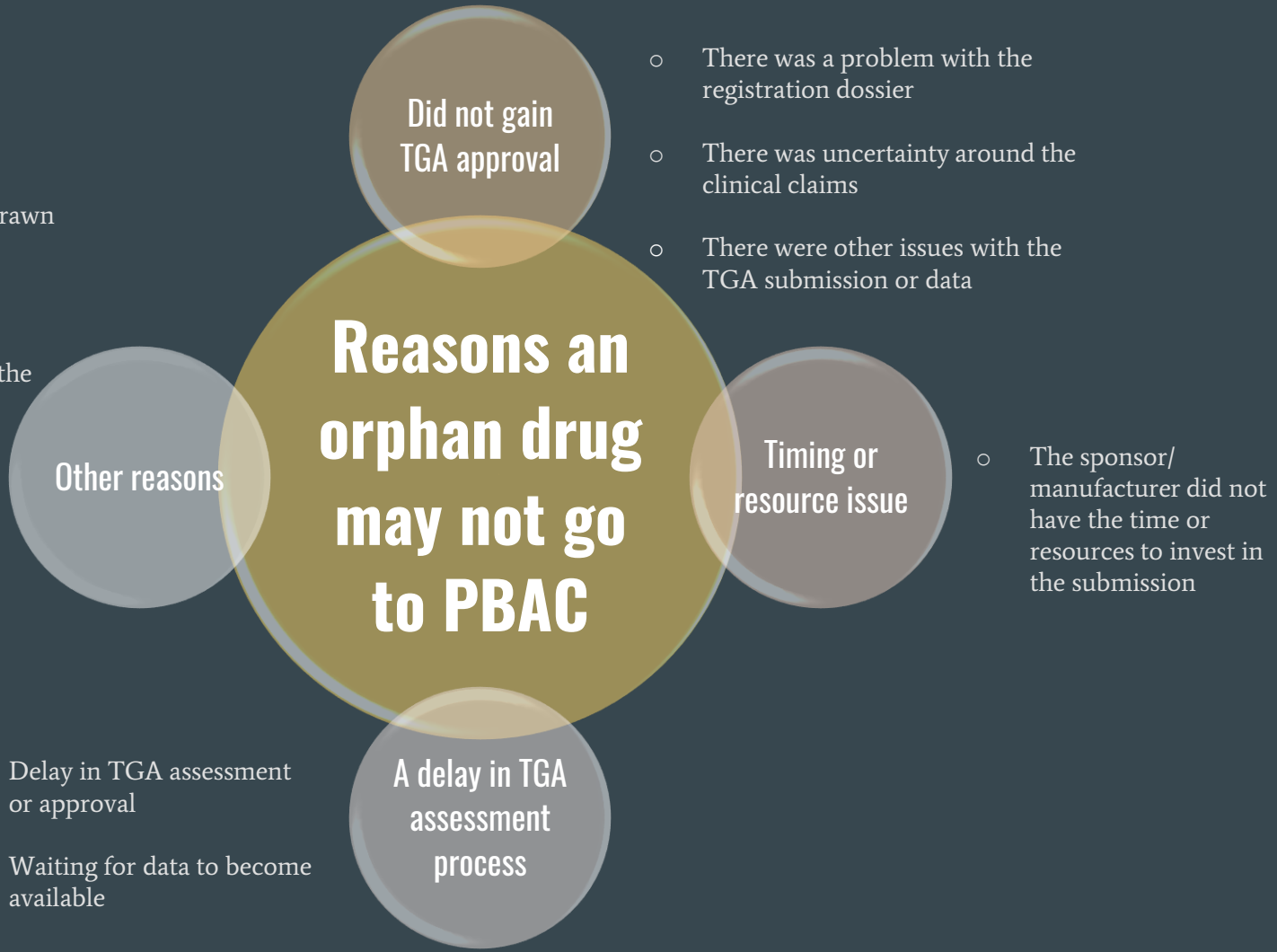
Current trends in orphan drug designation and funding

Results - Orphan designations

- On average around 25 (median: 25.5) orphan designations were granted per year by the TGA between 2016-2021 (this includes multiple designation notices for single molecules).
- The number of orphan designations is increasing.
- Of those molecules that received an orphan designation between 2016-2021, an average of 6.8 (Median: 8) have been considered each year by the PBAC.
- Overall, the number of orphan designations that were not considered by the PBAC between 2016-2021 (109 in total) was higher than the number considered (41 in total).

