

Impact of regulatory reforms on utilisation of opioids

Drug utilisation sub-committee (DUSC)

June 2023

Abstract

Purpose

DUSC requested a review of the utilisation of Pharmaceutical Benefits Scheme (PBS)-listed opioid analgesics to examine the impact of the 1 June 2020 regulatory reforms and associated PBS listing changes for opioid analgesics.

Data Source / methodology

Data were extracted from the Services Australia Supplied Prescriptions database based on Anatomic Therapeutic Classification codes for dates of supply from 1 January 2016 to 30 September 2022.

Key Findings

- The number of supplied prescriptions, defined daily doses (DDDs) and treated patients had decreased since 2018. In 2021 there was:
 - a 4.2% decrease of the number of supplied prescriptions,
 - a 10.8% decrease in the number of supplied DDDs, and
 - a 0.3% decrease of the number of treated patients.
- Tapentadol was the only drug in the opioids market with increased utilisation.
- The percentage of original prescriptions with prescribed repeats decreased from 13% in 2019 to 8% in 2021.
- Of the 14.5 million original prescriptions written in 2021, approximately 4% were written for listings of reduced pack sizes.
- For PBS listings that had the pack size reduced from 1 June 2020, only a very small proportion of these new listings were prescribed with repeats.
- After the introduction of new and amended listings to the Palliative Care Schedule from 1 June 2021, the supply of opioids from Palliative Care Schedule has increased from Q2 2021.

Purpose of analysis

To assess the impact of the 1 June 2020 regulatory reforms and associated PBS listing changes for opioid analgesics. Pregabalin, a common treatment for pain, is also included in the analysis to examine if its utilisation has been impacted by the reforms to opioids.

The analyses examine the use of opioids for analgesia on the Pharmaceutical Benefits Scheme (PBS) and the Repatriation PBS (RPBS) from January 2016 to the end of September 2022. This includes both single ingredient opioid analgesics and combination products; such as paracetamol with codeine and oxycodone with naloxone combinations. The analysis will not consider the use of non-PBS listed opioids or over-the-counter opioid preparations.

Background

Pharmacology

Opioids work by acting on opioid receptors on neuronal cell membranes in the central nervous system and, to a lesser extent, the peripheral nervous system. There are three main types of opioid receptors: μ , κ and δ (mu, kappa and delta). Agonist activity at mu opioid receptors is responsible for analgesia, respiratory depression, euphoria, sedation, decreased gastrointestinal motility leading to constipation and physical dependence. The analgesic activity of most clinically used opioids is due to their agonist activity at the mu receptor.

Therapeutic Goods Administration (TGA) approved indications

Table 1 presents the TGA approved analgesic indications of opioids and non-opioids listed on the PBS. These indications have changed since the previous DUSC review, as explained in the section 'Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC).'

Table 1: TGA analgesic indications of PBS listed opioids and non-opioids

Drug	Indication
Buprenorphine	<p>Buprenorphine sublingual tablets and injection are indicated for the short-term (not more than one week) management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.</p> <p>Buprenorphine patches are indicated for the management of severe pain where:</p> <ul style="list-style-type: none">• other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and• the pain is opioid-responsive, and• requires daily, continuous, long-term treatment.
Codeine	Temporary relief of acute moderate pain or short-term management of severe pain (includes fixed-dose combinations with aspirin, ibuprofen, paracetamol)
Fentanyl	<p>Moderate to severe acute or chronic pain.</p> <p>Fentanyl patches are indicated for the management of pain associated with cancer, palliative care, and other conditions in patients where:</p>

Drug	Indication
	<ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise • inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • severe enough to require daily, continuous, long term opioid treatment. <p>Fentanyl lozenges are indicated for the management of breakthrough cancer pain in patients with malignancies who are already receiving and are tolerant to opioid therapy for their underlying persistent cancer pain.</p> <p>Fentanyl injections are indicated for:</p> <ul style="list-style-type: none"> • analgesic action of short duration during anaesthetic periods, premedication, induction and maintenance, and in the immediate post-operative period (recovery room) as the need arises; • use as an opioid analgesic supplement in general and regional anaesthesia; and • administration with a neuroleptic such as droperidol injection as an anaesthetic premedication, for the induction of anaesthesia, and as an adjunct in the maintenance of general and regional anaesthesia.
Hydromorphone	<p>Hydromorphone tablets and injections are indicated for short-term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.</p> <p>Hydromorphone prolonged release tablets are indicated for management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long-term treatment. <p>Not indicated for use in chronic non-cancer pain other than in exceptional circumstances. Not indicated as an as-needed analgesia.</p>
Methadone	<p>Management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long-term treatment.
Morphine	<p>Morphine tablets and injections are indicated for</p> <ul style="list-style-type: none"> • short -term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain; or • treatment of chronic severe pain of cancer. <p>Morphine modified release tablets and capsules are indicated for management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long-term treatment. <p>Not indicated for use in chronic non-cancer pain other than in exceptional circumstances. Not indicated as an as-needed analgesia.</p>
Oxycodone	<p>Oxycodone tablets and injections are indicated for short-term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.</p>

Drug	Indication
	<p>Oxycodone modified release tablets are indicated for management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long-term treatment. <p>Not indicated for use in chronic non-cancer pain other than in exceptional circumstances. Not indicated as an as-needed analgesia.</p>
Oxycodone and naloxone	<p>Management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise, inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long term treatment. <p>Not indicated for use in chronic non-cancer pain other than in exceptional circumstances. Not indicated as an as-needed analgesia.</p> <p>The naloxone component in a fixed combination with oxycodone is indicated for the therapy and/or prophylaxis of opioid-induced constipation.</p> <p>Indicated as a second line symptomatic treatment of patients with severe to very severe idiopathic restless legs syndrome after failure of dopaminergic therapy.</p>
Tapentadol	<p>Tapentadol immediate release tablets are indicated for the short-term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.</p> <p>Tapentadol sustained release tablets are indicated for the management of severe pain where:</p> <ul style="list-style-type: none"> • other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and • the pain is opioid-responsive, and • requires daily, continuous, long-term treatment. <p>Not indicated for use in chronic non-cancer pain other than in exceptional circumstances. Not indicated as an as-needed analgesia.</p>
Tramadol	<p>Short-term management of severe pain for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain.</p>
Pregabalin	Neuropathic pain
Gabapentin	Neuropathic pain

Source: TGA Product Information, accessed 24/11/2022

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

Dosage and administration

The recommended dosages of these medicines are complex and vary widely within a medicine depending on use as acute/chronic treatment, mode of administration (i.e. intravenous (IV)/subcutaneous (SC)/oral/transdermal/rectal) and rate of release (immediate or controlled).

