Utilisation analysis of PBS-listed anti-epileptic drugs in a cohort of epilepsy patients

Drug Utilisation Sub-Committee (DUSC)

September 2023

Background

Previous PBAC consideration

PBAC Intracycle meeting, September 2020

The Pharmaceutical Benefits Advisory Committee (PBAC) recalled that in March 2020 it requested that the Department conduct research to consider the cost to the Pharmaceutical Benefits Scheme (PBS) of allowing women of childbearing potential to access the second-line anti-epileptic drugs (AEDs), levetiracetam (LEV) and lamotrigine (LTG), first-line. This request followed the PBAC's consideration of feedback from the Epilepsy Society of Australia (ESA) that best practice clinical management of epilepsy includes the availability of LEV and LTG as first-line agents for women of childbearing potential.

The PBAC noted that the current PBS restrictions for LEV and LTG restrict access to those patients who have failed to have their epilepsy controlled with other AEDs. The current restriction may result in prescribers continuing to use sodium valproate among women of childbearing potential when likely safer options are available. The PBAC acknowledged this was a quality use of medicines issue and accepted advice from the ESA on the need for clinicians to have the choice to prescribe alternative AEDs (i.e., LEV and LTG) in this population.

The PBAC recommended amending the current PBS restrictions to allow for the first-line use of LEV and LTG in women of childbearing potential. The PBAC accepted the utilisation data and estimates that suggested prescribing of LEV and LTG is already occurring in approximately 75% of women with epilepsy who are of childbearing potential. The PBAC noted that the financial impact to the PBS of expanding the current restrictions was estimated to be small and less than $10 million per year in Year 6. The PBAC considered the additional cost to the PBS of expanding the LEV and LTG restrictions acceptable.

Based on the information and clinical guidelines provided by the ESA, the PBAC requested that the Department provide estimates of the cost to the PBS of allowing first-line use of LEV and LTG in the remaining population with epilepsy (i.e., males and females of all ages) to the DUSC of the PBAC. In addition, the PBAC requested that the Department provide utilisation data and any further evidence on the broader use of other second-line AEDs to the DUSC in the same report.

Summary of PBS-listed anti-epileptic drugs

Table 1 provides a summary of the AEDs currently PBS-listed for epilepsy.

Table 1: Summary of PBS-listed anti-epileptic drugs [ATC code N03A – ANTIEPILEPTICS]

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
First-line treatment							
Carbamazepine	CR 200mg tab: $30.77 200mg tab: $30.41 100mg/5ml: $25.97 100mg tab: $23.41 CR 400mg tab: $46.77	Complex or simple partial seizures (with or without loss of consciousness), with or without secondary generalisation; Generalised tonic-clonic seizures; Mixed seizure patterns incorporating the above.	N/A	Unrestricted	N/A	D	December 1979
Ethosuximide	250mg/5ml: $73.58 250mg cap, 100 (2 pks): $295.85	Petit mal epilepsy	N/A	Unrestricted	N/A	D	May 1964
Phenobarbital (phenobarbitone)	219mg/ml inj: $36.02 30mg tab: $18.60	Epilepsy	Epilepsy	Restricted Benefit	N/A	D	May 1964
Phenytoin	50mg chew. tab: $65.17 30mg cap: $52.56 30mg/5ml liq: $26.11 100mg cap: $33.31	Generalised tonic-clonic (grand mal) and psychomotor seizures	N/A	Unrestricted	N/A	D	May 1964
Primidone	250mg tab: $69.89	Grand mal and psychomotor (temporal lobe) epilepsy: focal or Jacksonian seizures, myoclonic jerks and akinetic attacks.	N/A	Unrestricted	N/A	D	May 1964
Sulthiame	50mg tab: $69.15 200mg tab: $162.85	Behavioural disorders associated with epilepsy; hyperkinetic behaviour; temporal lobe epilepsy; myoclonic seizures; grand mal attacks; Jacksonian seizures.	N/A	Unrestricted	N/A	D	May 1964
Valproate	200mg/5ml liq: $40.95 100mg tab: $35.23 500mg EC tab: $32.71 200mg EC tab: $22.95	Primary generalised epilepsy (petit mal absences, various forms of myoclonic epilepsy and tonic-clonic grand mal seizures). Partial (focal) epilepsy either alone or as adjuvant therapy	N/A	Unrestricted	N/A	D	August 1984
Clonazepam	1 mg/mL injection [5 x 1 mL ampoules], 1 pack: $23.56 2.5 mg/mL (0.1 mg/drop) oral liquid, 10 mL (2 pks): $20.51 2 mg tablet, 100 (2 pks): $31.97	Tablets: Most types of epilepsy in infants and children, especially absences (petit mal), myoclonic seizures and tonic clonic fits, whether due to primary generalised epilepsy, or to secondary generalisation of partial epilepsy. In adults all varieties of generalised epilepsy (including myoclonic, akinetic, tonic and tonic clonic	Epilepsy	Restricted Benefit (for injection) Authority Required (other forms)	The condition must be neurologically proven.	B3	December 1976

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
	500 microgram tablet, 100 (2 pks): $26.53 500 microgram tablet, 50 (4 pks): $30.25	seizures), and in partial epilepsy (including psychomotor seizures). Injection: Intravenous (IV) use, for status epilepticus.					
Nitrazepam	5 mg tablet, 25: $18.41	N/A	Myoclonic epilepsy Malignant neoplasia (late stage) Insomnia	Authority Required	N/A	C	August 1968
Second-line treatment							
Gabapentin	100mg cap: $17.16 800mg tab: $46.14 300mg cap: $24.48 400mg cap: $28.66 600mg tab: $37.85	Partial seizures, including secondarily generalised tonic-clonic seizures, initially as add-on therapy in adults and children aged 3 years and above who have not achieved adequate control with standard anti-epileptic medications	Partial epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	B3	December 1994
Levetiracetam	500mg tab: $29.02 250mg tab: $22.61 1g tab: $39.71 100mg/ml liq: $75.35	Epileptic patients aged 4 years and older, initially as add-on therapy, in the treatment of partial onset seizures with or without secondary generalisation; monotherapy in the treatment of partial onset seizures, with or without secondary generalisation, in patients from 16 years of age with newly diagnosed epilepsy; add-on therapy in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with juvenile myoclonic epilepsy (JME); and add-on therapy in the treatment of primary generalized tonic-clonic seizures in adults and children from 4 years of age with idiopathic generalized epilepsy (IGE)	Partial epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs; OR Patient must be a woman of childbearing potential, AND The treatment must not be given concomitantly with brivaracetam, except for cross titration.	B3	August 2003
Tiagabine	15mg tab: $155.67 10mg tab: $110.77 5mg tab: $61.87	Partial seizures, as add on therapy in patients who are not controlled satisfactorily with other antiepileptic drug(s)	Partial epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	B3	February 1998

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
Zonisamide	100mg cap: $76.13 50mg cap: $31.94 25mg cap: $24.35	Monotherapy in the treatment of partial seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy who are intolerant to other agents or where other agents are contraindicated; adjunctive therapy in the treatment of adult patients with partial seizures, with or without secondary generalisation	Partial epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	D	April 2009
Lamotrigine	200mg tab: $34.30 100mg tab: $25.67 50mg tab: $20.60 25mg tab: $17.65 5mg tab: $19.31	Partial and generalised seizures in adults and children	Epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs; OR Patient must be a woman of childbearing potential.	D	December 1994
Vigabatrin	500mg tab: $86.75 500mg sachet: $60.74	Treatment of epilepsy which is not satisfactorily controlled by other antiepileptic drugs	Epileptic seizures	Authority Required (STREAMLINED)	The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	D	October 1993
Oxcarbazepine	300mg tab: $84.32 600mg tab: $133.13 150mg tab: $56.21 60mg/ml liq: $99.43	Monotherapy or adjunctive therapy for the treatment of partial seizures and generalised tonic-clonic seizures, in adults and children	Seizures	Authority Required (STREAMLINED)	Patient must have partial epileptic seizures; OR Patient must have primary generalised tonic-clonic seizures, AND The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	D	May 2002
Topiramate	50mg tab: $21.60 25mg tab: $18.28 200mg tab: $35.75 15mg cap: $24.30 100mg tab: $26.54 25mg cap: $22.30 50mg cap: $28.52	Adults and children, 2 years and over: monotherapy in patients with newly diagnosed epilepsy; for conversion to monotherapy in patients with epilepsy; add-on therapy in partial onset seizures (with or without secondary generalised seizures), primary generalised tonic-clonic seizures or drop attacks associated with Lennox-Gastaut syndrome	Seizures Migraines	Authority Required (STREAMLINED)	Patient must have partial epileptic seizures; OR Patient must have primary generalised tonic-clonic seizures; OR Patient must have seizures of the Lennox-Gastaut syndrome, AND The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs.	D	August 1997

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
Third-line treatment							
Brivaracetam	25mg tab: $164.66 50mg tab: $164.66 10mg/ml liq: $203.82 100mg tab: $164.66 75mg tab: $164.66	Add-on therapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 4 years of age with epilepsy	Intractable partial epileptic seizures	Authority Required (STREAMLINED)	Must be treated by a neurologist (for initiation) The treatment must be in combination with two or more anti-epileptic drugs which includes one second-line adjunctive agent, AND The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs, which includes at least one first-line anti-epileptic agent and at least two second-line adjunctive anti-epileptic agents, AND The treatment must not be given concomitantly with levetiracetam, except for cross titration.	B3	May 2018
Perampanel	12mg tab, 28: $303.16 6mg tab, 28: $229.39 2mg tab, 7 (2 pks): $48.13 10mg tab, 28: $303.16 8mg tab, 28: $303.16 4mg tab, 28: $155.59 Special Pricing Arrangements apply [2]	Adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients from 4 years of age with epilepsy; adjunctive treatment of primary generalised tonic-clonic seizures in patients from 7 years of age with idiopathic generalised epilepsy.	Intractable partial epileptic seizures [1]	Authority Required (STREAMLINED)	[1] The treatment must be in combination with two or more anti-epileptic drugs which includes one second-line adjunctive agent, AND The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs, which includes at least one first-line anti-epileptic agent and at least two second-line adjunctive anti-epileptic agents. Must be treated by a neurologist (for initiation).	B3	November 2014
			Idiopathic generalised epilepsy with primary generalised tonic-clonic seizures [2]		[2] Must be treated by a neurologist. The condition must have failed to be controlled satisfactorily by at least two anti-epileptic drugs, AND The treatment must be in combination with at least one PBS-subsidised anti-epileptic drug. Patient must be aged 12 years or older.		
Lacosamide	10mg/ml liq, 200mL: $124.75 [2 pks]; $358.29 [6 pks] 150mg tab (14): $50.22 150mg tab (56): $164.38 100mg tab (14): $37.82 200mg tab (56): $216.50 100mg tab (56): $112.30	Monotherapy in the treatment of partial seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older; add-on therapy in the treatment of partial seizures with or without secondary generalisation in	Intractable partial epileptic seizures [1]	Authority Required (STREAMLINED)	[1] Must be treated by a neurologist (for initiation). The treatment must be in combination with two or more anti-epileptic drugs which includes one second-line adjunctive agent, AND The condition must have failed to be controlled satisfactorily by other anti-epileptic drugs, which includes at least one first-line anti-epileptic agent	B3	May 2010

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
	50mg tab (14): $25.40 [1 pk]; $62.65 [4 pks]	patients with epilepsy aged 4 years and older; add-on therapy in the treatment of primary generalised tonic-clonic seizures in patients with idiopathic generalised epilepsy aged 4 years and older.			and at least two second-line adjunctive anti-epileptic agents.		
			Idiopathic generalised epilepsy with primary generalised tonic-clonic seizures [2]		[2] Must be treated by a neurologist; OR Must be treated by a paediatrician. AND Must be treated by an eligible practitioner type who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion. The condition must have failed to be controlled satisfactorily by at least two anti-epileptic drugs prior to when the drug is/was first commenced, AND The treatment must be (for initiating treatment)/have been (for continuing treatment) in combination with at least one PBS-subsidised anti-epileptic drug at the time the drug is/was first commenced.		
Cannabidiol	100 mg/mL oral liquid, 100 mL: $1534.84 Special Pricing Arrangements apply [2]	Adjunctive therapy of seizures associated with Lennox Gastaut syndrome (LGS) or Dravet syndrome (DS) for patients 2 years of age and older.	Severe myoclonic epilepsy in infancy (Dravet syndrome)	Authority Required	Patient must have (as an initiating patient)/have had (as a continuing patient), generalised tonic-clonic seizures or generalised clonic seizures that are not adequately controlled with at least two other anti-epileptic drugs, AND The treatment must be as adjunctive therapy to at least two other anti-epileptic drugs. Must be treated by a neurologist if treatment is being initiated; OR Must be treated by a neurologist if treatment is being continued or re-initiated; OR Must be treated by a paediatrician in consultation with a neurologist if treatment is being continued; OR Must be treated by a general practitioner in consultation with a neurologist if treatment is being continued.	B2	May 2021

Drug	DPMQ	TGA-approved epilepsy indication(s) [1]	PBS-listed indication	Restriction level	Restriction criteria	Pregnancy category [1]	Date of first PBS listing
Stiripentol	250 mg capsule, 60: $669.55 250 mg powder for oral liquid, 60 sachets: $669.55 500 mg capsule, 60: $1295.43 500 mg powder for oral liquid, 60 sachets: $1295.43	Adjunctive treatment of generalised tonic-clonic and clonic seizures associated with severe myoclonic epilepsy in infancy (SMEI, also known as Dravet syndrome) in patients whose seizures are not adequately controlled with a benzodiazepine (usually clobazam) and valproate.	Severe myoclonic epilepsy in infancy (Dravet syndrome)	Authority Required (STREAMLINED)	Patient must have (as an initiating patient)/have had (as a continuing patient), generalised tonic-clonic seizures or generalised clonic seizures that are not adequately controlled with at least two other anti-epileptic drugs, AND The treatment must be as adjunctive therapy to at least two other anti-epileptic drugs. Must be treated by a neurologist if treatment is being initiated; OR Must be treated by a neurologist if treatment is being continued or re-initiated; OR Must be treated by a paediatrician in consultation with a neurologist if treatment is being continued; OR Must be treated by a general practitioner in consultation with a neurologist if treatment is being continued.	B3	August 2021

Source: Extracted from PBS.gov.au on 29 August 2023.

[1] Per the Product Information (PI) accessed from the TGA website on 3 March 2023.

[2] Special Pricing Arrangements apply to perampanel and cannabidiol. The DPMQs noted above for these medicines are the published prices.

Epilepsy patient cohort utilisation analysis

In order to investigate the utilisation of PBS-listed AEDs for the treatment of epilepsy, an epilepsy patient cohort was defined for this analysis. This was done because the majority of the first-line PBS-listed AEDs are unrestricted benefits and some of these medicines are used for the treatment of conditions other than epilepsy.

Patients were included in the epilepsy patient cohort if 50% or more of their PBS-subsidised AED prescriptions (supplied between 1 January 2018 and the end of January 2023) were indicated for epilepsy after excluding prescriptions with an unknown indication (refer to 'Methods' below for further information).

The key findings from this analysis are summarised below.

Key findings

Patient utilisation trends

- The number of patients in the epilepsy patient cohort prevalent to a PBS-listed AED increased from 159,356 in 2018 to 184,043 in 2022 (an increase of 15.5%). The number of patients in the epilepsy patient cohort incident (initiating) to a PBS-listed AED declined from 38,549 in 2019 to 34,125 in 2022 (a decrease of 11.5%).
- In terms of prevalent patients, LEV (78,270 prevalent patients in 2022), LTG (55,952 prevalent patients in 2022) and valproate (34,018 prevalent patients in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort.
- In terms of incident (initiating) patients, LEV (16,814 incident patients in 2022), gabapentin (11,531 incident patients in 2022) and LTG (10,386 incident patients in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort.
- There were more females (99,490 patients) than males (84,553 patients) prevalent to a PBS-listed AED in the epilepsy patient cohort in 2022, and utilisation peaks at 50-54 years in females and 70-74 years in males.
- LTG was the most utilised PBS-listed AED for females aged 15-54 years in the epilepsy patient cohort, whilst LEV was the most utilised PBS-listed AED for females aged 55 years and over. LEV was the most utilised PBS-listed AED for males in the epilepsy patient cohort across all ages, except in males aged 25-29 years, where LTG had the highest utilisation.
- Monotherapy with LEV, gabapentin and LTG were the three most utilised PBS-listed AED initiation sequences in the epilepsy patient cohort. For drug initiation sequences consisting of two or more AEDs, LEV->valproate, valproate->LEV and valproate->LTG were the three most utilised treatment initiation sequences.