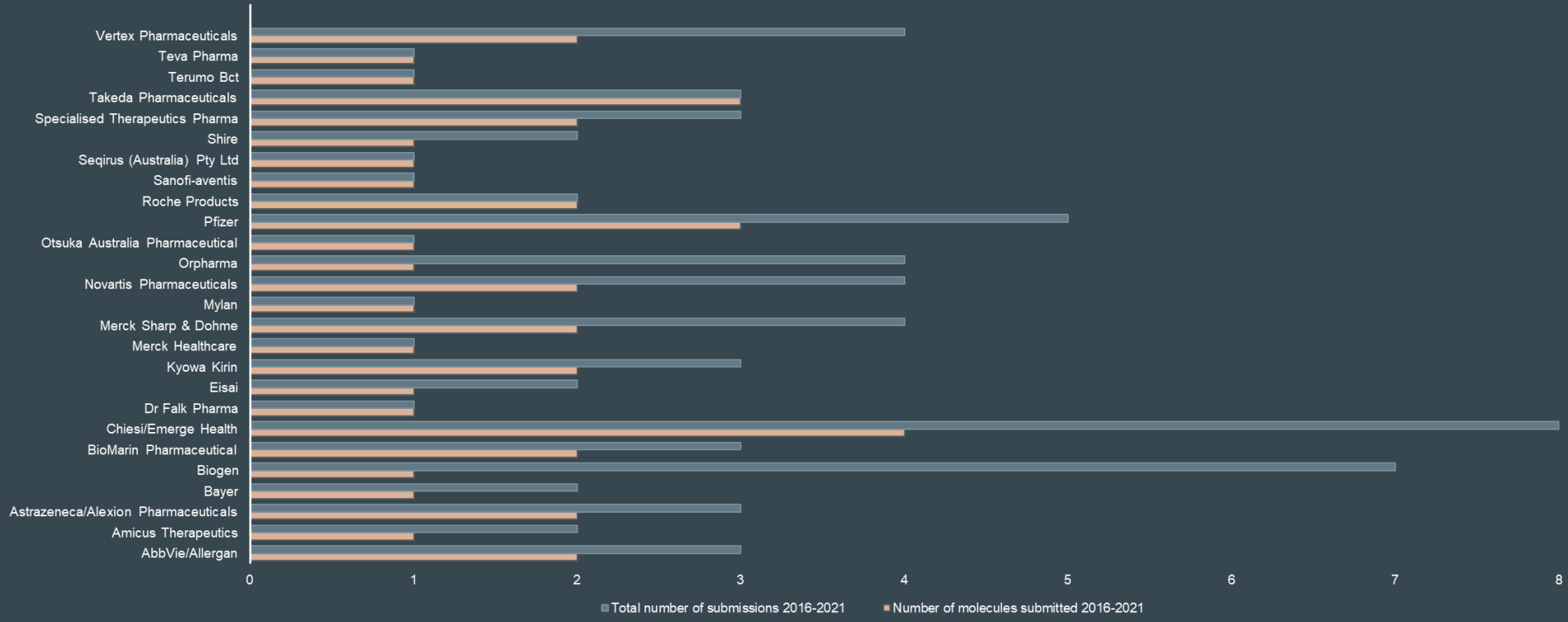


* It is likely that many orphan drugs considered by the PBAC in 2016 and 2017 would have received designation in 2015 or earlier and were not captured by this study.
** Orphan drugs designated in 2020 and 2021 may not be considered by PBAC until 2022 at the earliest.