Detailed dosing information can be found in the Australian Medicines Handbook online¹ and in [the TGA Product Information](#).

¹ <https://amhonline.amh.net.au/>

PBS listing details (as at 1 November 2022)

Table 2 presents an overview of opioid analgesics listed on the PBS. Current PBS listing details are available from the [PBS website](#).

Table 2: PBS restrictions for opioid analgesics and non-opioids

Drug and form	Restrictions (abridged)
Buprenorphine	
Buprenorphine patches	Chronic severe pain Severe disabling pain (palliative care)
Codeine	
Codeine tablets	Severe pain
Fentanyl	
Fentanyl patches	Chronic severe disabling pain Severe disabling pain (palliative care)
Fentanyl lozenge, sublingual tablet & orally disintegrating tablet	Breakthrough pain (palliative care)
Hydromorphone	
Hydromorphone tablets (standard release)	Severe pain Severe pain (palliative care)
Hydromorphone tablets (modified release)	Chronic severe pain Severe disabling pain (palliative care)
Hydromorphone injection	Severe pain Severe pain (palliative care)
Hydromorphone oral liquid	Severe pain Severe pain (palliative care)
Methadone	
Methadone tablet	Chronic severe disabling pain Severe disabling pain (palliative care)
Methadone oral liquid	Chronic severe disabling pain (palliative care)
Methadone injection	Chronic severe disabling pain Severe disabling pain (palliative care)
Morphine	
<i>Standard release tablets</i>	
Morphine sulfate tablet (10 or 20 mg, 0 repeats)	Cancer pain
Morphine sulfate tablet (30mg, 0 repeats)	Severe pain
Morphine sulfate tablet (10 or 20mg with 2 repeats)	Severe disabling pain (palliative care)
<i>Modified release tablets or capsules</i>	
Morphine sulfate modified tablets (up to 120mg/tablet)	Chronic severe pain Severe disabling pain (palliative care)
Morphine sulfate modified tablets (200mg)	Chronic severe disabling pain Severe disabling pain (palliative care)
<i>Oral liquids</i>	
Morphine hydrochloride oral liquid (standard release)	Severe pain Severe pain (palliative)
Morphine controlled release granules for oral suspension (up to 100mg)	Chronic severe pain Severe disabling pain (palliative care)
Morphine controlled release granules for oral suspension (200mg)	Chronic severe disabling pain Severe disabling pain (palliative care)
<i>Injections</i>	

Drug and form	Restrictions (abridged)
Morphine sulphate injections	Severe pain Severe pain (palliative care) Prescriber bag as Unrestricted benefit
Morphine hydrochloride injection	Severe pain (palliative care)
Oxycodone	
Oxycodone tablet or capsule (standard release)	Severe pain
Oxycodone tablet or capsule (5 mg modified release)	Severe pain
Oxycodone tablet (10 mg to 80 mg modified release)	Chronic severe pain Severe disabling pain (palliative care)
Oxycodone oral liquid	Severe pain
Oxycodone suppository	Severe pain
Oxycodone + naloxone	
Oxycodone + naloxone modified release tablet	Chronic severe pain Severe disabling pain (palliative care)
Paracetamol + codeine	
Paracetamol 500mg + codeine phosphate 30mg – 10 or 20 tablets	Severe pain
Tramadol	
Tramadol capsule 50mg (standard release)	Severe pain
Tramadol tablet (modified release)	Chronic severe pain
Tramadol oral liquid	Severe pain
Tramadol injection	Prescriber bag as Unrestricted benefit Severe pain
Tapentadol	
Tapentadol tablet (modified release)	Chronic severe pain
Gabapentinoids	
Pregabalin	Neuropathic pain
Gabapentin	Refractory neuropathic pain (RPBS only).

Source: November 2022 PBS Schedule

For details of the current PBS listing refer to the [PBS website](#).

Changes to listing

Since the previous DUSC review in February 2020 a number of changes have been implemented to PBS listings for opioids. The following changes were made from 1 June 2020.

- Smaller pack sizes for some items were intended to be listed. Prior to smaller pack sizes being available, new listings were created with a smaller maximum quantity of 0.5 packs. These are still listed.
- Authority level has increased for some listings, for example from Unrestricted to Restricted Benefit or from Restricted Benefit to Authority Required (Streamlined).
- Additional criteria added to PBS restrictions.
- The deletion of the listing for paracetamol 500 mg + codeine phosphate hemihydrate 30 mg tablet which allowed three packs of 20 tablets to be dispensed at once.
- The deletion of the listing for tramadol for dose titration.

From 1 October 2020, some revised changes were implemented to facilitate access to opioid medication to palliative care patients. PBS listings that require an annual secondary review were altered to allow a palliative care nurse practitioner to conduct the review, and the requirements for the annual secondary reviews were removed for patients whose clinical condition is such that a secondary review is rendered not possible.

From 1 June 2021, the Palliative Care Schedule (PCS) included new and amended listings for opioid medications. Following consideration of the Department of Health commissioned review of the PCS, the Pharmaceutical Benefits Advisory Committee recommended the inclusion of additional formulations of fentanyl, hydromorphone, methadone and morphine on PCS, and the addition of new listings for oxycodone and oxycodone with naloxone modified release products. These changes reflect the PBAC’s recommendations and were intended to further reduce barriers to the prescribing and timely supply of opioid analgesic medications for palliative care patients.

From 1 August 2022 amendments in the below table were made to the PBS listings of hydromorphone oral solutions to allow pharmacists to dispense volumes smaller than a whole bottle at PBS subsidised prices.²

Table 3: Amendments to hydromorphone oral solution effective 1 August 2022

Change	Previous listing	Amendments from 1 August 2022
Legislative Instrument form descriptions	Oral solution containing hydromorphone hydrochloride 1 mg per mL, 473 mL	Oral solution containing hydromorphone hydrochloride 1 mg per mL, 1 mL
Pharmaceutical Item value	1 unit (i.e. bottle)	473 units (i.e. millilitres)
Pack Qty	1	473
Pricing Qty	1	473
Max Qty Units	1	473

Current PBS listing details are available from the [PBS website](#).

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

At its December 2019 meeting, the PBAC considered a number of proposed changes to the listing of opioids on the PBS.