Prescription utilisation trends

- The number of prescriptions for PBS-listed AEDs supplied to the epilepsy patient cohort increased from 1,893,392 in 2018 to 2,269,474 in 2022 (an increase of 19.9%).
- The PBS benefits paid (based on published prices) for prescriptions for PBS-listed AEDs supplied to the epilepsy patient cohort increased from $56,497,715 in 2018 to $77,045,926 in 2022 (an increase of 36.4%).

- In terms of prescriptions supplied, LEV (800,384 prescriptions in 2022), LTG (567,972 prescriptions in 2022) and valproate (207,633 prescriptions in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort. Based on prescription numbers, LEV had the greatest market share (35%) followed by LTG (25%) and valproate (9%).
- LEV ($18,871,016 in 2022), lacosamide ($13,322,267 in 2022) and LTG ($8,324,978 in 2022) were the PBS-listed AEDs supplied to the epilepsy patient cohort that incurred the highest cost to the PBS. Based on PBS benefits paid, LEV had the greatest market share (24%) followed by lacosamide (17%) and LTG (11%).
- The second-line PBS-listed AEDs had the highest utilisation in the epilepsy patient cohort (1,747,804 prescriptions in 2022), followed by the first-line AEDs (366,419 prescriptions in 2022) and the third-line AEDs (155,251 prescriptions in 2022).
- The second-line PBS-listed AEDs incurred the highest cost to the PBS ($37,803,913 in 2022), followed by the third-line AEDs ($29,468,860 in 2022) and the first-line AEDs ($9,773,153 in 2022).
- Vocationally registered general practitioners (VRGPs) prescribed the most prescriptions for PBS-listed AEDs to the epilepsy patient cohort (1,616,346 prescriptions in 2022), followed by neurologists (197,080 prescriptions in 2022) and GP trainees (166,132 prescriptions in 2022).
- A substantial number of prescriptions for third-line PBS-listed AEDs that require a prescription from a neurologist or paediatrician (e.g., brivaracetam and perampanel) were prescribed by GPs. This may be partly explained by prescribers/pharmacists selecting an incorrect PBS item code at the time of prescribing/dispensing.
- There was no clear impact to the utilisation trends of LEV and LTG after the PBS restrictions for these medicines were expanded on 1 January 2021 to allow for their first-line use in women of childbearing potential. This is consistent with the PBAC's September 2020 advice that prescribing these medicines first-line in women of childbearing potential was likely already occurring in practice.
- There was a slight increase in the number of women of childbearing potential prevalent to lacosamide in 2021-2022. There was also a decline in the number of women of childbearing potential incident (initiating) to brivaracetam and perampanel in 2021-2022. Overall, it is unclear if these changes to the utilisation of the third-line PBS-listed AEDs (brivaracetam, perampanel and lacosamide) are flow-on effects after the PBS restrictions for LEV and LTG were expanded on 1 January 2021 to allow for their first-line use in women of childbearing potential.

Methods

In order to investigate the utilisation of PBS-listed AEDs for the treatment of epilepsy, an epilepsy patient cohort was defined for this analysis. This was done because the majority of the first-line PBS-listed AEDs are unrestricted benefits, and some of these medicines are used for the treatment of conditions other than epilepsy. For example: carbamazepine can also be used for bipolar disorder and trigeminal and glossopharyngeal neuralgias; and valproate can also be used for bipolar disorder and migraine prevention.

Patients were included in the epilepsy patient cohort if 50% or more of their PBS-subsidised AED prescriptions (supplied between 1 January 2018 and the end of January 2023) were indicated for epilepsy after excluding prescriptions with an unknown indication (i.e.,

unrestricted benefits or missing authority information). A 50% cut-off was used to prevent including patients who are being treated for conditions such as migraines who are erroneously supplied prescriptions under authority codes for epilepsy. For example, topiramate is PBS-listed under the same PBS code for both migraines and seizures but with different authority codes for each indication. Therefore, it is likely that prescribers and pharmacists may occasionally select an incorrect authority code at the time of prescribing/dispensing. Indications were determined by PBS item code for those codes that are indication specific and by authority approval data for those that are not. Once a patient was included in the epilepsy patient cohort, all their prescriptions (including unknown and non-epilepsy indication prescriptions) were considered to be for epilepsy. A total of 308,424 patients were included in the epilepsy patient cohort used in this analysis.

A limitation of defining epilepsy patients, as described above, is that it will exclude some epilepsy patients who have only received treatment with an unrestricted first-line PBS-listed AED. For example, as valproate is unrestricted, it will only appear in the data if the patient is included in the epilepsy patient cohort via the additional use of non-unrestricted first-line PBS-listed AEDs (phenobarbital, clonazepam or nitrazepam) or via a second- or third-line AED. This means that a patient who has only received prescriptions for first-line valproate, for example, will not appear in the data as this patient will not be included in the epilepsy patient cohort.

The data used for this analysis included all prescriptions supplied to patients included in the epilepsy patient cohort during the period 1 January 2018 to 31 January 2023 for the PBS item codes specified in Table 2.

Table 2: PBS codes included in the utilisation analysis [ATC code N03A – ANTIEPILEPTICS]

Drug	Form, strength & pack size	PBS code	Treatment phase	Restriction level
First-line AEDs				
Carbamazepine [1]	100 mg/5 mL oral liquid, 300 mL	2427R	N/A	Unrestricted
	100 mg tablet, 100	2422L	N/A	Unrestricted
	200 mg tablet, 100	1706T	N/A	Unrestricted
	200 mg modified release tablet, 200	2426Q	N/A	Unrestricted
	400 mg modified release tablet, 200	2431Y	N/A	Unrestricted
Ethosuximide	250 mg capsule, 200	1413J	N/A	Unrestricted
	250 mg/5 mL oral liquid, 200 mL	1414K	N/A	Unrestricted
	250 mg capsule, 100	11703Y	N/A	Unrestricted
	250 mg capsule, 56	13127X	N/A	Unrestricted
Phenobarbital (phenobarbitone)	30 mg tablet, 200	1850J	N/A	Restricted Benefit
	200 mg (equivalent to phenobarbital (phenobarbitone) sodium 219 mg)/mL injection, 5 x 1 mL ampoules	2138M	N/A	Restricted Benefit
Phenytoin	30 mg/5 mL oral liquid, 500 mL	2692Q	N/A	Unrestricted
	50 mg chewable tablet, 200	1249R	N/A	Unrestricted
	100 mg capsule, 200	1874P	N/A	Unrestricted

Drug	Form, strength & pack size	PBS code	Treatment phase	Restriction level
	30 mg capsule, 200	1873N	N/A	Unrestricted
Primidone	250 mg tablet, 200	1939C	N/A	Unrestricted
	250 mg tablet, 100	11883K [2]	N/A	N/A
Sulthiame	200 mg tablet, 200	2100M	N/A	Unrestricted
	50 mg tablet, 200	2099L	N/A	Unrestricted
Valproate (sodium)	100 mg tablet, 100	2294R	N/A	Unrestricted
	200 mg enteric tablet, 100	2289L	N/A	Unrestricted
	500 mg enteric tablet, 100	2290M	N/A	Unrestricted
	200 mg/5 mL oral liquid, 300 mL	2293Q	N/A	Unrestricted
	200 mg/5 mL oral liquid, 300 mL	2295T	N/A	Unrestricted
Clonazepam [3]	1 mg/mL injection [5 x 1 mL ampoules] (&) inert substance diluent [5 x 1 mL ampoules], 1 pack	1807D	N/A	Restricted Benefit
	2.5 mg/mL (0.1 mg/drop) oral liquid, 10 mL	1808E	N/A	Authority Required
	2 mg tablet, 100	1806C	N/A	Authority Required
	500 microgram tablet, 100	1805B	N/A	Authority Required
	500 microgram tablet, 50	11559J	N/A	Authority Required
Nitrazepam [4]	5 mg tablet, 25	2732T	N/A	Authority Required
Second-line AEDs				
Gabapentin	800 mg tablet, 100	8389M	N/A	Authority Required (STREAMLINED)
	100 mg capsule, 100	8505P	N/A	Authority Required (STREAMLINED)
	300 mg capsule, 100	1834M	N/A	Authority Required (STREAMLINED)
	400 mg capsule, 100	1835N	N/A	Authority Required (STREAMLINED)
	600 mg tablet, 100	8559L	N/A	Authority Required (STREAMLINED)
Levetiracetam	100 mg/mL oral liquid, 300 mL	9169N	N/A	Authority Required (STREAMLINED)
	1 g tablet, 60	8656N	N/A	Authority Required (STREAMLINED)
	250 mg tablet, 60	8654L	N/A	Authority Required (STREAMLINED)
	500 mg tablet, 60	8655M	N/A	Authority Required (STREAMLINED)
Tiagabine	10 mg tablet, 50	8222R	N/A	Authority Required (STREAMLINED)
	15 mg tablet, 50	8223T	N/A	Authority Required (STREAMLINED)
	5 mg tablet, 50	8221Q	N/A	Authority Required (STREAMLINED)
Zonisamide	100 mg capsule, 56	9390F	N/A	Authority Required (STREAMLINED)
	25 mg capsule, 56	9388D	N/A	Authority Required (STREAMLINED)

Drug	Form, strength & pack size	PBS code	Treatment phase	Restriction level
	50 mg capsule, 56	9389E	N/A	Authority Required (STREAMLINED)
Lamotrigine	5 mg tablet, 56	8063J	N/A	Authority Required (STREAMLINED)
	50 mg tablet, 56	2849Y	N/A	Authority Required (STREAMLINED)
	100 mg tablet, 56	2850B	N/A	Authority Required (STREAMLINED)
	200 mg tablet, 56	2851C	N/A	Authority Required (STREAMLINED)
	25 mg tablet, 56	2848X	N/A	Authority Required (STREAMLINED)
Vigabatrin	500 mg tablet, 100	2667J	N/A	Authority Required (STREAMLINED)
	500 mg powder for oral liquid, 60 sachets	2668K	N/A	Authority Required (STREAMLINED)
Oxcarbazepine	60 mg/mL oral liquid, 250 mL	8588B	N/A	Authority Required (STREAMLINED)
	150 mg tablet, 100	8584T	N/A	Authority Required (STREAMLINED)
	300 mg tablet, 100	8585W	N/A	Authority Required (STREAMLINED)
	600 mg tablet, 100	8586X	N/A	Authority Required (STREAMLINED)
Topiramate	15 mg capsule, 60	8371N	N/A	Authority Required (STREAMLINED)
	25 mg tablet, 60	8163P [5]	N/A	Authority Required (STREAMLINED)
	50 mg tablet, 60	8164Q [5]	N/A	Authority Required (STREAMLINED)
	25 mg capsule, 60	8372P	N/A	Authority Required (STREAMLINED)
	50 mg capsule, 60	8520K	N/A	Authority Required (STREAMLINED)
	100 mg tablet, 60	8165R [5]	N/A	Authority Required (STREAMLINED)
	200 mg tablet, 60	8166T	N/A	Authority Required (STREAMLINED)
Third-line AEDs				
Brivaracetam	10 mg/mL oral liquid, 300 mL	11349H	Initial treatment	Authority Required (STREAMLINED)
	10 mg/mL oral liquid, 300 mL	11358T	Continuing treatment	Authority Required (STREAMLINED)
	100 mg tablet, 56	11339T	Initial treatment	Authority Required (STREAMLINED)
	100 mg tablet, 56	11357R	Continuing treatment	Authority Required (STREAMLINED)
	25 mg tablet, 56	11327E	Continuing treatment	Authority Required (STREAMLINED)
	25 mg tablet, 56	11328F	Initial treatment	Authority Required (STREAMLINED)
	50 mg tablet, 56	11334M	Initial treatment	Authority Required (STREAMLINED)
	50 mg tablet, 56	11338R	Continuing treatment	Authority Required (STREAMLINED)

Drug	Form, strength & pack size	PBS code	Treatment phase	Restriction level
	75 mg tablet, 56	11350J	Continuing treatment	Authority Required (STREAMLINED)
	75 mg tablet, 56	11356Q	Initial treatment	Authority Required (STREAMLINED)
Perampanel	2 mg tablet, 7	10157N	Initial	Authority Required (STREAMLINED)
	2 mg tablet, 7	11436X	Initial treatment	Authority Required (STREAMLINED)
	6 mg tablet, 28	10163X	Continuing	Authority Required (STREAMLINED)
	6 mg tablet, 28	11407J	Continuing treatment	Authority Required (STREAMLINED)
	8 mg tablet, 28	10160R	Continuing	Authority Required (STREAMLINED)
	8 mg tablet, 28	11429M	Continuing treatment	Authority Required (STREAMLINED)
	10 mg tablet, 28	10151G	Continuing	Authority Required (STREAMLINED)
	10 mg tablet, 28	11428L	Continuing treatment	Authority Required (STREAMLINED)
	12 mg tablet, 28	10159Q	Continuing	Authority Required (STREAMLINED)
	12 mg tablet, 28	11409L	Continuing treatment	Authority Required (STREAMLINED)
	4 mg tablet, 28	10162W	Continuing	Authority Required (STREAMLINED)
	4 mg tablet, 28	11418Y	Continuing treatment	Authority Required (STREAMLINED)
Lacosamide	10 mg/mL oral liquid, 200 mL	11694L	Initial treatment Continuing treatment	Authority Required (STREAMLINED)
	10 mg/mL oral liquid, 200 mL	12628P	N/A	Authority Required (STREAMLINED)
	100 mg tablet, 56	12634Y	N/A	Authority Required (STREAMLINED)
	100 mg tablet, 56	9335H	Initial treatment Continuing treatment	Authority Required (STREAMLINED)
	150 mg tablet, 56	12627N	N/A	Authority Required (STREAMLINED)
	150 mg tablet, 56	9337K	Initial treatment Continuing treatment	Authority Required (STREAMLINED)
	200 mg tablet, 56	12658F	N/A	Authority Required (STREAMLINED)
	200 mg tablet, 56	9338L	Initial treatment Continuing treatment	Authority Required (STREAMLINED)
	50 mg tablet, 14	10293R	Continuing treatment	Authority Required (STREAMLINED)
	50 mg tablet, 14	12626M	N/A	Authority Required (STREAMLINED)
	50 mg tablet, 14	9333F	Initial treatment	Authority Required (STREAMLINED)
	100 mg tablet, 14	12633X	Dose titration at the start of therapy, during therapy or to gradually cease treatment	Authority Required (STREAMLINED)
	100 mg tablet, 14	9334G	Initial treatment	Authority Required (STREAMLINED)

Drug	Form, strength & pack size	PBS code	Treatment phase	Restriction level
	150 mg tablet, 14	12649R	Dose titration at the start of therapy, during therapy or to gradually cease treatment	Authority Required (STREAMLINED)
	150 mg tablet, 14	9336J	Initial treatment	Authority Required (STREAMLINED)
Cannabidiol	100 mg/mL oral liquid, 100 mL	12467E	N/A	Authority Required
Stiripentol	500 mg powder for oral liquid, 60 sachets	12088F	N/A	Authority Required (STREAMLINED)
	250 mg capsule, 60	12103B	N/A	Authority Required (STREAMLINED)
	250 mg powder for oral liquid, 60 sachets	12106E	N/A	Authority Required (STREAMLINED)
	500 mg capsule, 60	12107F	N/A	Authority Required (STREAMLINED)

[1] Dentist listings were excluded from the utilisation analysis.
[2] This item code was deleted from the PBS on 1 December 2022 but was included in the utilisation analysis.
[3] Palliative care listings were excluded from the utilisation analysis.
[4] This PBS code includes three indications – myoclonic epilepsy, malignant neoplasia (late stage) and insomnia.
[5] This PBS code includes two indications – seizures and migraine.

Results

Patient utilisation trends

Prevalence, incidence and patient demographics

Figure 1 shows the number of prevalent, incident (initiating) and re-initiating patients to PBS-listed AED therapy in the epilepsy patient cohort by year of supply from 2018 to 2022.

Note that the incident patient count starts one year after the prevalent patient count. This is because if a patient's first prescription in the data is in the first year of the data period (2018), it is not clear if this is their initiating prescription, or a continuing prescription and they initiated prior to the data period. Therefore, the use of a 12 month "no prescription" waiting period provides a reasonable degree of confidence that a patient's first prescription in the data is their initiating prescription.

Re-initiating patients are patients who have had a longer than 12 month gap in PBS-listed AED therapy before re-initiating.