Reasons an orphan drug may not go to PBAC
Did not gain TGA approval
There was a problem with the registration dossier
There was uncertainty around the clinical claims
There were other issues with the TGA submission or data
Timing or resource issue
The sponsor/ manufacturer did not have the time or resources to invest in the submission
A delay in TGA assessment process
Delay in TGA assessment or approval
Waiting for data to become available
Other reasons
The TGA or PBAC submission was withdrawn by the sponsor/ manufacturer
The molecule is not suitable for listing on the PBS

Results – PBAC submissions by company

In total 26 companies submitted orphan drugs to PBAC. The company with the most orphan drugs and submissions between 2016-2021 was Chiesi (formerly Emerge Health) with 8 submissions for 4 orphan drugs.

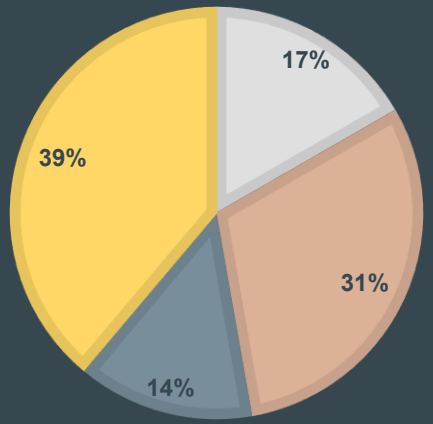


Results – PBAC decision

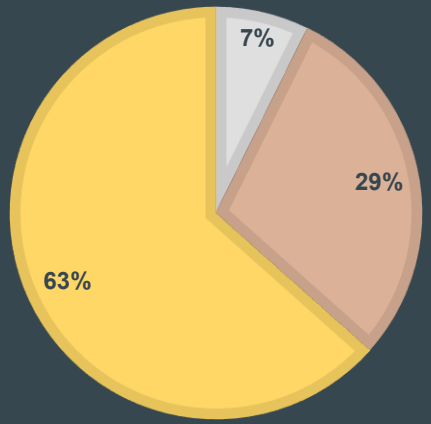
- Of all orphan drug submissions between 2016-2021 (including multiple submissions for single molecules, n=72), 39% of submissions received a positive recommendation.
- Of all molecules with orphan designation that were considered by the PBAC between 2016-2021 (n=41), 63% in total have received a positive recommendation.
- For the initial submission to the PBAC, the recommendation rate for orphan drugs is 32%
- On average, orphan designated drug required 2 (median: 2) submissions before receiving a positive recommendation.

Results – PBAC decision cont.