In July 2019, in response to a submission sponsored by Mundipharma Pty Ltd to register a smaller pack size for oxycodone 5mg capsules, the PBAC recommended the Restricted Benefit listing of a new maximum quantity (MQ) of 10 for oxycodone 5 mg capsules and tablets. The PBAC acknowledged the potential quality use of medicine benefit of reduced maximum quantities for opioids used in the acute pain setting (e.g. after surgery).

² PBS website, Changes to PBS listing of hydromorphone oral solution <https://www.pbs.gov.au/info/news/2022/08/changes-to-pbs-listing-of-hydromorphone-oral-solution>

The TGA was undertaking regulatory measures which aimed to reduce the harms associated with prescription opioid dependence and inappropriate use, including overdose fatalities. The regulatory measures were based on the findings from the TGA's 2018 prescription opioid review, and advice received from the Opioid Regulatory Advisory Group (ORAG). The TGA opioid reform regulatory measures were:

- Registration of smaller pack sizes for immediate release opioid products indicated for acute pain, including oxycodone, tramadol, tramadol/paracetamol, paracetamol/codeine, codeine, hydromorphone, morphine, tapentadol, and buprenorphine.
- Restricting the indications for fentanyl patches to the management of pain associated with cancer, palliative care and other conditions in opioid-tolerant patients.
- Revised indications for immediate- and modified- release prescription opioids.
- Boxed warnings and class statements in the Product Information (PI) of all prescription opioids, and stronger warnings in the Consumer Medicines Information (CMI).

The PBAC recommended changes to opioids listed on the PBS as:

- implementing new Restricted Benefit listings for smaller maximum quantities of immediate release opioids with no increased quantities or repeats for patients requiring short-term relief of acute severe pain that is unresponsive to non-opioid analgesics;
- amending the listings for immediate- and modified-release opioids to support the appropriate prescribing and use of opioids.

The PBAC noted that the smaller maximum quantity listings would be priced proportionally to the existing listings, in accordance with the requirements of Section 85D of the *National Health Act 1953* (the Act).

The PBAC noted that the TGA had revised the indications of several opioid analgesics, including fentanyl patches, to broadly categorise them into opioids for acute severe pain and for chronic severe pain. The PBAC recommended that the PBS restrictions for immediate- and modified-release opioids should be changed in the following manner to align with the TGA indication changes:

- Opioids for short-term use in the first-line setting (codeine tablets, codeine + paracetamol tablets, tramadol capsule, injection, and oral drops, and oxycodone tablets, capsules, suppository, and oral solution) to be Restricted Benefits limited to patients who have not responded to, are intolerant to or whose condition would not respond to non-opioid analgesics.
- Opioids for short-term use in the second-line setting (hydromorphone tablets, injections, and oral liquid, morphine tablets, oral solution and injections) to be Restricted Benefits limited to patients who have not responded to, are intolerant to or whose condition would not respond to non-opioid nor other opioid analgesics.
- Opioids for long-term use in the first-line setting (buprenorphine transdermal patches, morphine capsules, tablets and granules, oxycodone tablets, oxycodone with naloxone tablets, tapentadol tablets, and tramadol tablets) to have authority level increased to Authority Required (STREAMLINED) for daily, continuous, long-term management of

pain due to cancer or who have not responded to, are intolerant to or who experience inadequate pain management at maximum doses of non-opioid or other opioid analgesics.

- Opioids for long-term use in the second-line setting (hydromorphone tablets, methadone tablets and injection, fentanyl transdermal patches) to have authority level increased to Authority Required (STREAMLINED) with the same restrictions as opioids in the long-term first-line setting with the additional requirement that the patient must not be opioid-naïve, and the additional advice to “Consider consultation with a multidisciplinary pain service prior to, or after commencement of this medication”.

The PBAC noted that the opioids for long-term use in the first- and second- line settings were currently listed as Restricted Benefits on the PBS. The PBAC recommended an increase in the authority level to Authority Required (STREAMLINED) in line with the aims of the TGA’s opioid reforms. The PBAC also noted that, as was currently the case for these items, authority requests for increased quantities to extend treatment up to one month will still need to be made by telephone, and treatment beyond one month and up to three months will require a written authority requesting additional repeats.

The PBAC recommended additional criteria be added to the PBS restrictions as described in Section 9 (pp13-112) of the Public Summary Document:

- For the short term pain indication in first or second line setting, under the PBS indication for severe pain, new criteria that:
 - Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid analgesics OR
 - Patient must be unable to use non-opioid analgesics due to contraindications or intolerance.
- For the short term pain indication in first or second line setting, under the PBS indication for cancer pain (standard release morphine tablets 10 and 20 mg), new criteria that:
 - Patient must have cancer pain AND
 - Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid analgesics OR
 - Patient must be unable to use non-opioid analgesics due to contraindications or intolerance.
- For the short term pain indication in first or second line setting, under the PBS indication for severe pain (morphine injections), new criteria that:
 - Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid analgesics OR
 - Patient must be unable to use non-opioid analgesics due to contraindications or intolerance OR
 - The treatment must be part of pre-operative care OR
 - The treatment must be used as an analgesic adjunct in general anaesthesia.
- For PBS restrictions for reduced pack sizes in the first line setting, new criteria that:
 - The treatment must be for short term therapy of acute severe pain AND

- Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid analgesics OR
- Patient must be unable to use non-opioid analgesics due to contraindications or intolerance.
- For the long term pain indication in first line setting, under the PBS criteria for chronic severe pain or chronic severe disabling pain, new criteria that:
 - The condition must require daily, continuous, long term opioid treatment OR
 - Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid or other opioid analgesics OR
 - Patient must be unable to use non-opioid or other opioid analgesics due to contraindications or intolerance.
- For the long term pain indication in second line setting (fentanyl patches, hydromorphone MR tablets, methadone injection and IR tablet), under the PBS criteria for chronic severe pain or chronic severe disabling pain, new criteria that:
 - The condition must require daily, continuous, long term opioid treatment AND
 - Patient must not be opioid naïve AND
 - Patient must have cancer pain OR
 - Patient must have had or would have inadequate pain management with maximum tolerated doses of non-opioid or other opioid analgesics OR
 - Patient must be unable to use non-opioid or other opioid analgesics due to contraindications or intolerance.

The PBAC noted that paracetamol with codeine had two listings, one of which allowed up to a 6 month supply on a single script with a written authority. The PBAC noted that this was inconsistent with other opioids listings on the PBS, for which written authority for increased quantity and repeats can only provide a supply for up to 3 months. The PBAC considered that this listing should be brought in line with all other opioid analgesics, noting that it may result in an increased volume of authority requests to Services Australia.