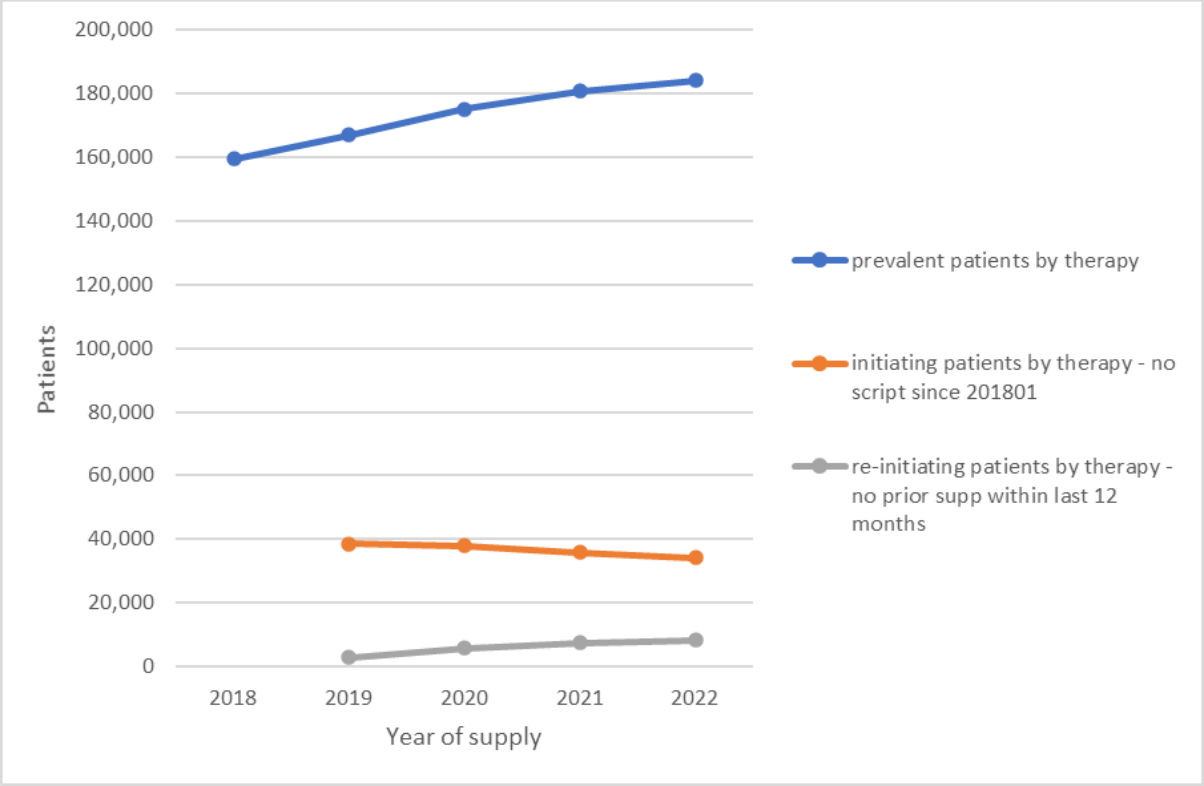

Figure 1: Prevalent, incident (first initiating) and re-initiating patients to PBS-listed AED therapy in the epilepsy patient cohort by year of supply (2018-2022)

As shown in Figure 1, the number of patients in the epilepsy patient cohort prevalent to a PBS-listed AED increased from 159,356 in 2018 to 184,043 in 2022 (an increase of 15.5%). The number of patients in the epilepsy patient cohort incident (initiating) to a PBS-listed AED declined from 38,549 in 2019 to 34,125 in 2022 (a decrease of 11.5%).

Figure 2 shows the number of prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by drug and year of supply from 2018 to 2022. *Note that patients can be prevalent to more than one AED in a year.* In terms of prevalent patients, LEV (78,270 prevalent patients in 2022), LTG (55,952 prevalent patients in 2022) and valproate (34,018 prevalent patients in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort.

Figure 3 shows the number of incident (initiating) patients to PBS-listed AED therapy in the epilepsy patient cohort by drug and year of supply from 2019 to 2022. *Note that patients can be incident to more than one AED in a year.* In terms of incident (initiating) patients, LEV (16,814 incident patients in 2022), gabapentin (11,531 incident patients in 2022) and LTG (10,386 incident patients in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort.

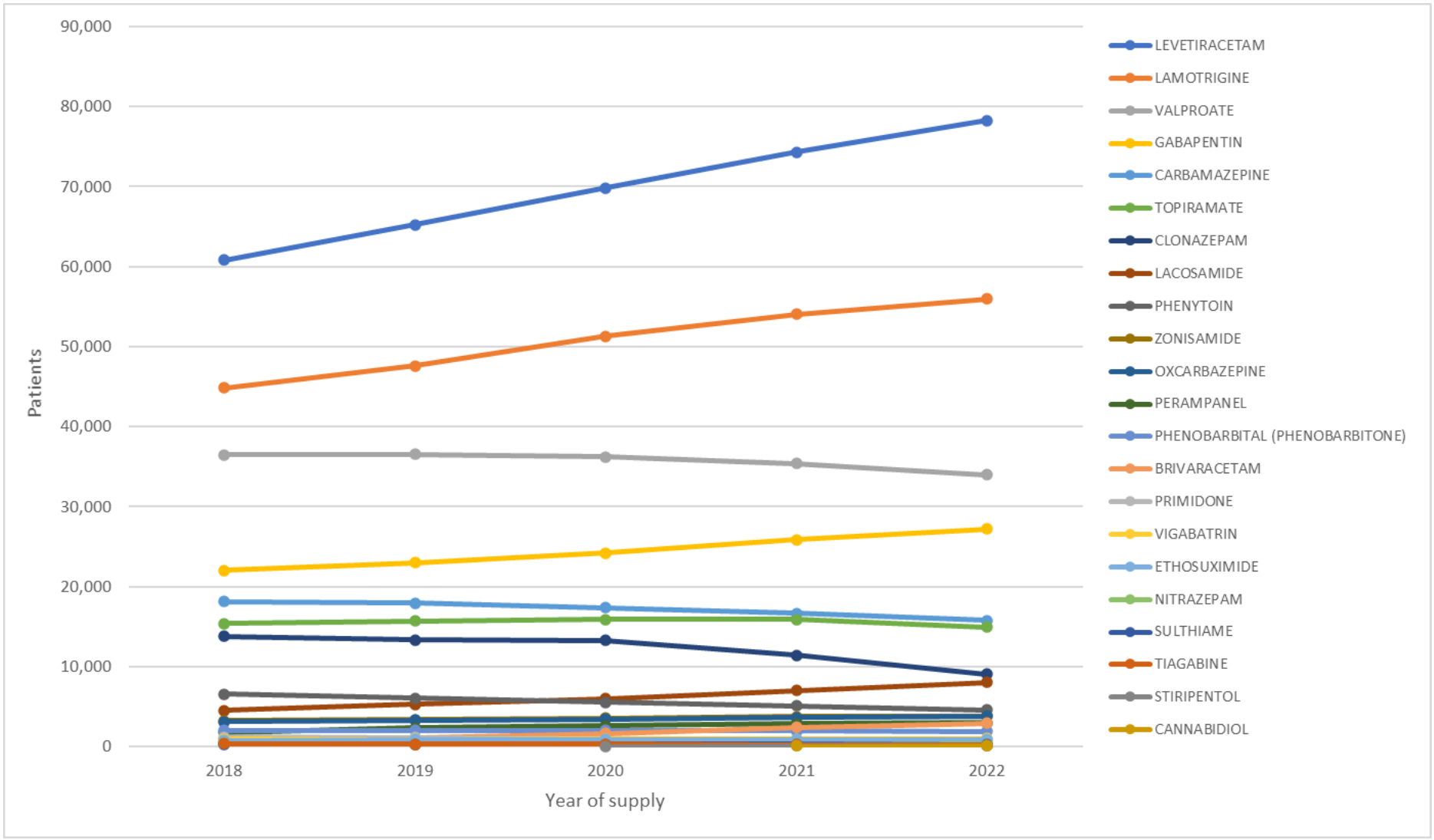

Figure 2: Prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by drug and year of supply (2018-2022)

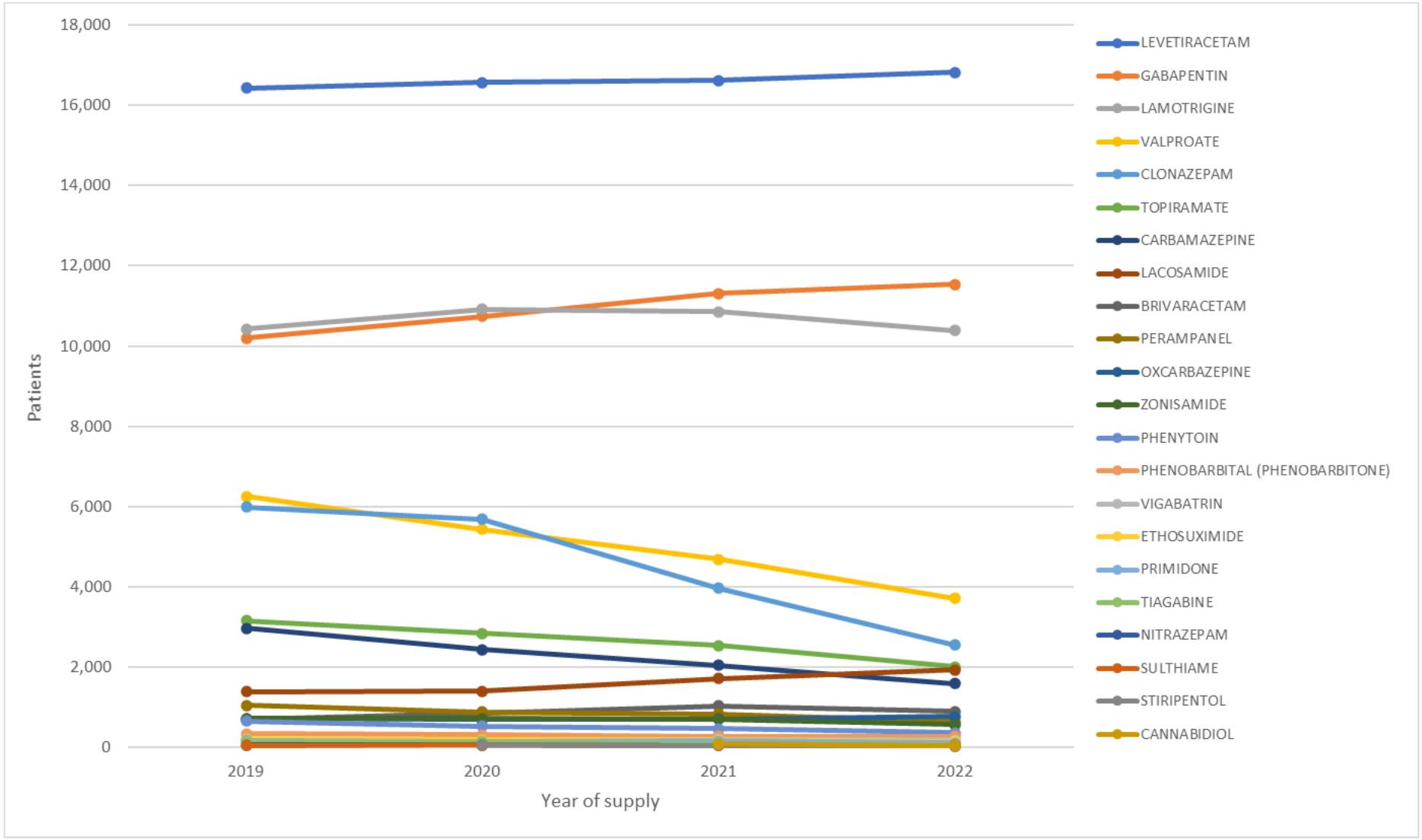

Figure 3: Incident (initiating) patients to PBS-listed AED therapy in the epilepsy patient cohort by drug and year of supply (2019-2022)

Figure 4 shows the number of prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by age and gender in 2022. Note that age and gender data was based on the patient details associated with their first prescription in 2022. Therefore, even if a patient changes age group during 2022, they will not be double counted in that year.

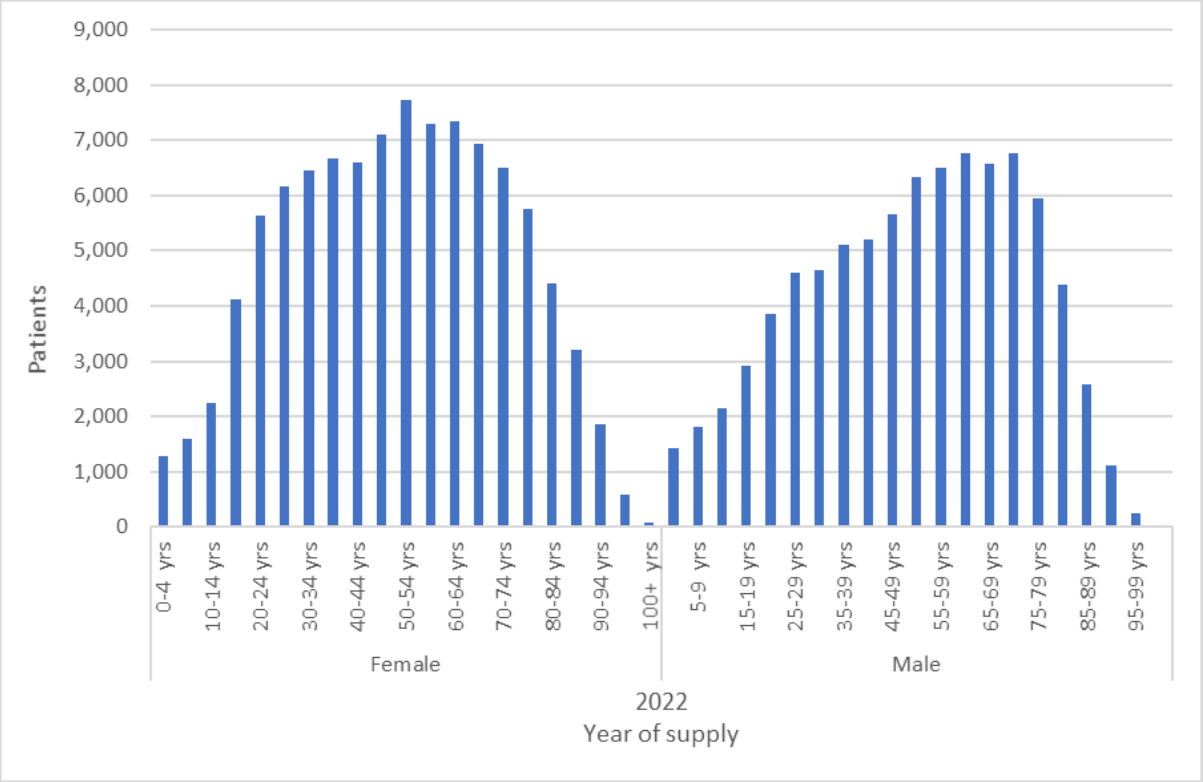

Figure 4: Prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by age and gender (2022)

As shown in Figure 4, there were more females (99,490 patients) than males (84,553 patients) prevalent to a PBS-listed AED in the epilepsy patient cohort in 2022, and utilisation peaks at 50-54 years in females and 70-74 years in males.

Figure 5 shows the number of prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by age, gender and drug in 2022. LTG was the most utilised PBS-listed AED for females aged 15-54 years in the epilepsy patient cohort, whilst LEV was the most utilised PBS-listed AED for females aged 55 years and over. LEV was the most utilised PBS-listed AED for males in the epilepsy patient cohort across all ages, except in males aged 25-29 years, where LTG had the highest utilisation.