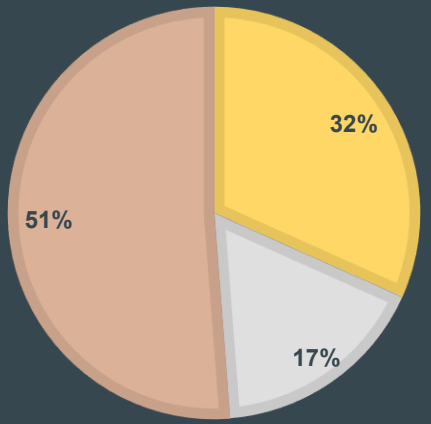
All submissions



All molecules



Initial submission



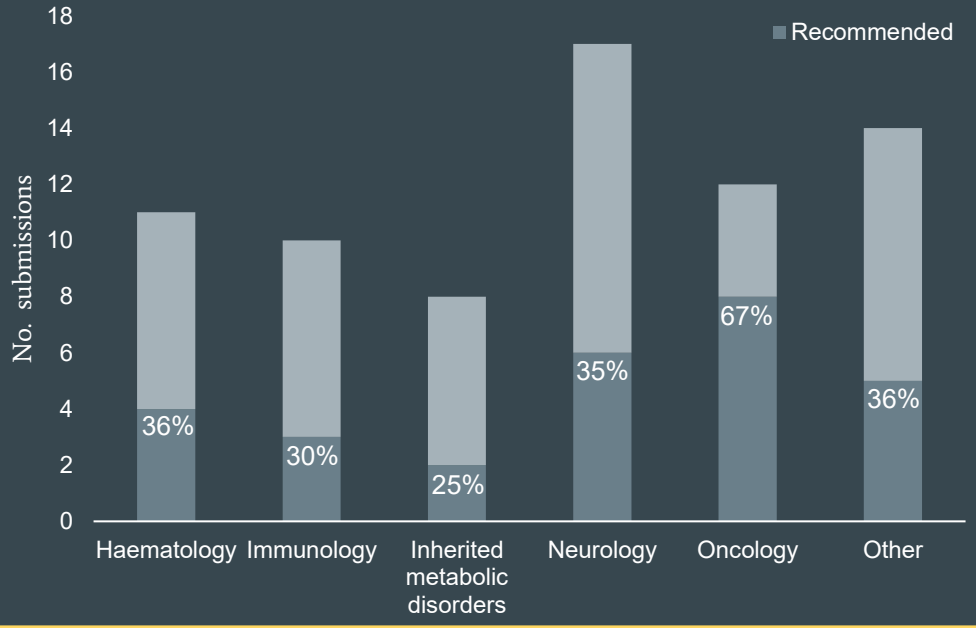
Deferred First Rejection Subsequent Rejection Recommended

PBAC Decision	Total no. submissions	Percentage	Total no. molecules	Percentage	Initial submission	Percentage
Deferred	12	17%	3	7%	7	17%
First Rejection	22	31%	12 (total rejected)	29%	21	51%
Subsequent Rejection	10	14%	–	–	–	–
Recommended	28	39%	26	63%	13	32%
Total	**72**	**100%**	**41**	**100%**	**41**	**100%**

Results – PBAC decision by therapeutic area

- The therapeutic area with the highest number of submissions between 2016-2021 was Neurology with 17 submissions in total (including multiple submissions for the same molecule).

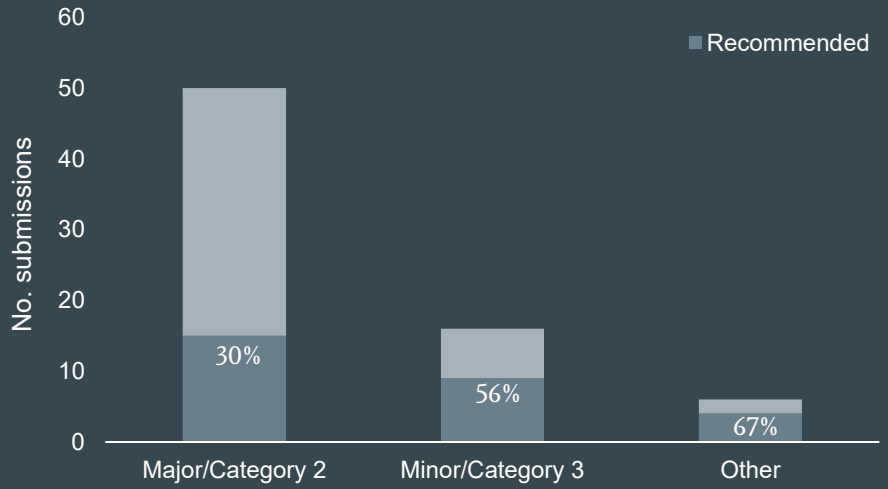
- The therapeutic area with the highest success rate was Oncology with 67% of all submissions receiving a positive recommendation.