The PBAC noted that tramadol immediate release tablets also had two restricted benefits listings, one indicated for acute pain with no repeats, and another indicated for dose-titration in chronic pain with 2 repeats. The PBAC considered that there was no need for a specific dose-titration listing, and that the proposed restriction changes outlined in above would encompass the intent of the existing listings as well as the intent of the new TGA indication for short-term pain management. The PBAC therefore considered that there should only be one listing for tramadol immediate release tablets as proposed, and that the listing for dose-titration should be deleted.

The PBAC expressed its concern regarding the high number of deaths and hospitalisations caused by prescription opioids in Australia, and acknowledged the significant work being undertaken by the TGA to help tackle the problem. The PBAC considered that its recommended changes to opioid listings on the PBS would complement the TGA's efforts to support the safe and clinically appropriate use of opioids while recognising the important role they play in providing pain relief for many people.

For further details refer to the [Public Summary Document](#) from the December 2019 PBAC meeting.

Approach taken to estimate utilisation

Due to the broken pack fees, the estimated net cost to the PBS was approximately \$3 million per year. Sensitivity analyses were conducted to estimate an upper and lower limit of the net costs. If 99% of scripts switched to the smaller maximum quantity, the net cost to the PBS/RPBS was estimated to be around \$4.9 million per year. If only 20% of scripts switched to the smaller maximum quantity, the net cost was estimated to be around \$1.0 million per year.

Previous reviews by the DUSC

The utilisation of opioids was reviewed by DUSC at its February 2008, February 2010, October 2014 and February 2020 meetings. In addition, a 24 month predicted versus actual analysis of pregabalin was considered at the October 2015 DUSC meeting and its use was included in the February 2020 report.

October 2014

The report examined PBS opioid use from October 2009 to March 2014. The key findings were:

- 2,968,733 people received at least one PBS-listed opioid analgesic in the 12 months from April 2013 to March 2014. Of these individuals, approximately 5% (approximately 150,000 people) accounted for 61% of opioid use over the year.
- Total use of opioids, in terms of prescriptions and defined daily doses (DDDs)/1000 population/day had continued to increase.
- Paracetamol with codeine had the highest rate of use in terms of DDDs/1000 population/day. In 2013, oxycodone became the second highest used opioid analgesic, exceeding the use of tramadol.
- Utilisation of oxycodone, fentanyl, buprenorphine and hydromorphone was increasing. The utilisation of morphine and tramadol appeared to be decreasing.

For details of the DUSC consideration of opioids in October 2014 refer to the [Public Release Document](#) from the October 2014 DUSC meeting.

February 2020

The report examined PBS opioid use from April 2012 to September 2019. The key findings were:

- Pregabalin had become the most supplied analgesic in the opioid and pregabalin analgesic market.
- Pregabalin and tapentadol were the only two drugs in this market currently not decreasing in utilisation. Tapentadol was increasing and pregabalin had plateaued and may have been starting to decrease.
- The up-scheduling by the TGA of low dose codeine combination products to Schedule 4 Prescription Only on 1 February 2018 had a minor upward impact on the utilisation of PBS listed high dose codeine (i.e. 30mg) combination products. The low dose codeine combination products were not PBS listed, so had to be supplied as private

prescriptions. This may have provided a financial incentive to substitute low dose codeine private prescriptions with high dose PBS subsidised prescriptions.

- Prescriptions from the palliative care schedule accounted for only 0.8% of the opioid market in 2019 Q3. However prescriptions for palliative care patients accounted for at least 7.1% of the opioid market and 5.0% of the pregabalin market in the same period.

The patient drug regimen analysis showed that:

- The listing of pregabalin for neuropathic pain in March 2013 coincided with the start of an increase in both two product and more than two product drug regimens.
- As at August 2019, 5 of the 10 most common two-product regimens contain pregabalin and 8 of the 10 most common three-product regimens contain pregabalin.
- At the time of reporting, 79%, 17% and 4% of patients were on a one, two or more than two product drug regimens respectively.
- The number of patients on two or more than two product drug regimens had started to decrease.

For details of the DUSC consideration of opioids in February 2020 refer to the [Public Release Document](#) from the February 2020 DUSC meeting.

Methods

Data extracted from the PBS claims database maintained by the Department of Health and Aged Care and processed by Services Australia were used for the analyses. Prescription data were extracted from 1 January 2016 up to and including 30 September 2022 based on the date of supply. Prescription data were linked to date of death data, which was last updated 24 August 2022.

Data were extracted for:

- N02A (analgesics – opioids).
- N02BG (Other analgesics and antipyretics) – pregabalin and gabapentin.
- Where the PBS restriction included ‘pain’.

These data were used to determine the prescription and patients counts for the opioid analgesic market counted by supply quarter, supply month and calendar year. Counts of initiating patients are presented from 1 January 2018 to allow for a two year lookback.

The number of prescriptions supplied through the palliative care schedule compared to general schedule is presented over time, and compared to the number of prescriptions supplied to palliative patients, where a patient was determined to be palliative for all prescriptions supplied subsequent to their first opioid prescription supply from the palliative care schedule.

Age and gender is presented for patients supplied an opioid or non-opioid in 2021. Patients are only counted for their first treatment in 2021 (for all use) and last treatment in 2021 (for patients who were supplied a prescription under a palliative care item code) to ensure they are only included in one age group.

The number and percent of patients who were supplied two or more medicines under different item codes on the same day at least once in a calendar year was calculated for 2019 and 2021.

The number and percent of repeats was calculated as the number of supplied prescriptions as either original or repeat prescriptions, and as the number of original prescriptions written with repeats or no repeats prescribed.

The utilisation of PBS listings that had reduced pack sizes as a result of the reforms is presented over time, and the number of original prescriptions written with repeats or no repeats prescribed for these listings is analysed.

Sequence analysis lists the drugs that a patient was supplied, for cohort of patients who initiated in 2019. Medicines are only counted once for each patient, for example if a patient is supplied A > B > A this is counted as A > B.

The mean quantity over time is presented by year and by drug and form. Strength is not included.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data.³

Data were extracted on 16 November 2022. Data manipulation was undertaken using SAS.

³ PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

Results

Analysis of drug utilisation

Overall utilisation

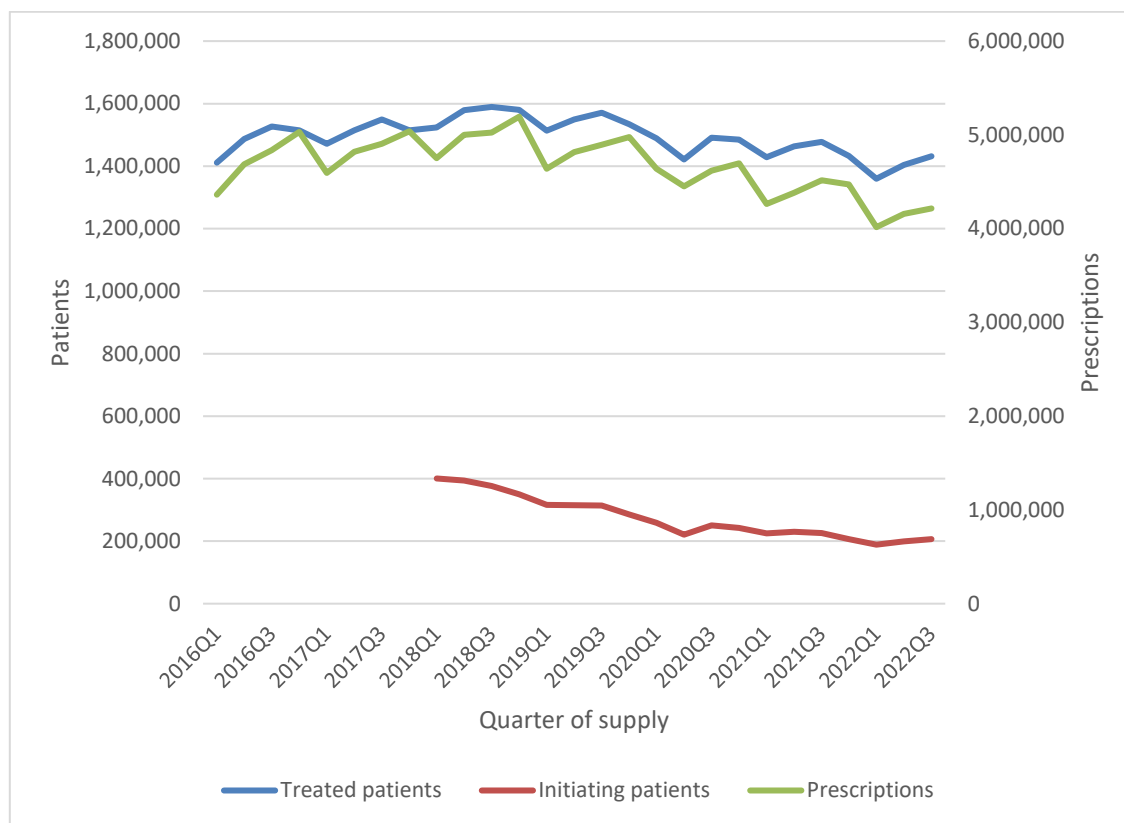


Figure 1: Number of treated patients, initiating patients and prescriptions over time

It appears the number of initiating patients is decreasing over time and has been since before the TGA reform changes. This may be partly because patients are less likely to be counted as initiating the further from the first date of including initiating patient counts.

Figure 2 shows the utilisation of PBS prescriptions for opioids and other selected analgesics by drug.

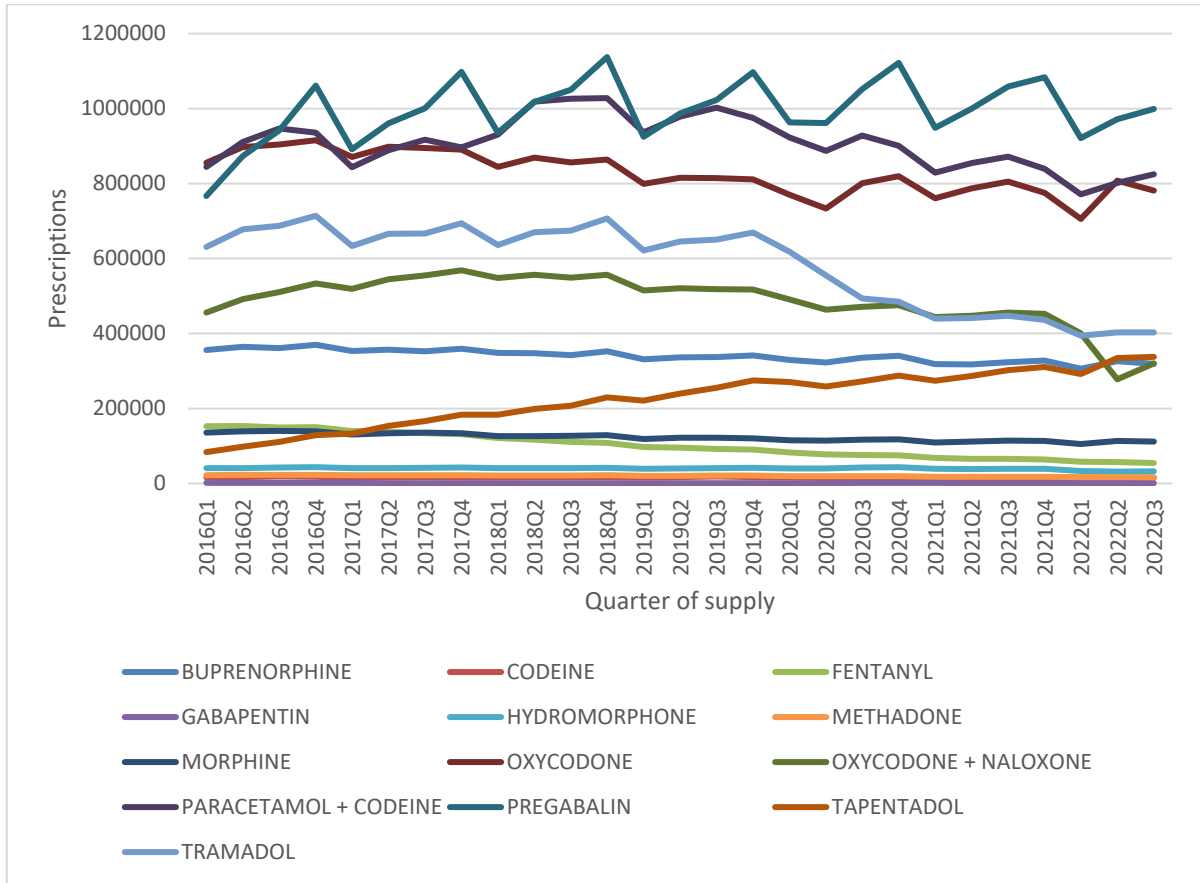


Figure 2: Number of prescriptions by quarter and by drug

It appears the medicine that has decreased the most in prescriptions supplied over this time is tramadol, while tapentadol appears to have increased the most. This is confirmed by table 4 below.