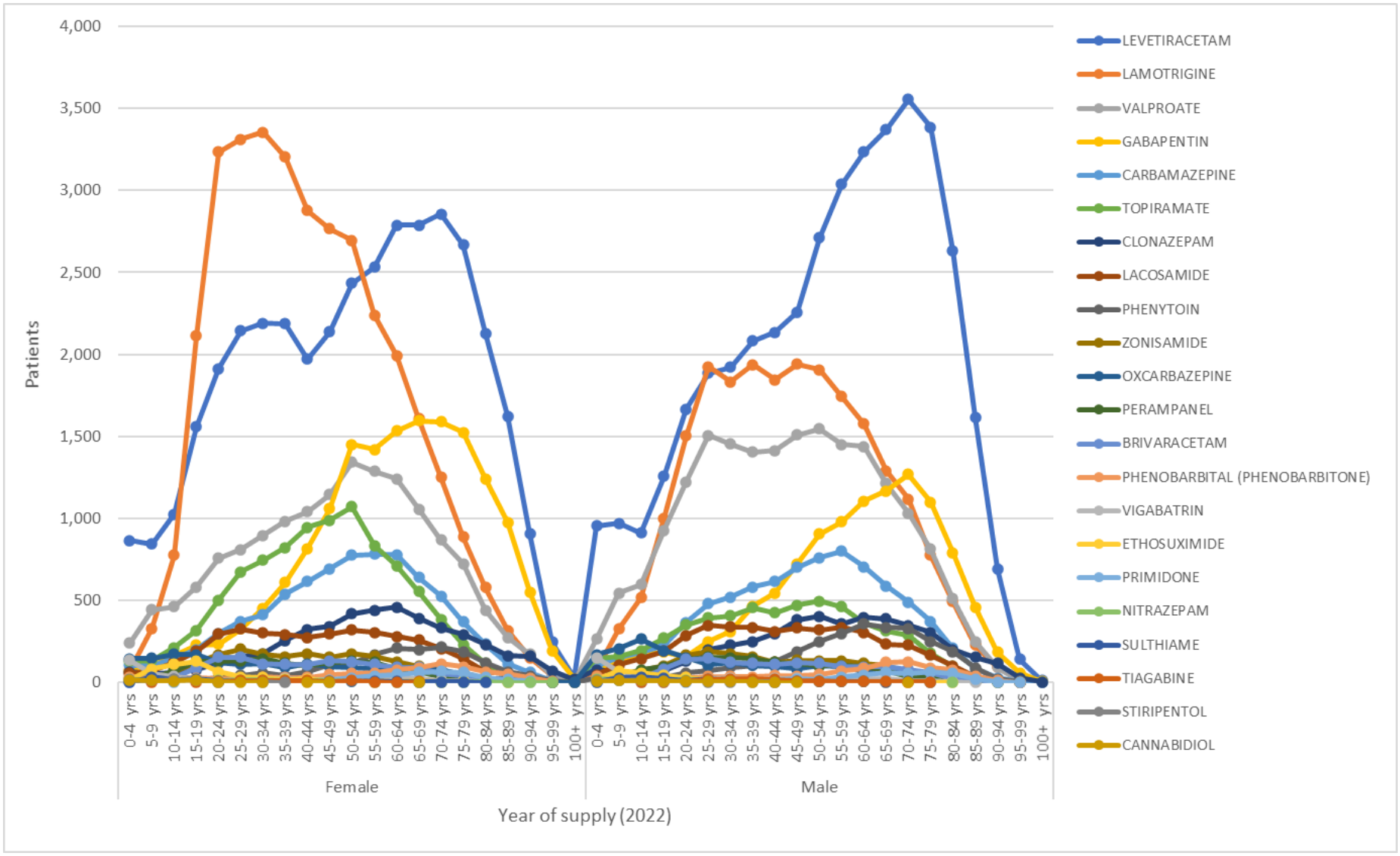

Figure 5: Prevalent patients to PBS-listed AED therapy in the epilepsy patient cohort by age, gender and drug (2022)

Drug sequence analysis

In order to investigate how PBS-listed AEDs are used concomitantly and to determine the extent of monotherapy versus combination therapy, a drug sequence analysis was conducted in the epilepsy patient cohort.

Table 3 shows the most utilised drug sequences by the number of patients treated in the epilepsy patient cohort who commenced PBS-listed AED treatment between 1 January 2019 to 31 January 2023. Because patients in the epilepsy patient cohort who commenced AED therapy in 2018 may be continuing patients from 2017, these patients have been excluded from the analysis.

Whilst the below sequence analysis does not show concomitant PBS-listed AED use directly, if different AEDs are supplied on the same day, or the sequence alternates between two AEDs, then this provides some evidence of concomitant use.

Table 3: Most utilised drug sequences by the number of patients treated in the epilepsy patient cohort who commenced PBS-listed AED treatment between 1 January 2019 to 31 January 2023

Drug sequences	Patients
LEVETIRACETAM	40,898
GABAPENTIN	36,478
LAMOTRIGINE	24,231
CLONAZEPAM	10,609
TOPIRAMATE	4,484
VALPROATE->LAMOTRIGINE	1,236
LEVETIRACETAM->VALPROATE	1,145
VALPROATE->LEVETIRACETAM	1,077
OXCARBAZEPINE	647
LAMOTRIGINE->VALPROATE	602
CARBAMAZEPINE->LEVETIRACETAM	587
LEVETIRACETAM->LAMOTRIGINE	492
CARBAMAZEPINE->GABAPENTIN	485
PHENOBARBITAL (PHENOBARBITONE)	383
LACOSAMIDE	347
LEVETIRACETAM->CLONAZEPAM	337
CARBAMAZEPINE->LAMOTRIGINE	311
TIAGABINE	310
VALPROATE->GABAPENTIN	301
LEVETIRACETAM->CARBAMAZEPINE	296
GABAPENTIN->CARBAMAZEPINE	291
GABAPENTIN->VALPROATE	284
ZONISAMIDE	235
TOPIRAMATE->LAMOTRIGINE	233
VALPROATE->CLONAZEPAM	231
LAMOTRIGINE->LEVETIRACETAM	194
LEVETIRACETAM->VALPROATE(sd)	188
LEVETIRACETAM->VALPROATE->LEVETIRACETAM	186
LEVETIRACETAM->CLONAZEPAM->LEVETIRACETAM	179
TOPIRAMATE->GABAPENTIN	172
LAMOTRIGINE->TOPIRAMATE	162
CARBAMAZEPINE->OXCARBAZEPINE	153
PHENYTOIN->LEVETIRACETAM	147
VIGABATRIN	143
VALPROATE->LAMOTRIGINE->VALPROATE	136
GABAPENTIN->TOPIRAMATE	136
LEVETIRACETAM->BRIVARACETAM	136
VALPROATE->LEVETIRACETAM->VALPROATE	132
LEVETIRACETAM->LAMOTRIGINE->LEVETIRACETAM->LAMOTRIGINE	130
LAMOTRIGINE->CARBAMAZEPINE	129
LEVETIRACETAM->VALPROATE->LEVETIRACETAM->VALPROATE	128
LEVETIRACETAM->LACOSAMIDE	121
VALPROATE->TOPIRAMATE	120
BRIVARACETAM	113
VALPROATE->LEVETIRACETAM->VALPROATE(sd)->LEVETIRACETAM	111
LEVETIRACETAM->LAMOTRIGINE->LEVETIRACETAM(sd)->LAMOTRIGINE	110
CLONAZEPAM->VALPROATE	106

(sd) = same day of supply as the previous drug in the sequence

Only drug sequences including more than 100 patients treated have been presented in the table above.

Table 4 shows the most utilised drug initiation sequences by the number of patients treated in the epilepsy patient cohort who commenced PBS-listed AED treatment between 1 January 2019 to 31 January 2023. Because patients in the epilepsy patient cohort who commenced AED therapy in 2018 may be continuing patients from 2017, these patients have been excluded from the analysis.

Note: The analysis presented in Table 4 is similar to that presented in Table 3 above, except that Table 4 shows the sequence of drug initiations in the epilepsy patient cohort (i.e., a drug is not repeated in the sequence).

Table 4: Most utilised drug initiation sequences by the number of patients treated in the epilepsy patient cohort who commenced PBS-listed AED treatment between 1 January 2019 to 31 January 2023

Drug initiation sequences	Patients
LEVETIRACETAM	40,898
GABAPENTIN	36,478
LAMOTRIGINE	24,231
CLONAZEPAM	10,609
TOPIRAMATE	4,484
LEVETIRACETAM->VALPROATE	2,228
VALPROATE->LEVETIRACETAM	2,014
VALPROATE->LAMOTRIGINE	1,978
LEVETIRACETAM->LAMOTRIGINE	1,428
LAMOTRIGINE->VALPROATE	884
CARBAMAZEPINE->LEVETIRACETAM	857
LEVETIRACETAM->CARBAMAZEPINE	722
LEVETIRACETAM->CLONAZEPAM	691
OXCARBAZEPINE	647
CARBAMAZEPINE->GABAPENTIN	622
VALPROATE->GABAPENTIN	477
LEVETIRACETAM->VALPROATE(sd)	475
CARBAMAZEPINE->LAMOTRIGINE	447
LAMOTRIGINE->LEVETIRACETAM	439
LEVETIRACETAM->LACOSAMIDE	432
GABAPENTIN->VALPROATE	429
VALPROATE->CLONAZEPAM	425
GABAPENTIN->CARBAMAZEPINE	403
PHENOBARBITAL (PHENOBARBITONE)	383
LACOSAMIDE	347
TOPIRAMATE->LAMOTRIGINE	319
TIAGABINE	310
LAMOTRIGINE->TOPIRAMATE	306
LEVETIRACETAM->TOPIRAMATE	257
ZONISAMIDE	235
LEVETIRACETAM->GABAPENTIN	227
TOPIRAMATE->GABAPENTIN	215
PHENYTOIN->LEVETIRACETAM	214
GABAPENTIN->TOPIRAMATE	208

VALPROATE->TOPIRAMATE	206
LAMOTRIGINE->CARBAMAZEPINE	198
LACOSAMIDE->LEVETIRACETAM(sd)	193
CARBAMAZEPINE->OXCARBAZEPINE	185
LEVETIRACETAM->OXCARBAZEPINE	184
LEVETIRACETAM->BRIVARACETAM	169
GABAPENTIN->LEVETIRACETAM	160
LAMOTRIGINE->VALPROATE(sd)	156
LAMOTRIGINE->LEVETIRACETAM(sd)	156
LAMOTRIGINE->GABAPENTIN	152
TOPIRAMATE->VALPROATE	151
LEVETIRACETAM->VALPROATE->LAMOTRIGINE	146
LEVETIRACETAM->PHENYTOIN	144
VIGABATRIN	143
CLONAZEPAM->VALPROATE	138
TOPIRAMATE->LEVETIRACETAM	137
VALPROATE->LEVETIRACETAM->LAMOTRIGINE	137
LEVETIRACETAM->PHENYTOIN(sd)	136
CARBAMAZEPINE->LEVETIRACETAM(sd)	136
GABAPENTIN->CLONAZEPAM	134
CLONAZEPAM->LEVETIRACETAM	130
GABAPENTIN->LAMOTRIGINE	129
CLONAZEPAM->LEVETIRACETAM(sd)	122
BRIVARACETAM	113

(sd) = same day of supply as the previous drug in the sequence
Only drug initiation sequences including more than 100 patients treated have been presented in the table above.

As shown in Table 4, monotherapy with LEV, gabapentin and LTG were the three most utilised PBS-listed AED initiation sequences in the epilepsy patient cohort. For drug initiation sequences consisting of two or more AEDs, LEV->valproate, valproate->LEV and valproate->LTG were the three most utilised treatment initiation sequences.

Prescription utilisation trends

Figure 6 shows the total number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort from 2018 to 2022.

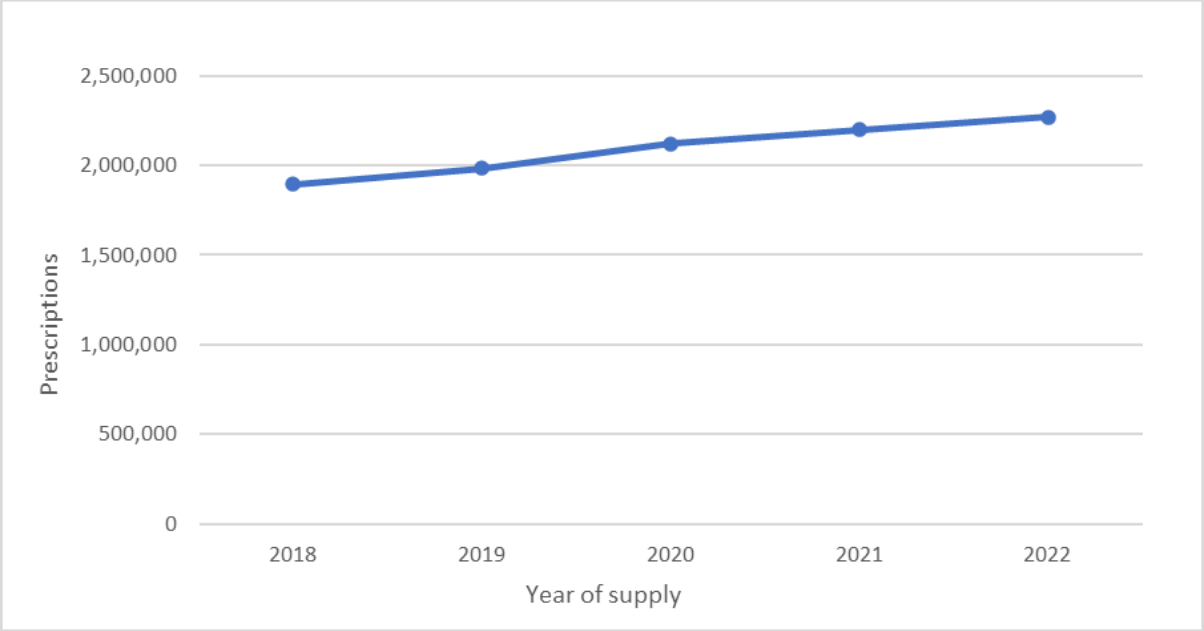

Figure 6: PBS-listed AED prescriptions supplied to the epilepsy patient cohort by year of supply (2018-2022)

As shown in Figure 6, the number of prescriptions for PBS-listed AEDs supplied to the epilepsy patient cohort increased from 1,893,392 in 2018 to 2,269,474 in 2022 (an increase of 19.9%).

Figure 7 shows the total PBS benefits paid (based on published prices) for PBS-listed AED prescriptions supplied to the epilepsy patient cohort from 2018 to 2022.

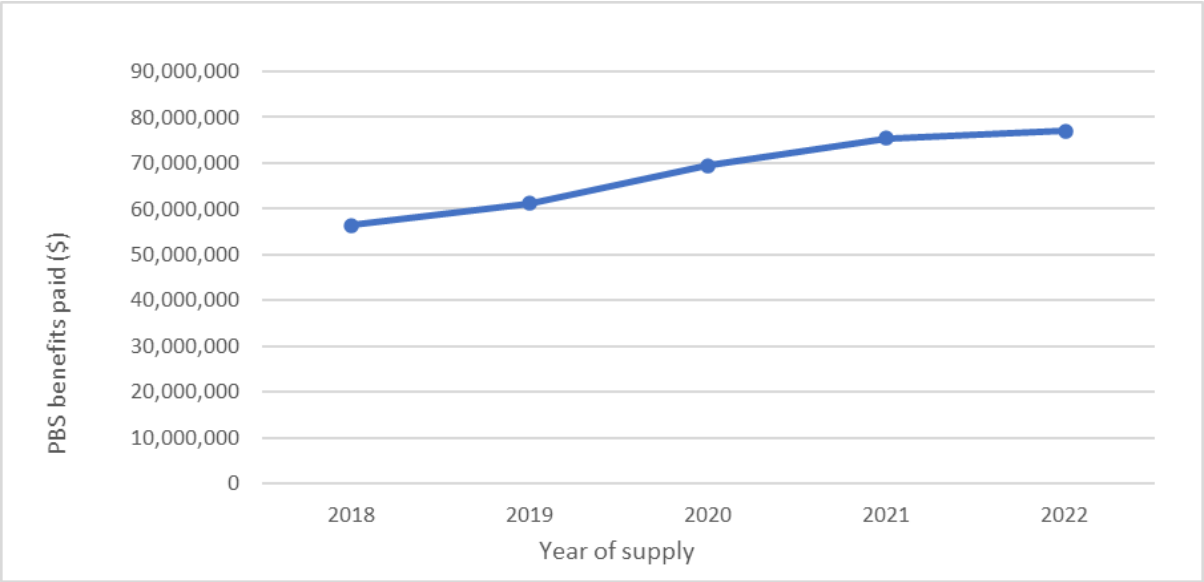

Figure 7: PBS benefits paid for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by year of supply (2018-2022) [published prices]

As shown in Figure 7, the PBS benefits paid for prescriptions for PBS-listed AEDs supplied to the epilepsy patient cohort increased from $56,497,715 in 2018 to $77,045,926 in 2022 (an increase of 36.4%).

Figure 8 shows the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug from 2018 to 2022. In terms of prescriptions supplied, LEV (800,384 prescriptions in 2022), LTG (567,972 prescriptions in 2022) and valproate (207,633

prescriptions in 2022) were the PBS-listed AEDs with the highest utilisation in the epilepsy patient cohort.

Figure 9 shows the market share based on the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug in 2022. Based on prescription numbers, LEV had the greatest market share (35%) followed by LTG (25%) and valproate (9%).