Therapeutic area	Deferred	First Rejection	Subsequent Rejection	Recommended	Total	Recommendation rate
Haematology	0	6	1	4	11	36%
Immunology	3	3	1	3	10	30%
Inherited metabolic disorders	1	2	3	2	8	25%
Neurology	4	5	2	6	17	35%
Oncology	1	2	1	8	12	67%
Other	3	4	2	5	14	36%
Total	**12**	**22**	**10**	**28**	**72**	**39%**

Results – PBAC decision by submission type (all submissions)

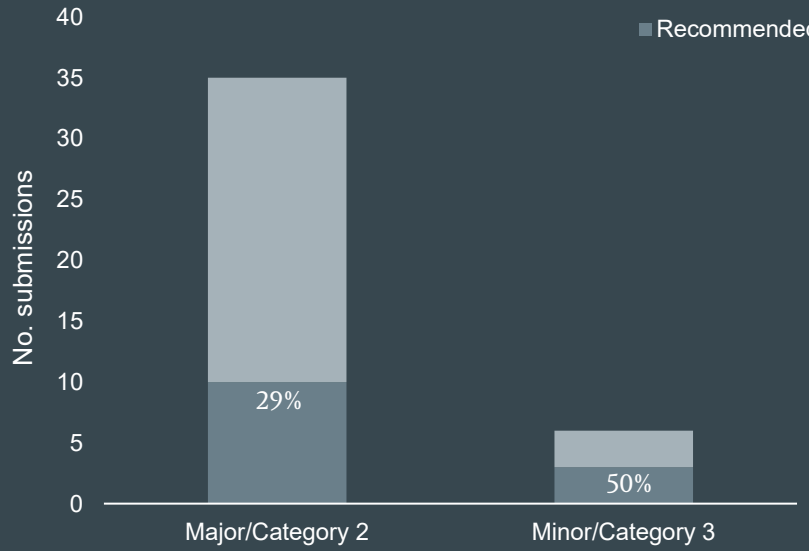
- Of all orphan drug submissions between 2016-2021 (including multiple submissions for single molecules), major/category 2 submissions were the most common (n=50), however, minor/category 3 submissions were more successful with 56% receiving a positive recommendation.



Submission type	Deferred	First Rejection	Subsequent Rejection	Recommended	Grand Total	Recommendation rate
Major/Category 2	10	20	5	15	50	30%
Minor/Category 3	2	1	4	9	16	56%
Other	0	1	1	4	6	67%
Total	**12**	**22**	**10**	**28**	**72**	**39%**

Results – PBAC decision by submission type (initial submission)

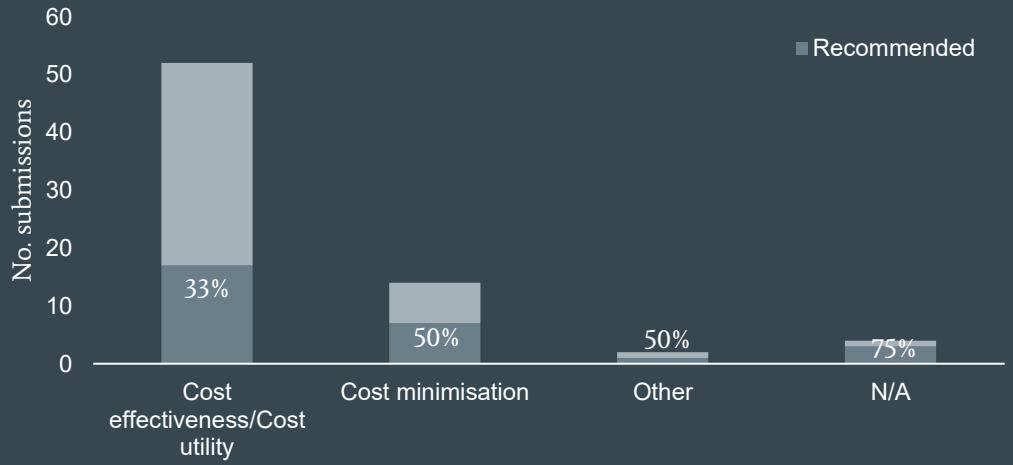
- In terms of the initial submission of an orphan drug to the PBAC between 2016-2021, a minor/category 3 submission had a greater success rate (50%) than a major/category 2 submission (29%)