Table 4: Number of prescriptions and rate of growth from previous year

	2016	2017	2018	2019	2020	2021
BUPRENORPHINE	1,450,629	1,422,313 (-1.95%)	1,390,820 (-2.21%)	1,346,354 (-3.20%)	1,327,970 (-1.37%)	1,287,078 (-3.08%)
CODEINE	68,496	63,632 (-7.10%)	67,100 (5.45%)	67,372 (0.41%)	51,118 (-24.13%)	54,356 (6.33%)
FENTANYL	604,910	543,196 (-10.2%)	456,579 (-15.95%)	375,352 (-17.79%)	310,915 (-17.17%)	262,045 (-15.72%)
GABAPENTIN	5,516	3,877 (-29.71%)	3,366 (-13.18%)	3,529 (4.84%)	4,182 (18.50%)	3,878 (-7.27%)
HYDROMORPHONE	167,472	165,512 (-1.17%)	163,464 (-1.24%)	161,088 (-1.45%)	165,279 (2.60%)	155,894 (-5.68%)
METHADONE	90,211	87,818 (-2.65%)	85,399 (-2.75%)	81,964 (-4.02%)	77,636 (-5.28%)	71,931 (-7.35%)
MORPHINE	553,040	532,823 (-3.66%)	508,097 (-4.64%)	482,166 (-5.10%)	463,776 (-3.81%)	447,400 (-3.53%)
OXYCODONE	3,572,372	3,553,863 (-0.52%)	3,433,501 (-3.39%)	3,239,540 (-5.65%)	3,123,233 (-3.59%)	3,128,491 (0.17%)
OXYCODONE + NALOXONE	1,992,434	2,188,057 (9.82%)	2,210,758 (1.04%)	2,071,159 (-6.31%)	1,900,625 (-8.23%)	1,798,620 (-5.37%)
PARACETAMOL + CODEINE	3,638,329	3,546,024 (-2.54%)	4,004,165 (12.92%)	3,892,053 (-2.80%)	3,639,428 (-6.49%)	3,394,697 (-6.72%)
PREGABALIN	3,644,033	3,951,026 (8.42%)	4,141,471 (4.82%)	4,032,332 (-2.64%)	4,098,539 (1.64%)	4,090,620 (-0.19%)
TAPENTADOL	421,131	635,853 (50.99%)	819,534 (28.89%)	990,826 (20.90%)	1,089,257 (9.93%)	1,173,306 (7.72%)
TRAMADOL	2,709,328	2,661,166 (-1.78%)	2,688,619 (1.03%)	2,586,222 (-3.81%)	2,151,893 (-16.79%)	1,764,083 (-18.02%)
TOTAL PRESCRIPTIONS	18,917,901	19,355,160 (2.31%)	19,972,873 (3.19%)	19,329,957 (-3.22%)	18,403,851 (-4.79%)	17,632,399 (-4.19%)
TREATED PATIENTS	3,335,666	3,364,710 (0.87%)	3,450,825 (2.56%)	3,387,099 (-1.85%)	3,193,524 (-5.72%)	3,183,838 (-0.30%)

Note: Year to date of 2022 is not included

Table 4 confirms that there was a decrease in the total number of prescriptions supplied in each year included in the analysis. In 2020 there was a 4.8% reduction and a 4.2% reduction in 2021. The number of treated patients grew in 2017 and 2018, and has been declining since 2019. The largest percent reduction was in 2020 (5.7%).

Table 4 also confirms that fentanyl and tramadol have had consistent reductions in the number of supplied prescriptions over time. The use of codeine reduced by almost 25% in 2020, but grew modestly in 2021. The use of tapentadol, which is available as a modified release formulation, is the only medicine which shows consistent growth in prescriptions supplied over the last five calendar years.

Figure 3 shows the utilisation of PBS prescriptions for opioids and other selected analgesics by drug by months from January 2019 to show the COVID-19 pandemic lockdown effect.