Figure 10 shows the PBS benefits paid (based on published prices) for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug from 2018 to 2022. LEV ($18,871,016 in 2022), lacosamide ($13,322,267 in 2022) and LTG ($8,324,978 in 2022) were the PBS-listed AEDs supplied to the epilepsy patient cohort that incurred the highest cost to the PBS.

Figure 11 shows the market share based on PBS benefits paid for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug in 2022. Based on PBS benefits paid, LEV had the greatest market share (24%) followed by lacosamide (17%) and LTG (11%).

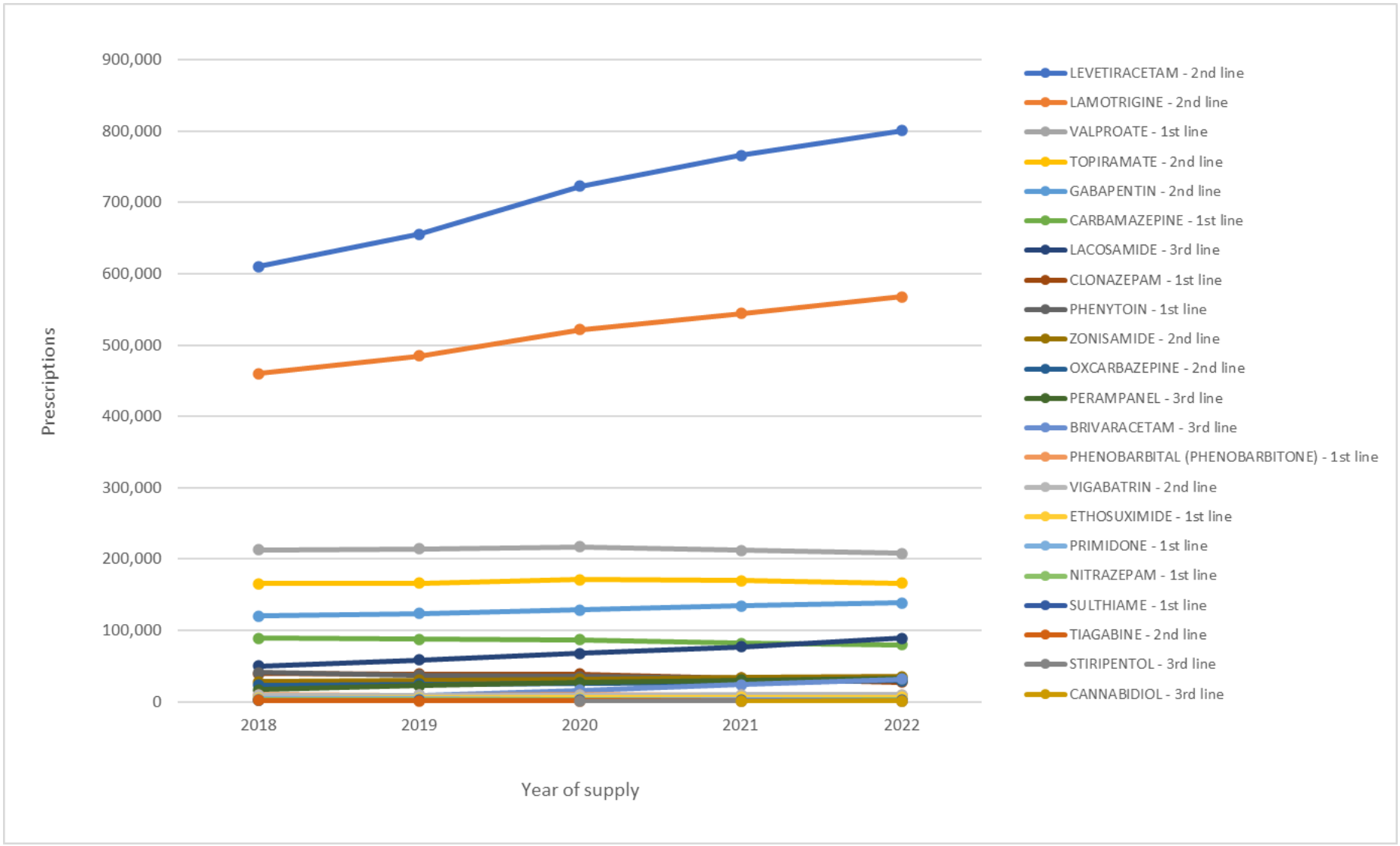

Figure 8: PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug and year of supply (2018-2022)

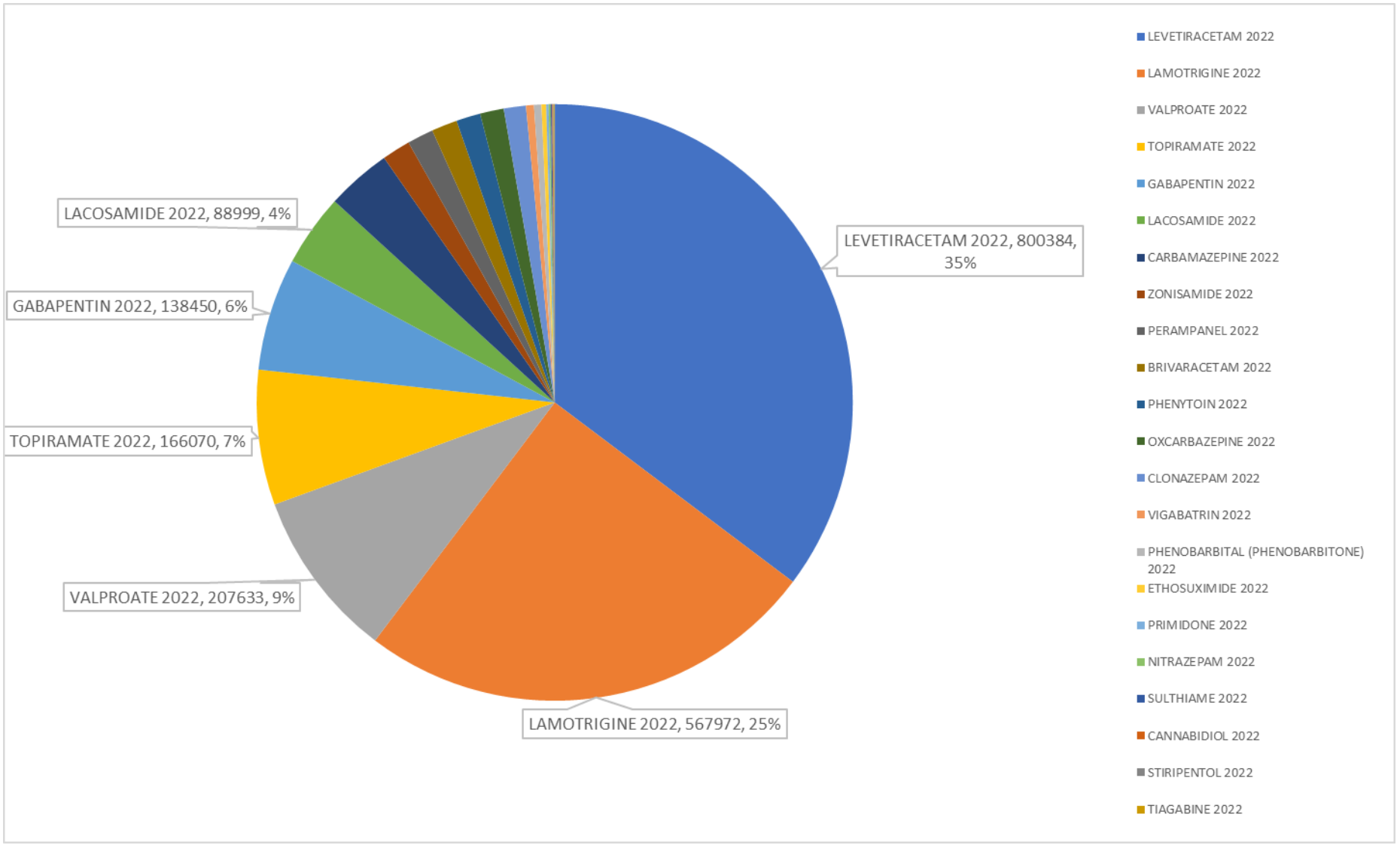

Figure 9: Market share based on the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug (2022)

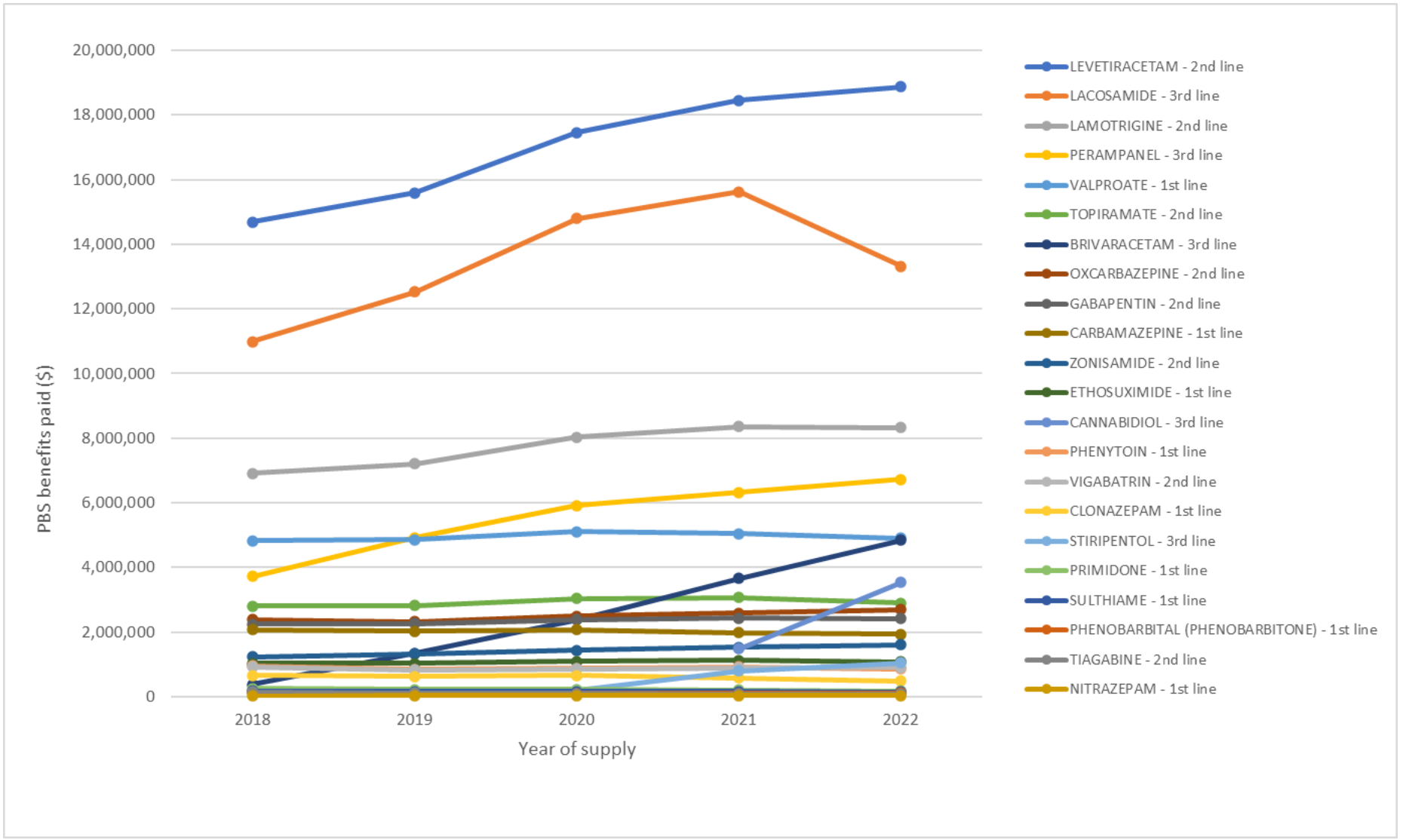

Figure 10: PBS benefits paid for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug and year of supply (2018-2022) [published prices]

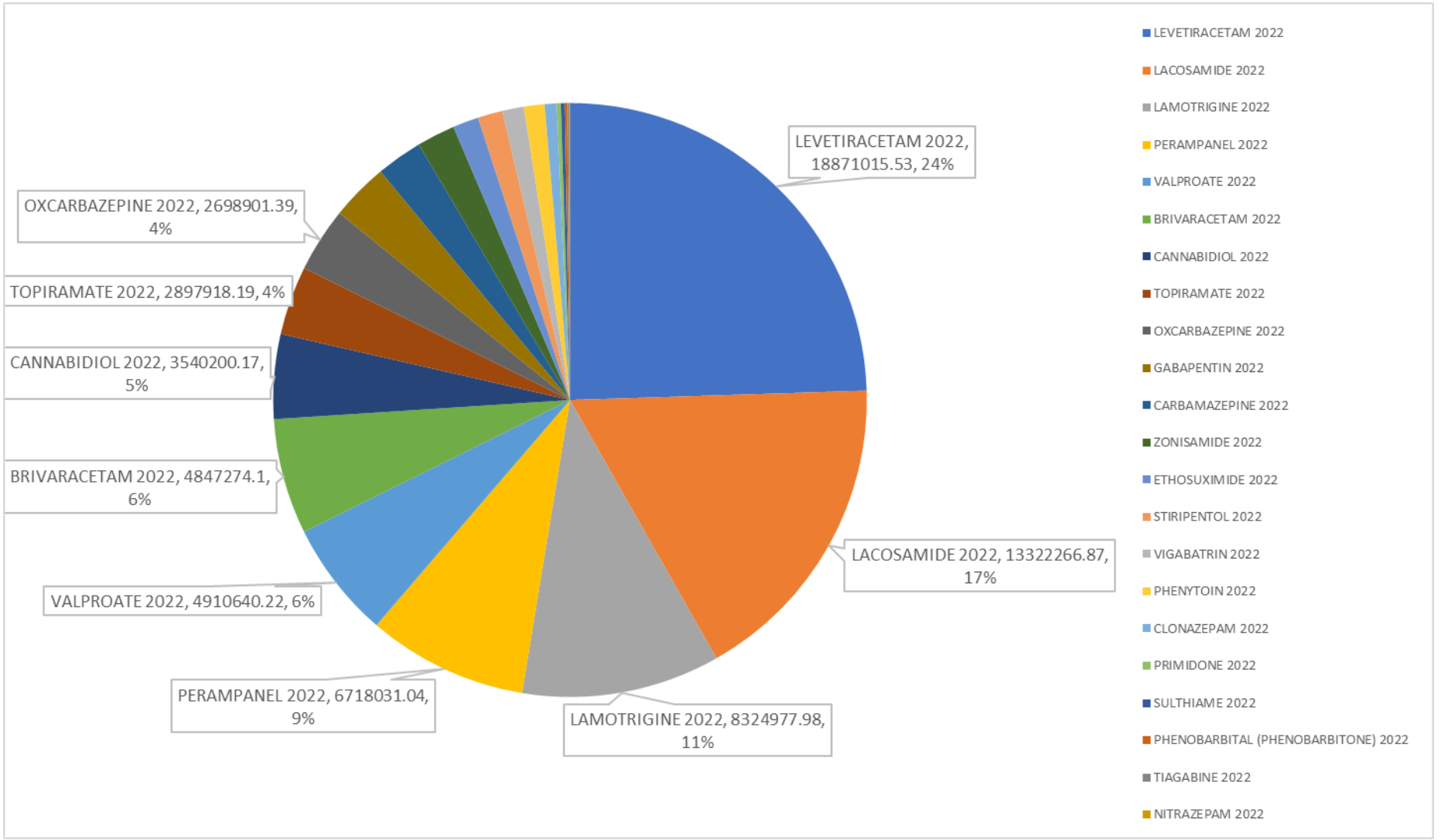

Figure 11: Market share based on PBS benefits paid for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by drug (2022) [based on published prices]

Line of therapy

As presented in Table 1, PBS-listed AEDs can be classified into three lines of therapy. The first-line AEDs listed on the PBS include carbamazepine, ethosuximide, phenobarbital, phenytoin, primidone, sulthiame, valproate, clonazepam and nitrazepam. The second-line AEDs listed on the PBS include gabapentin, LEV, tiagabine, zonisamide, LTG, vigabatrin, oxcarbazepine and topiramate. The third-line AEDs listed on the PBS include brivaracetam, perampanel, lacosamide, cannabidiol and stiripentol.

Figure 12 shows the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by line of therapy from 2018 to 2022.