Submission type	Deferred	First Rejection	Recommended	Grand Total	Recommendation rate
Major/Category 2	5	20	10	35	29%
Minor/Category 3	2	1	3	6	50%
Total	**7**	**21**	**13**	**41**	**32%**

Results – PBAC decision by economic evaluation (all submissions)

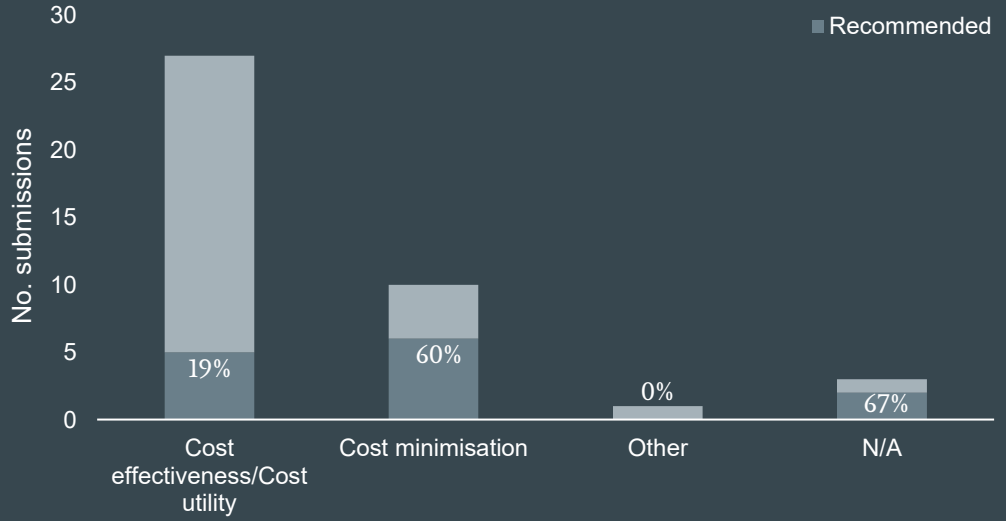
- Of all orphan drug submissions between 2016-2021 (including multiple submissions for single molecules), cost effective/cost utility evaluations were the most common (n=52), however, cost minimisation evaluations were more successful with 50% receiving a positive recommendation.



Economic evaluation	Deferred	First Rejection	Subsequent Rejection	Recommended	Grand Total	Recommendation rate
Cost effectiveness/Cost utility	10	18	7	17	52	33%
Cost minimisation	1	3	3	7	14	50%
Other	0	1	0	1	2	50%
N/A	1	0	0	3	4	75%
Total	**12**	**22**	**10**	**28**	**72**	**39%**

Results – PBAC decision by economic evaluation (initial submission

- In terms of the initial submission of an orphan drug to the PBAC between 2016-2021, a cost effective/cost utility evaluation had a lower success rate (19%) than a cost minimisation submission (60%)