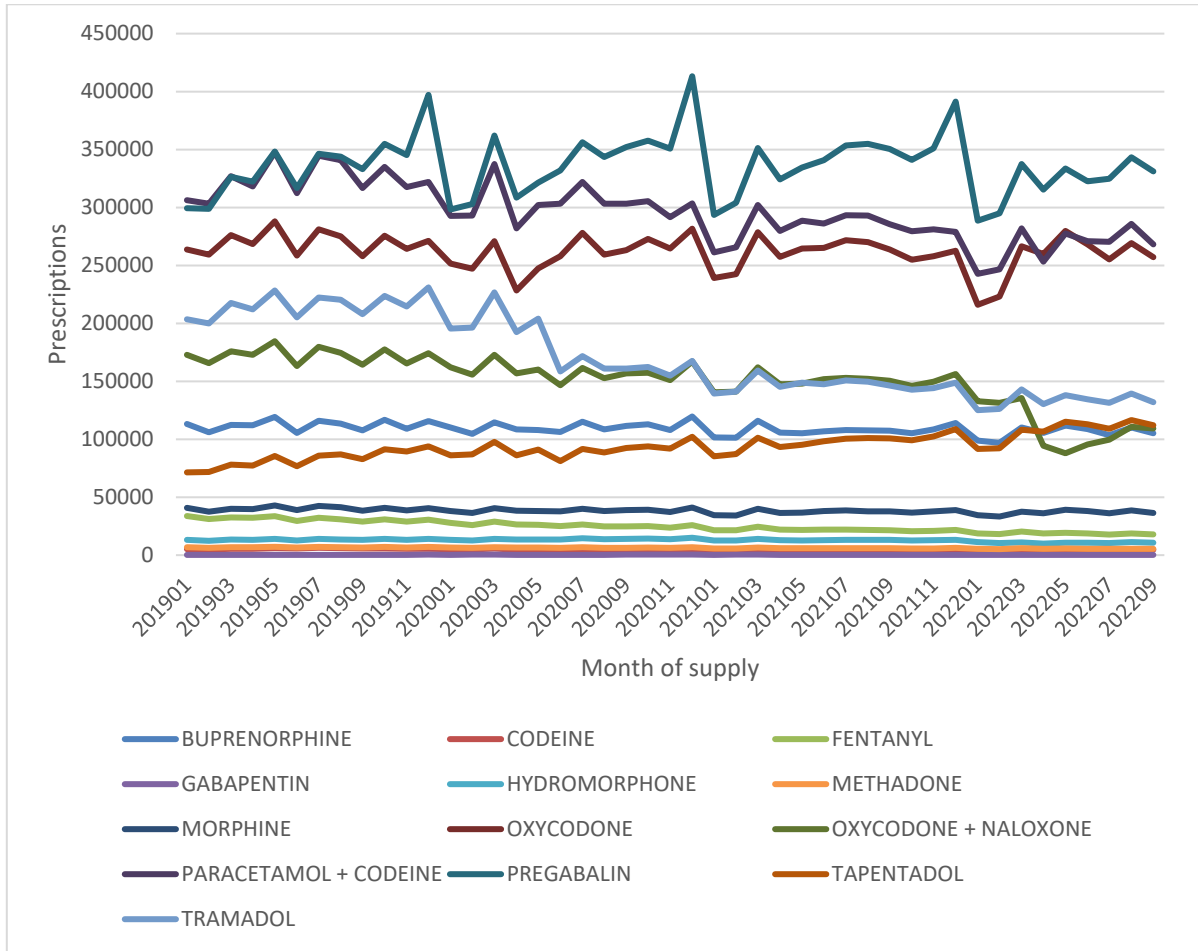


Figure 3: Number of prescriptions by month

It appears there was some stockpiling of prescriptions in March 2020 and a subsequent reduction in April 2020. This effect is close to the opioid reform date of 1 June 2020 and so the quarterly graphs in this report may be slightly confounded by the impact of social distancing restrictions during the COVID-19 pandemic, with 2020 Q1 being slightly higher than expected and 2020 Q2 being slightly lower than expected. Despite this, the subsequent figures in this report use a time period of quarters rather than months as the latter makes the figures too variable and harder to discern trends.

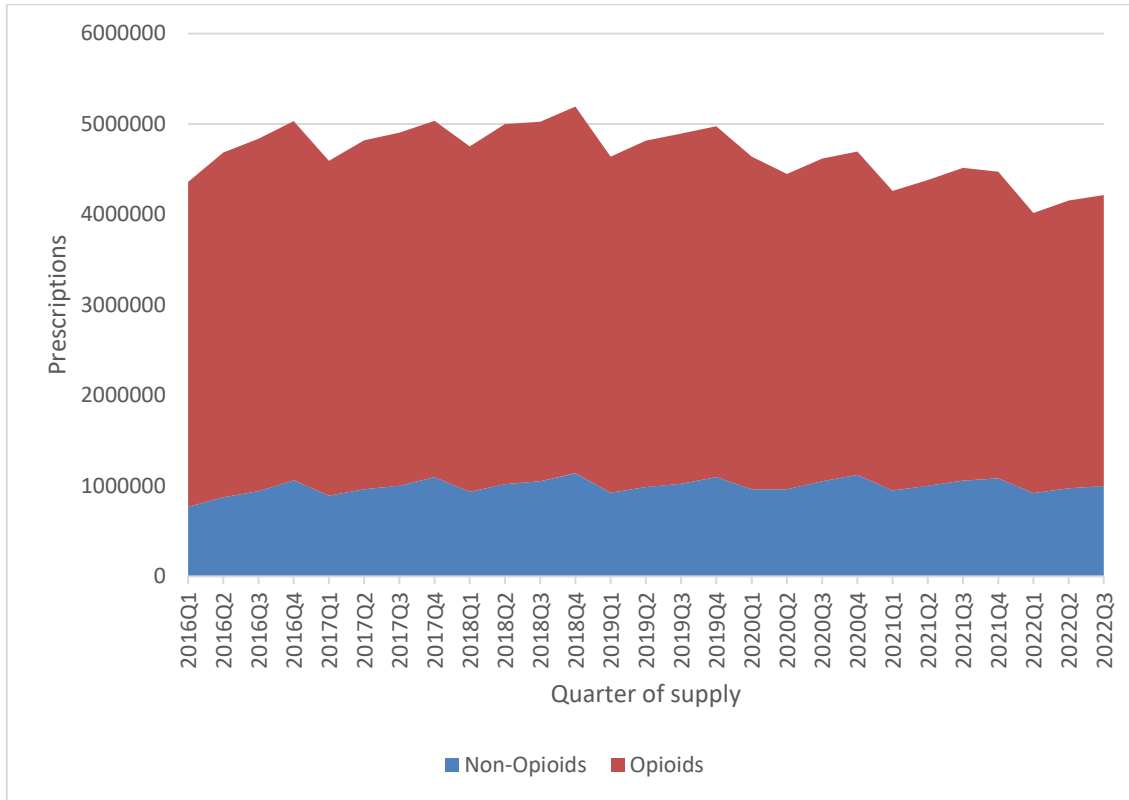


Figure 4: Prescriptions of opioids and non-opioids over time

Figure 4 shows the total PBS prescriptions for opioids and non-opioids. Figure 4 shows that the combined PBS opioid and non-opioid prescription market expanded until 2018 and then began to decrease.

Figure 5 shows prescriptions broken down by whether or not the PBS item is from the palliative care schedule.