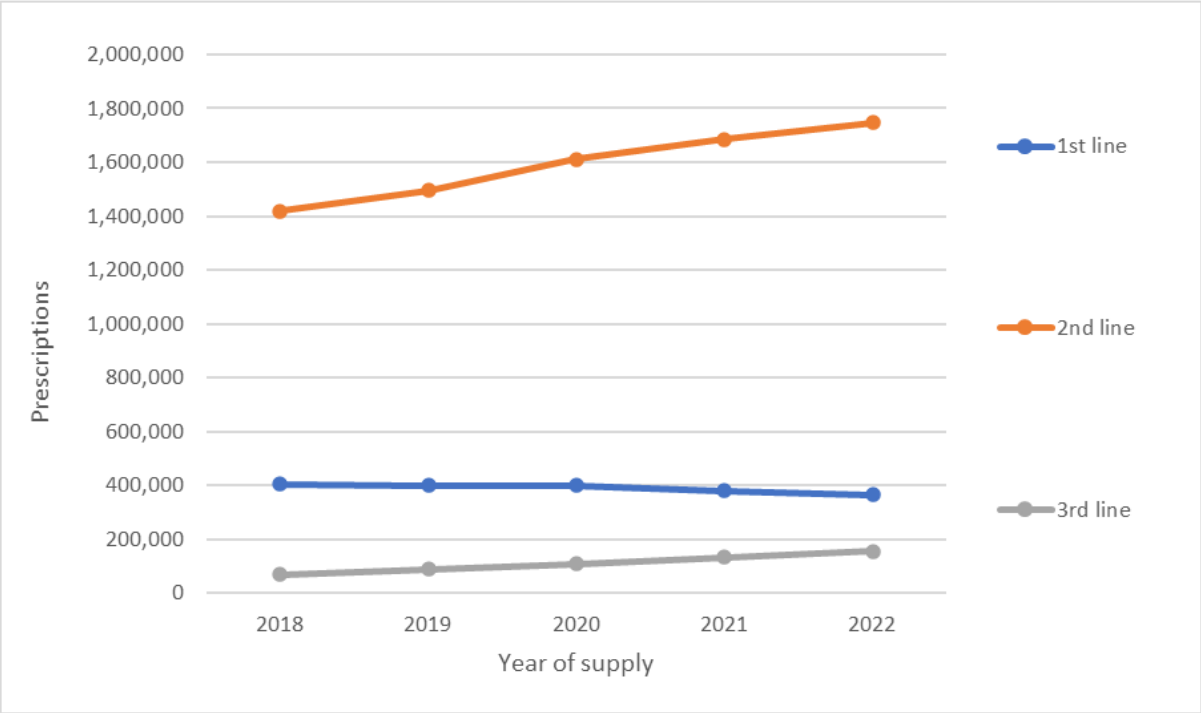

Figure 12: PBS-listed AED prescriptions supplied to the epilepsy patient cohort by line of therapy and year of supply (2018-2022)

As shown in Figure 12, the second-line PBS-listed AEDs had the highest utilisation in the epilepsy patient cohort (1,747,804 prescriptions in 2022), followed by the first-line AEDs (366,419 prescriptions in 2022) and the third-line AEDs (155,251 prescriptions in 2022).

Figure 13 shows the PBS benefits paid (based on published prices) for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by line of therapy from 2018 to 2022.

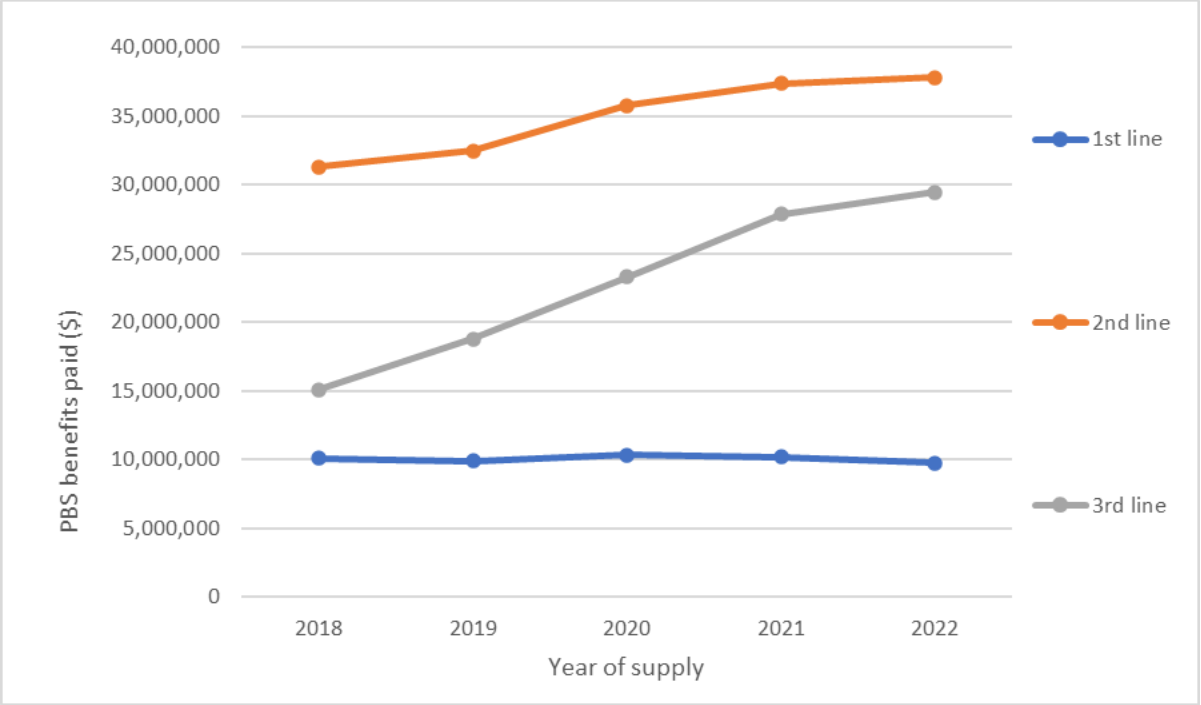

Figure 13: PBS benefits paid for PBS-listed AED prescriptions supplied to the epilepsy patient cohort by line of therapy and year of supply (2018-2022) [based on published prices]

As shown in Figure 13, the second-line PBS-listed AEDs incurred the highest cost to the PBS ($37,803,913 in 2022), followed by the third-line AEDs ($29,468,860 in 2022) and the first-line AEDs ($9,773,153 in 2022).

Prescriber type analysis

In order to investigate how PBS-listed AEDs are prescribed by health practitioners in Australian clinical practice, an analysis of prescriber types was conducted based on the AED prescriptions supplied to the epilepsy patient cohort via the PBS.

Figure 14 shows the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by prescriber type from 2018 to 2022. VRGPs prescribed the most prescriptions for PBS-listed AEDs to the epilepsy patient cohort (1,616,346 prescriptions in 2022), followed by neurologists (197,080 prescriptions in 2022) and GP trainees (166,132 prescriptions in 2022).

Figure 15 shows the number of PBS-listed AED prescriptions supplied to the epilepsy patient cohort by prescriber type and line of therapy from 2018 to 2022.

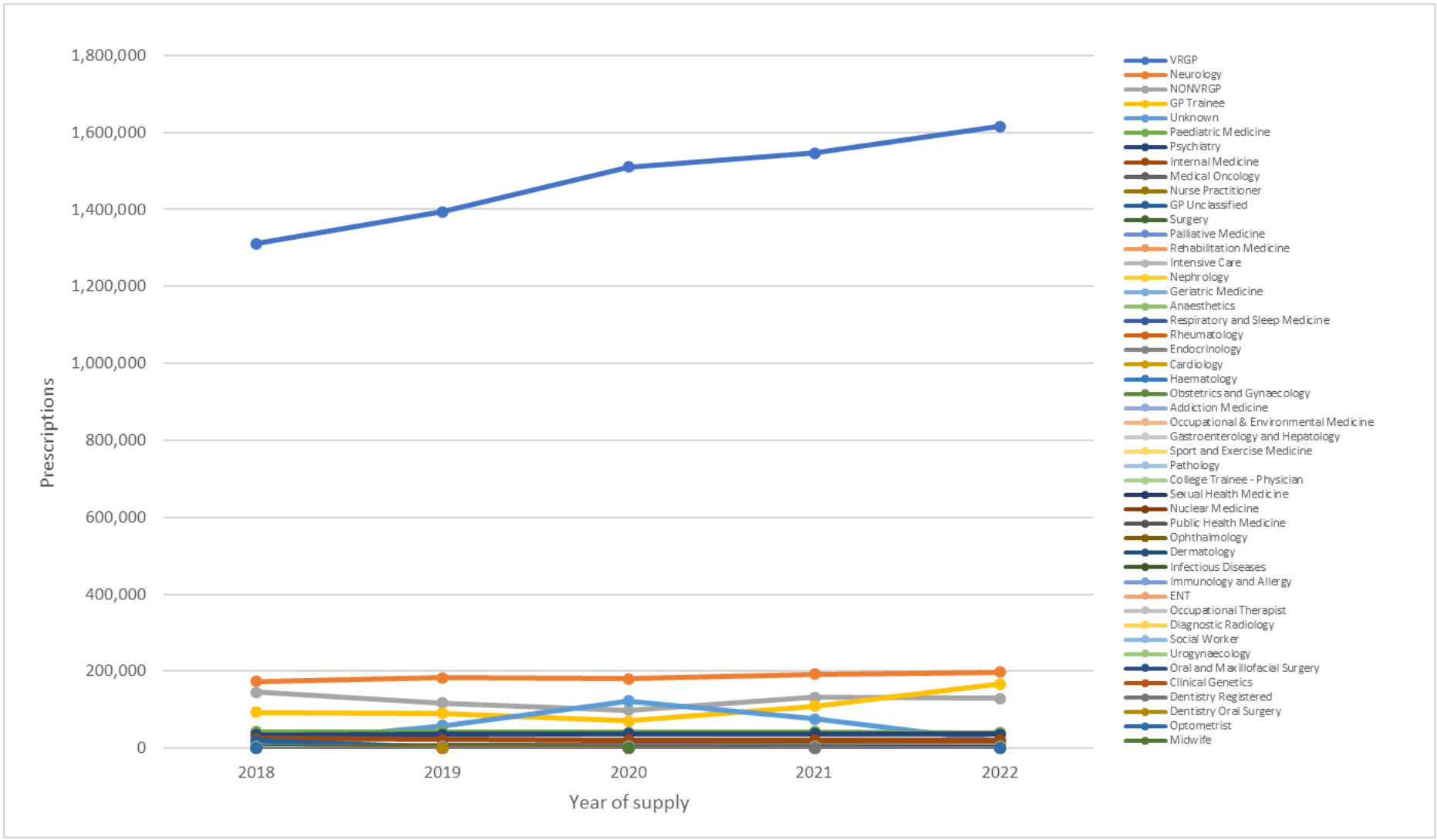

Figure 14: PBS-listed AED prescriptions supplied to the epilepsy patient cohort by prescriber type and year of supply (2018-2022)

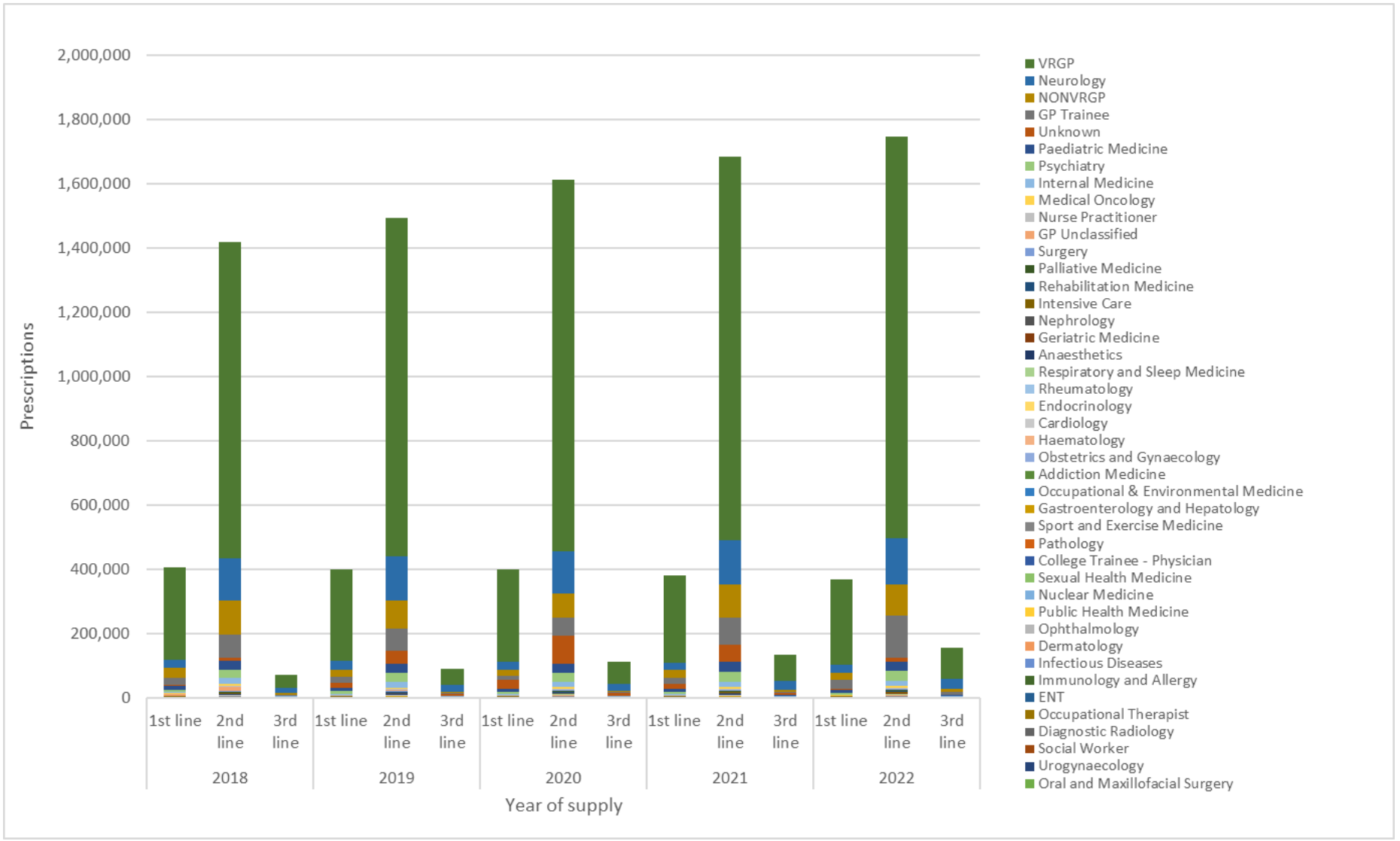

Figure 15: PBS-listed AED prescriptions supplied to the epilepsy patient cohort by prescriber type and line of therapy (2018-2022)

Prescriber compliance with the PBS restrictions for the third-line PBS-listed AEDs

Some of the PBS item codes for the third-line AEDs (brivaracetam, perampanel and lacosamide) require a prescription from a neurologist or paediatrician according to the PBS treatment criteria: *"must be treated by a neurologist" OR "must be treated by a paediatrician*." These item codes are presented in Table 5 below.

Table 5: PBS item codes for third-line AEDs that require a prescription from a neurologist or paediatrician

Third-line AED	PBS code	Treatment phase	Restriction level	PBS treatment criteria
Brivaracetam	11349H	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	11339T	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	11328F	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	11334M	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	11356Q	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
Perampanel	10157N	Initial	Authority Required (STREAMLINED)	Must be treated by a neurologist
	11436X	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
Lacosamide	9333F	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	12633X	Dose titration at the start of therapy, during therapy or to gradually cease treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist; OR Must be treated by a paediatrician.
	9334G	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist
	12649R	Dose titration at the start of therapy, during therapy or to gradually cease treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist; OR Must be treated by a paediatrician.
	9336J	Initial treatment	Authority Required (STREAMLINED)	Must be treated by a neurologist

An analysis of the prescriber type associated with prescriptions supplied to the epilepsy patient cohort under the PBS item codes above was conducted to assess prescriber compliance with the PBS restrictions (Figure 16).