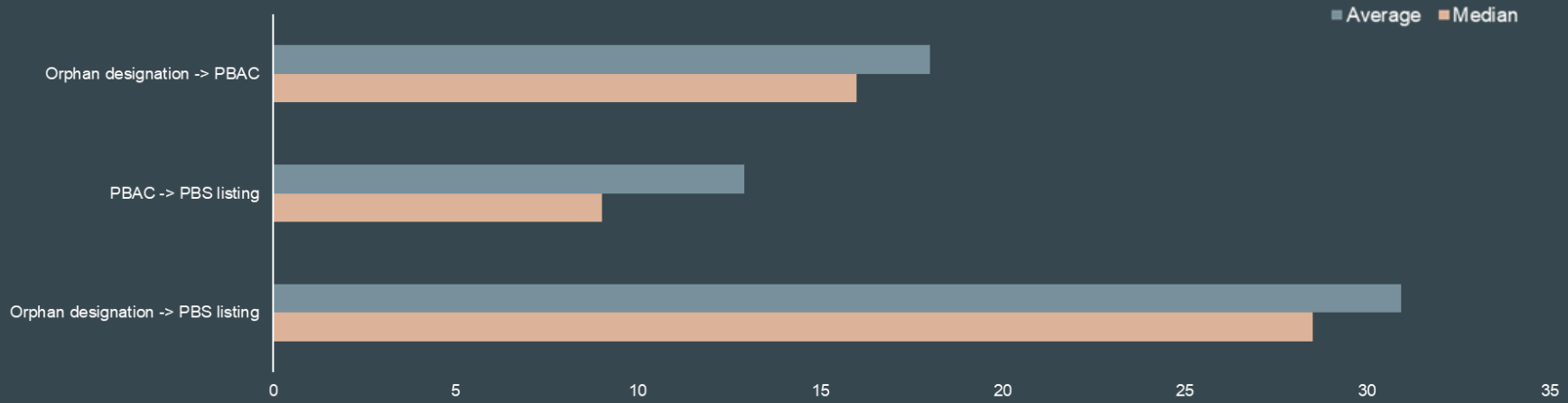
Economic evaluation	Deferred	First Rejection	Recommended	Grand Total	Recommendation rate
Cost effectiveness/Cost utility	5	17	5	27	19%
Cost minimisation	1	3	6	10	60%
Other	0	1	0	1	0%
N/A	1	0	2	3	67%
Total	**7**	**21**	**13**	**41**	**32%**

Results – Time from TGA -> PBAC -> PBS

- Between 2016-2021 the average time it took for a brand new orphan drug (i.e. the molecule has never been listed on the PBS previously, n=13) to go to the PBAC from the date of designation was 18 months (median: 16). This analysis included only molecules that went on to receive a positive recommendation between 2016-2021

- The average time from the PBAC meeting where the treatment received a positive recommendation to PBS listing was 13 months (median: 9)

- Overall, the average number of months from orphan designation to PBS listing was 31 (median: 29).



Summary and conclusions

Summary and conclusions

- Results from the study suggest that orphan designated drugs make up a small proportion of the drugs that go to the PBAC each year (mean: 6.8 per year, median: 8).

- The majority of drugs that receive an orphan designation do not make it to PBAC evaluation (150 designations total vs 41 PBAC considerations). This may be due to a number of reasons including: timing, delays, problems with the clinical trials/data and the fact that not all orphan drugs would be appropriate for PBAC evaluation.

- The largest group of orphan drugs that are submitted to the PBAC are drugs for neurological diseases and conditions, however, oncology drugs are the most successful with an overall positive recommendation rate of 67%.

- In terms of submission types and economic evaluation options for orphan drugs, the most successful submissions are minor/category 2 submissions and cost minimisation analyses. On initial submission to the PBAC, a minor submission has a 50% chance success rate, however, the majority of initial submissions are major submissions with a success rate of 29%. The most commonly used economic analysis is a cost effectiveness/cost utility approach, however, the most successful initial submissions use a cost minimisation approach with a 60% chance success rate vs 19% for cost effective/cost utility analyses.

- The time it takes to get an orphan drug listed on the PBS from the date of designation is likely to be >2 years. Once an orphan drug has been recommended, the time from the PBAC meeting to the PBS listing date is likely to be around 12 months on average.

References:

1. TGA. *Reform of the orphan drug program*. 2018 [cited December 2021]; Available from: https://www.tga.gov.au/node/842961.
2. TGA. *Fees and charges: summary, December 2021*. 2021 [cited 2021 December]; Available from: https://www.tga.gov.au/sites/default/files/fees-and-charges-summary-1-december-2021.pdf
3. PBS. *Cost Recovery Fees and Charges*. 2021 [cited December 2021]; Available from: https://www.pbs.gov.au/info/industry/listing/elements/fees-and-charges.

The Team

illuminate

Health Consulting Pty Ltd

Peter Davey, BA (Econ) MA (Econ)	Sarah Campbell, BSc MRes	Sahan Amarathunga, BSc BBus
General Manager	Health Outcomes Analyst	Pricing & Data Analyst