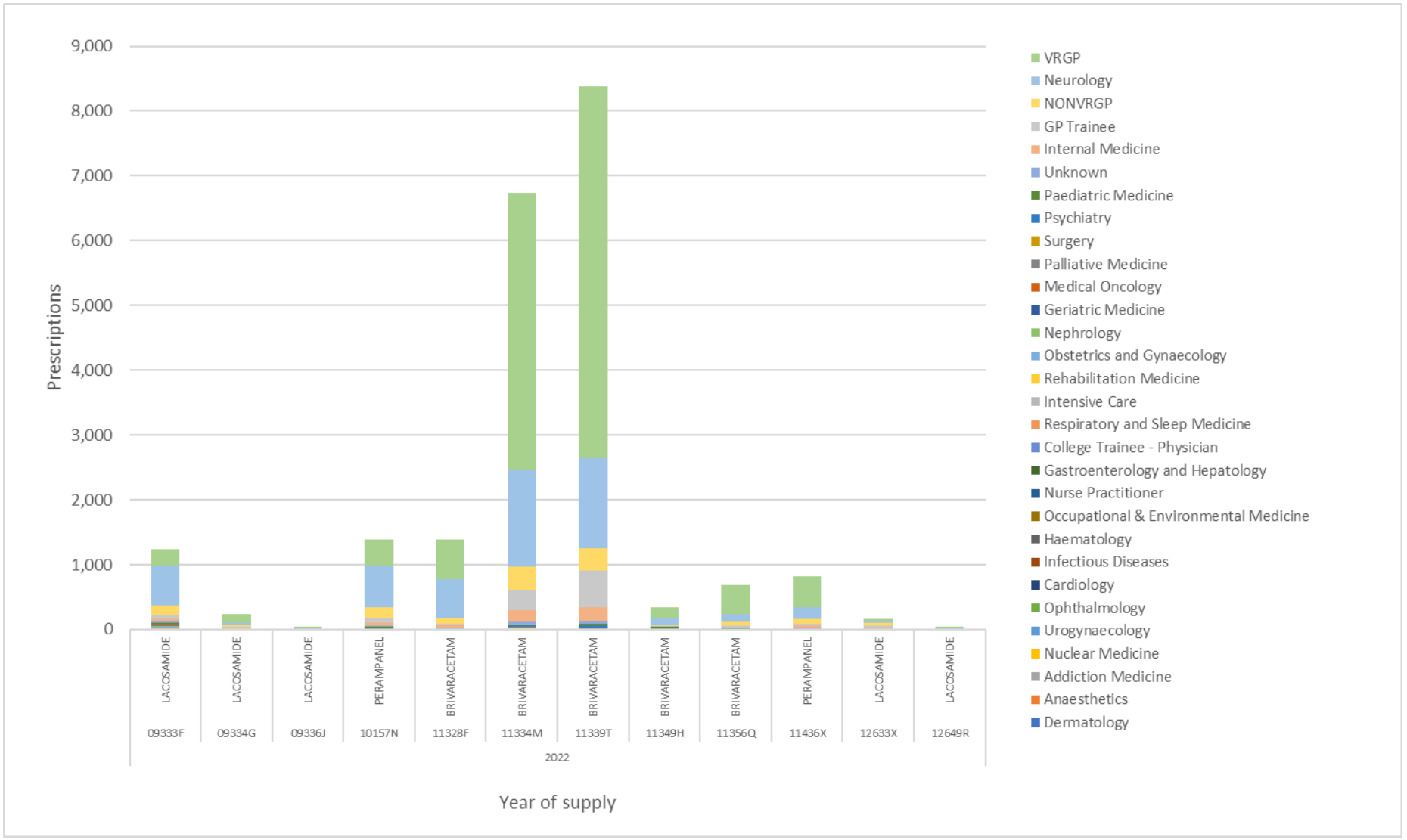

Figure 16: PBS item codes for third-line AEDs that require a prescription from a neurologist, or a paediatrician supplied to the epilepsy patient cohort by prescriber type (2022)

Figure 16 shows that a substantial number of prescriptions for third-line PBS-listed AEDs that require a prescription from a neurologist or paediatrician (e.g., brivaracetam and perampanel) were prescribed by GPs. This may be partly explained by prescribers/pharmacists selecting an incorrect PBS item code at the time of prescribing/dispensing. For example, a GP may intend to prescribe brivaracetam under a continuing treatment code, consistent with the PBS restrictions, but erroneously select a PBS code for initial treatment which requires a prescription from a neurologist.

Utilisation of LEV and LTG post-PBS changes in January 2021

As detailed above, the PBS restrictions for LEV and LTG were expanded on 1 January 2021 to allow for the first-line use of these medicines in women of childbearing potential. In order to understand the impact to the PBS of these changes, this section of the utilisation analysis looks specifically at the utilisation of LEV and LTG in the epilepsy patient cohort during the period 1 January 2018 to 31 December 2022.

Figure 17 shows the number of prescriptions for LEV and LTG supplied to the epilepsy patient cohort by quarter from 2018 to 2022.

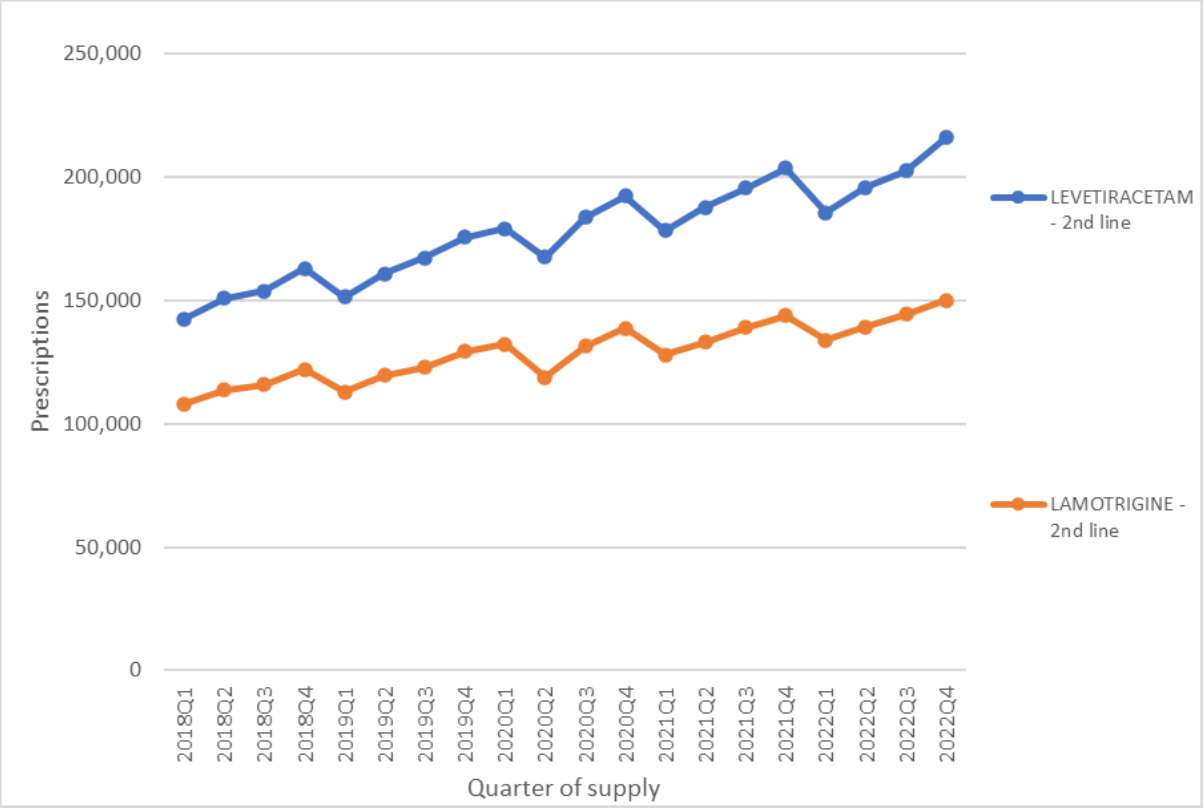

Figure 17: LEV and LTG prescriptions supplied to the epilepsy patient cohort by quarter of supply (2018-2022)

Figure 18 shows the PBS benefits paid for LEV and LTG prescriptions supplied to the epilepsy patient cohort by quarter from 2018 to 2022.

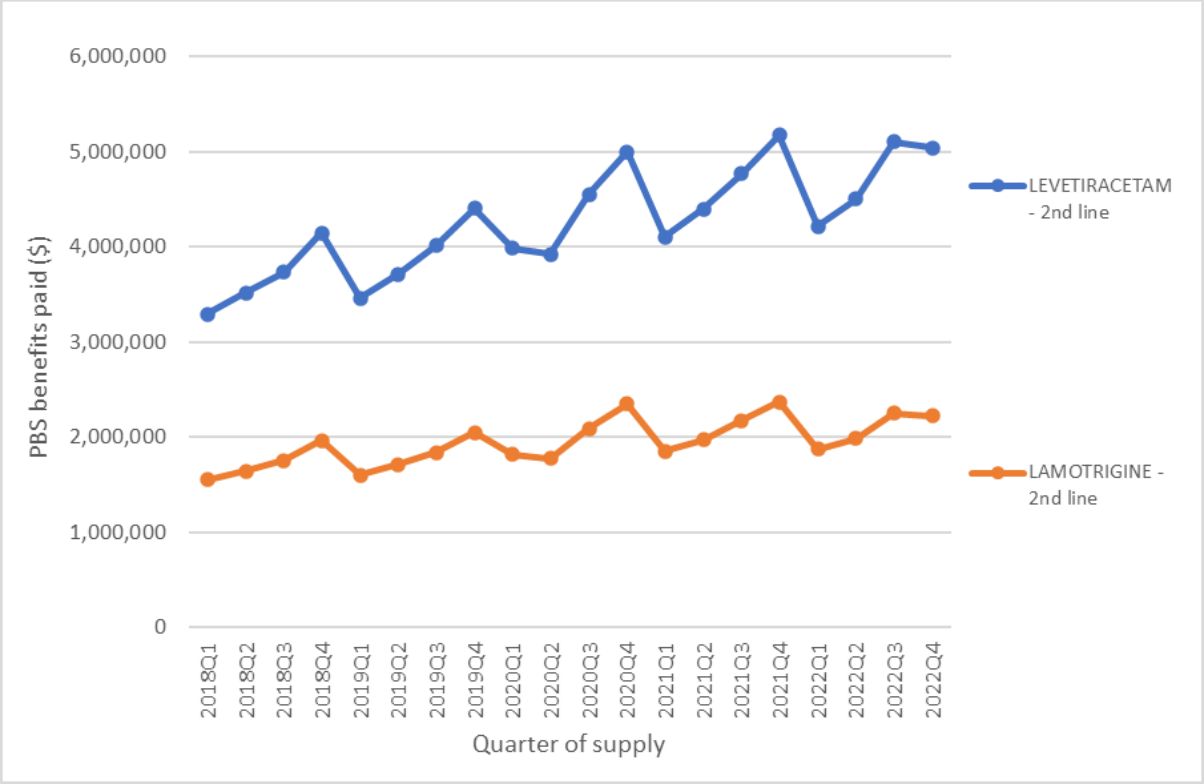

Figure 18: PBS benefits paid for LEV and LTG prescriptions supplied to the epilepsy patient cohort by quarter of supply (2018-2022)

Figure 19 shows the number of women of childbearing potential (i.e., female patients aged 15-49 years[1]) within the epilepsy patient cohort prevalent to LEV and LTG by year of supply from 2018 to 2022. *Note that patients can be prevalent to more than one AED in a year.*

Figure 20 shows the number of women of childbearing potential[1] within the epilepsy patient cohort incident (initiating) to LEV and LTG by year of supply from 2019 to 2022. *Note that the incident patient count starts one year after the prevalent patient count and that patients can be incident to more than one AED in a year.*

[1] Women of childbearing potential were defined in accordance with the World Health Organization (WHO) definition i.e., women aged 15-49 years. https://www.who.int/data/gho/indicator-metadata-registry/imr-details/women-of-reproductive-age-(15-49-years)-population-(thousands). Accessed 5 July 2023.

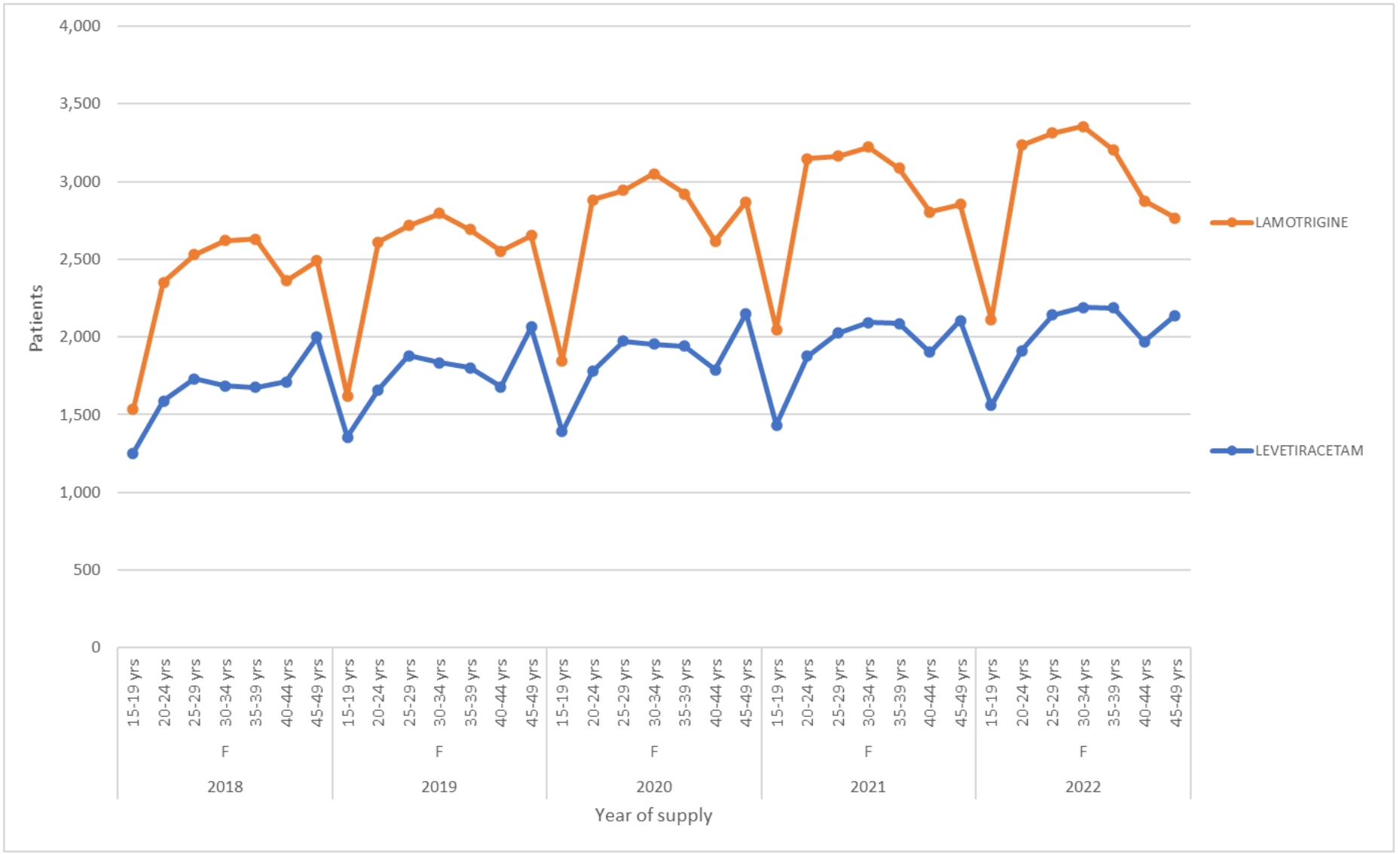

Figure 19: Women of childbearing potential within the epilepsy patient cohort prevalent to LEV and LTG by year of supply (2018-2022)

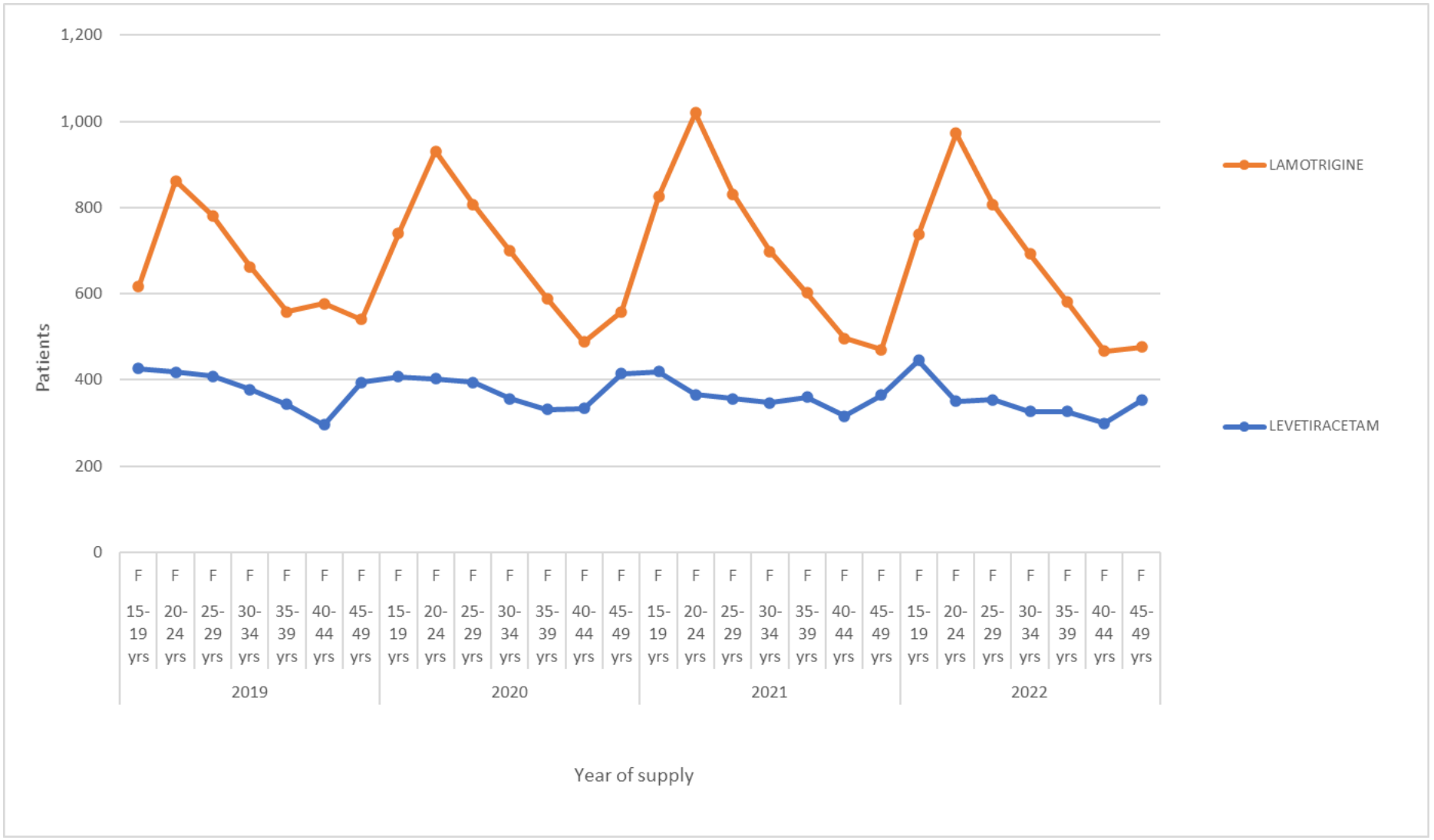

Figure 20: Women of childbearing potential within the epilepsy patient cohort incident (initiating) to LEV and LTG by year of supply (2019-2022)

Based on Figures 17-20, there was no clear impact to the utilisation trends of LEV and LTG after the PBS restrictions for these medicines were expanded on 1 January 2021 to allow for their first-line use in women of childbearing potential. This is consistent with the PBAC's September 2020 advice that prescribing these medicines first-line in women of childbearing potential was likely already occurring in practice.

Utilisation of the third-line PBS-listed AEDs after the PBS changes to LEV and LTG in January 2021

As illustrated in Table 1, the PBS restrictions for the third-line PBS-listed AEDs indicated for intractable partial epileptic seizures (brivaracetam, perampanel and lacosamide) require that a patient use these medicines: *"in combination with two or more anti-epileptic drugs which includes one second-line adjunctive agent" AND that "the condition must have failed to be controlled satisfactorily by other anti-epileptic drugs, which includes at least one first-line anti-epileptic agent and at least two second-line adjunctive anti-epileptic agents."*

In addition, the PBS restrictions for the third-line PBS-listed AEDs indicated for idiopathic generalised epilepsy with primary generalised tonic-clonic seizures (perampanel and lacosamide) require that a patient use these medicines: *"in combination with at least one PBS-subsidised anti-epileptic drug" AND that "the condition must have failed to be controlled satisfactorily by at least two anti-epileptic drugs."*

In order to assess whether allowing the first-line use of LEV and LTG in women of childbearing potential had flow-on effects to the utilisation of the third-line PBS-listed AEDs, this section of the utilisation analysis looks specifically at the utilisation of brivaracetam, perampanel and lacosamide in the women of childbearing potential included in the epilepsy patient cohort during the period 1 January 2018 to 31 December 2022.

Note: This analysis excludes the additional third-line PBS-listed AEDs, cannabidiol (PBS-listed May 2021) and stiripentol (PBS-listed August 2021), as these medicines were listed after the restriction changes were made to LEV and LTG in January 2021. Furthermore, because these medicines are PBS-listed for severe myoclonic epilepsy in infancy (Dravet syndrome) utilisation in the women of childbearing potential population is low.

Figure 21 shows the number of women of childbearing potential (i.e., female patients aged 15-49 years) within the epilepsy patient cohort prevalent to brivaracetam, perampanel and lacosamide by year of supply from 2018 to 2022. *Note that patients can be prevalent to more than one of these AEDs in a year.*

Figure 22 shows the number of women of childbearing potential within the epilepsy patient cohort incident (initiating) to brivaracetam, perampanel and lacosamide by year of supply from 2019 to 2022. *Note that the incident patient count starts one year after the prevalent patient count and that patients can be incident to more than one of these AEDs in a year.*

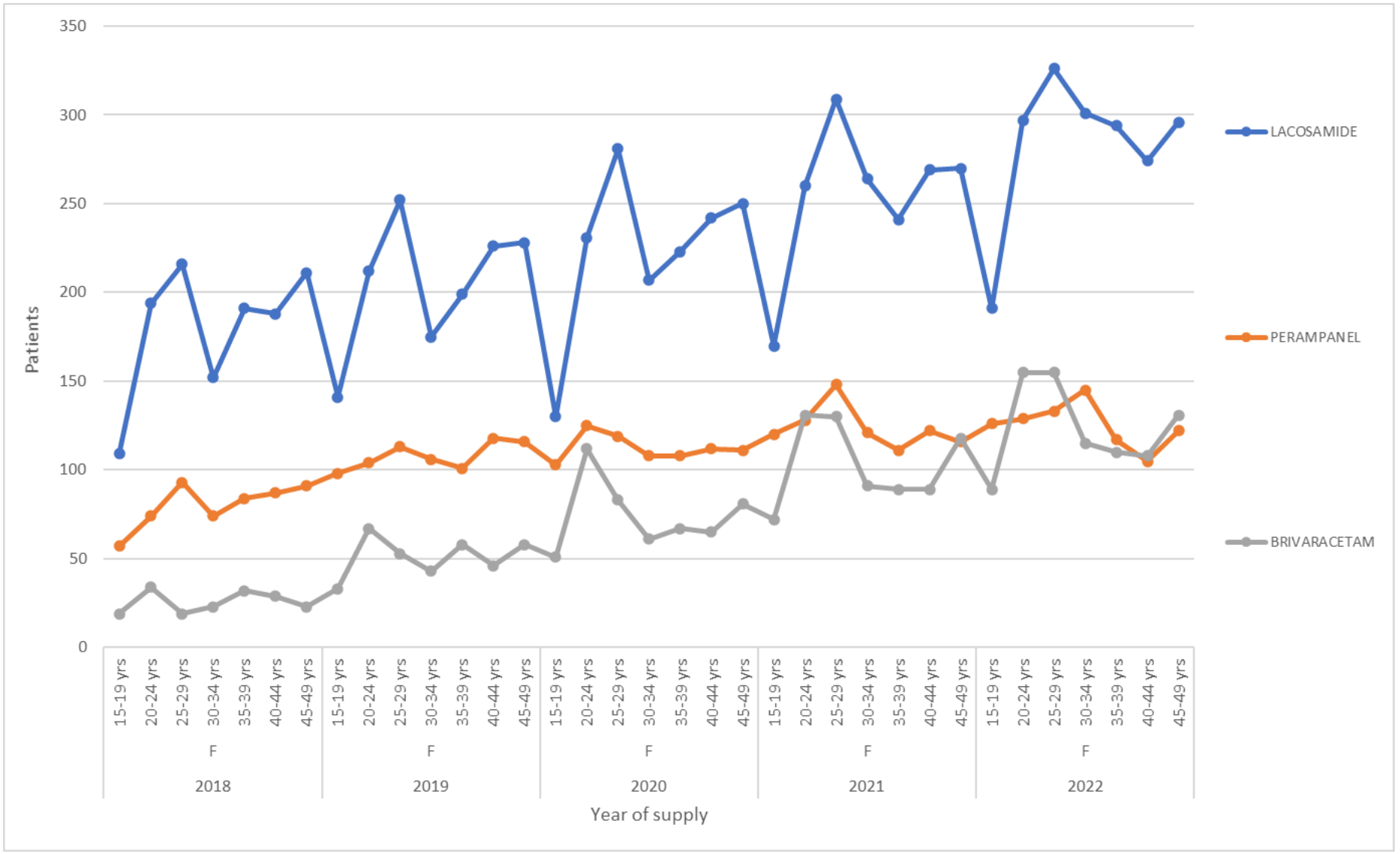

Figure 21: Women of childbearing potential within the epilepsy patient cohort prevalent to brivaracetam, perampanel and lacosamide by year of supply (2018-2022)

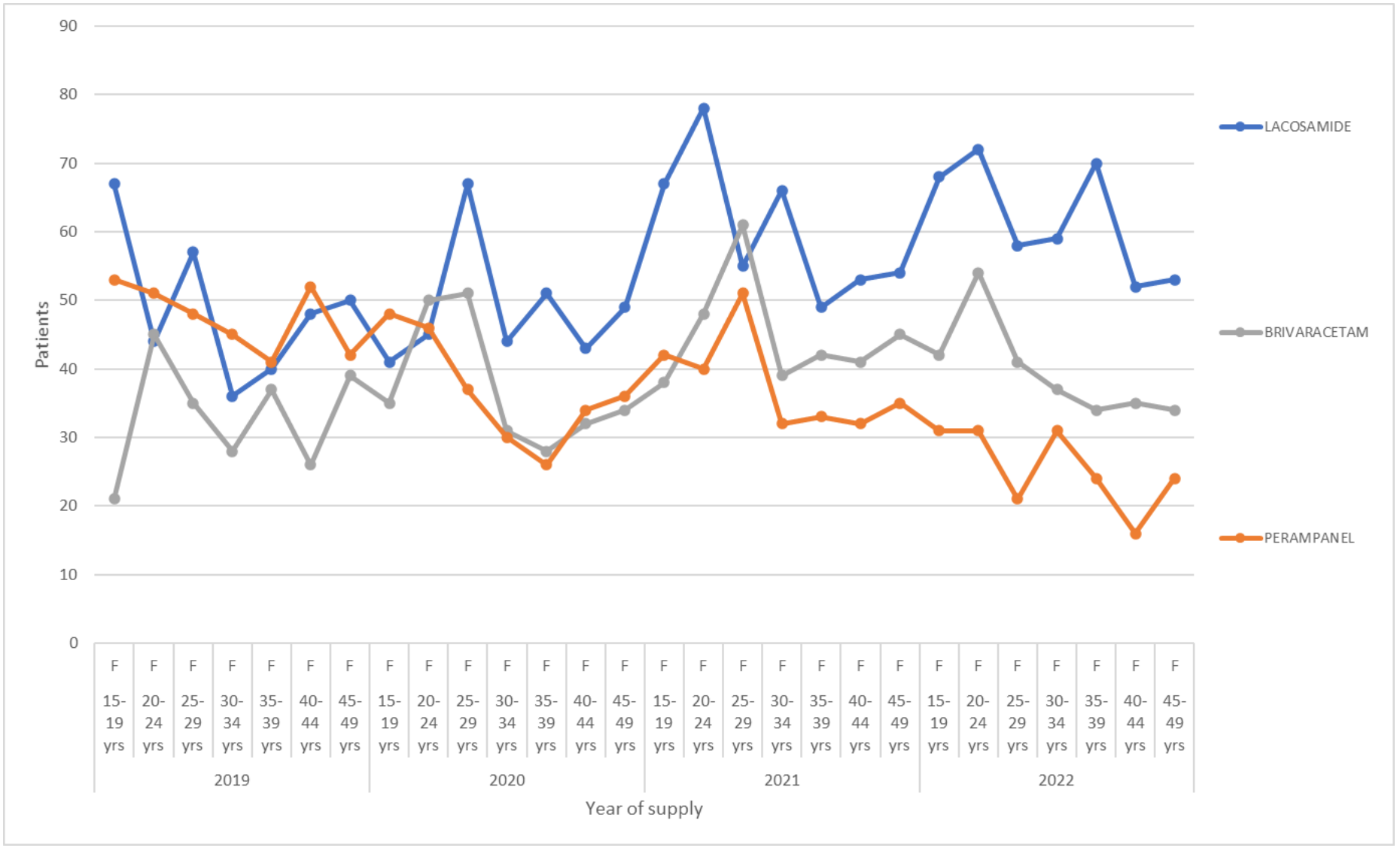

Figure 22: Women of childbearing potential within the epilepsy patient cohort incident (initiating) to brivaracetam, perampanel and lacosamide by year of supply (2019-2022)

As shown in Figure 21, there appears to be a slight increase in the number of women of childbearing potential prevalent to lacosamide in 2021-2022 with no apparent change to the utilisation trends of brivaracetam and perampanel.

Figure 22 shows that there was a decline in the number of women of childbearing potential incident (initiating) to brivaracetam and perampanel in 2021-2022 with no apparent change to the utilisation trend of lacosamide.

Overall, it is unclear if the utilisation changes for brivaracetam, perampanel and lacosamide described above are flow-on effects after the PBS restrictions for LEV and LTG were expanded on 1 January 2021 to allow for their first-line use in women of childbearing potential.

Discussion and DUSC interpretation

The DUSC noted that patients were included in the epilepsy patient cohort for the utilisation analysis if 50% or more of their PBS-subsidised AED prescriptions were indicated for epilepsy after excluding prescriptions with an unknown indication. The DUSC noted that 308,424 patients were included in the epilepsy patient cohort and that 402,842 patients who had received a PBS-listed AED were excluded based on this criteria.

The DUSC noted that a limitation of defining epilepsy patients in this way is that it will exclude a number of epilepsy patients who have only received treatment with an unrestricted first-line PBS-listed AED such as valproate and carbamazepine. As these medicines are used for conditions other than epilepsy however, this approach does allow confidence that the analysis addresses the use of PBS-listed AEDs for the treatment of epilepsy and not for other conditions.

The DUSC noted that the number of patients in the epilepsy patient cohort prevalent to a PBS-listed AED increased from 159,356 in 2018 to 184,043 in 2022 (an increase of 15.5%), whilst the number of incident (initiating) patients decreased from 38,549 in 2019 to 34,125 in 2022 (a decrease of 11.5%). The DUSC considered that the decrease in patients incident to a PBS-listed AED over this time may reflect a delay in epilepsy diagnoses as a result of the COVID-19 pandemic.

The DUSC noted that there were significantly more females (99,490 patients) than males (84,553 patients) prevalent to a PBS-listed AED in the epilepsy patient cohort (in 2022) and that this discrepancy was particularly marked in younger males (aged 15-49 years). The DUSC considered that younger males may be using the first-line AEDs (such as valproate and carbamazepine) more than younger females due to the known teratogenic effects of these medicines and may have therefore been excluded from the epilepsy patient cohort. In addition, younger males who do not meet the PBS criteria for second-line LEV and LTG may be accessing these medicines via a private prescription.

The DUSC advised that this group of younger males may impact the cost estimates if they switch to PBS-subsidised LEV or LTG if the restrictions for these medicines are expanded to allow their first-line use in the general population with epilepsy. The DUSC advised that GP prescribing data might help to quantify the size of this group.

The DUSC noted that there was no apparent impact to the utilisation of LEV and LTG in the women of childbearing population included in the epilepsy patient cohort following the January 2021 PBS restriction changes for these medicines. The DUSC considered that this was consistent with the PBAC's September 2020 advice that prescribing of LEV and LTG is likely already occurring in the majority of women with epilepsy who are of childbearing potential.

The DUSC noted that there was a slight increase in the number of women of childbearing potential prevalent to the third-line AED lacosamide in 2021-2022 following the PBS restriction changes to LEV and LTG. The DUSC noted that is unclear from the available data whether this change was a flow-on effect after the PBS restrictions for LEV and LTG were expanded in January 2021.

The DUSC advised that LEV and LTG were the most prevalent PBS-listed AEDs overall and stratified by gender. Therefore, it was likely that these medicines are already being used first-line in the majority of patients with epilepsy and any potential impacts on the third-line AEDs from allowing first-line use of LEV and LTG in the general population are already occurring.

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.

Disclaimer

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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