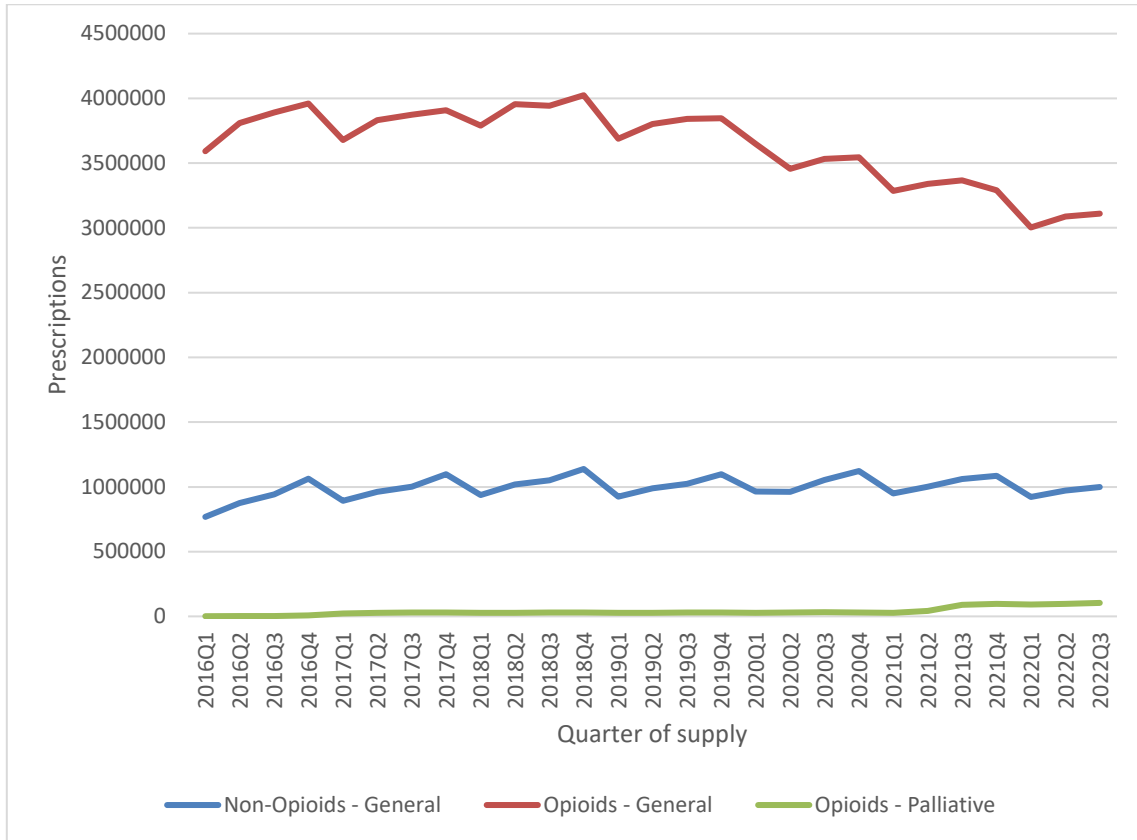


Figure 5: Prescriptions of opioids and non-opioids over time through the General Schedule vs. Palliative Care Schedule

Figure 5 shows that prescriptions for palliative care items are a small proportion of the overall opioid market. However, it is possible for palliative care patients to be prescribed opioids using non-palliative care items (e.g. items from the General Schedule). The products on the palliative schedule are often replicated in the General Schedule, but with lower maximum quantities and repeats.

Figure 6 shows prescriptions supplied to palliative care patients. Palliative care prescriptions were defined as all opioid prescriptions supplied to a patient subsequent to their first opioid prescription supply from the palliative care schedule.

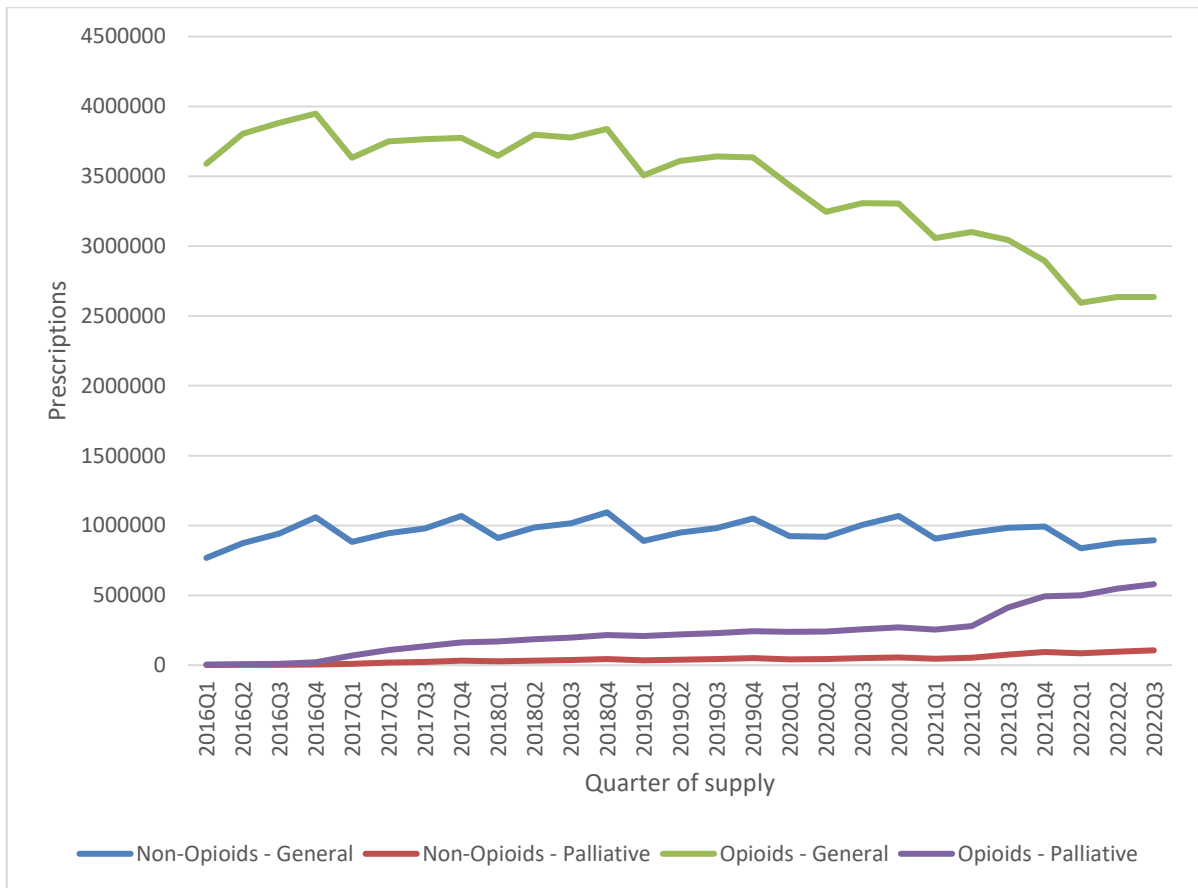


Figure 6: Prescriptions of opioids and non-opioids over time to palliative care patients

Figure 6 shows that there were many more opioid prescriptions for palliative care patients from the General Schedule than from the palliative care schedule (figure 5). In 2021 Q1, prescriptions for palliative care patients were 8% of the opioid market and 5% of the non-opioid market. These may be an underestimate, as some palliative care patients may only be supplied opioid prescriptions from the General Schedule and would not be identified by this method.

It can be seen that there was an increase in the number of opioid scripts for palliative care patients from the second quarter of 2021. This is likely due to a change in the palliative care schedule on 1 June 2021. In 2022 Q1, prescriptions for palliative care patients were 16% of the opioid market and 9% of the non-opioid market.

Age and gender of treated patients

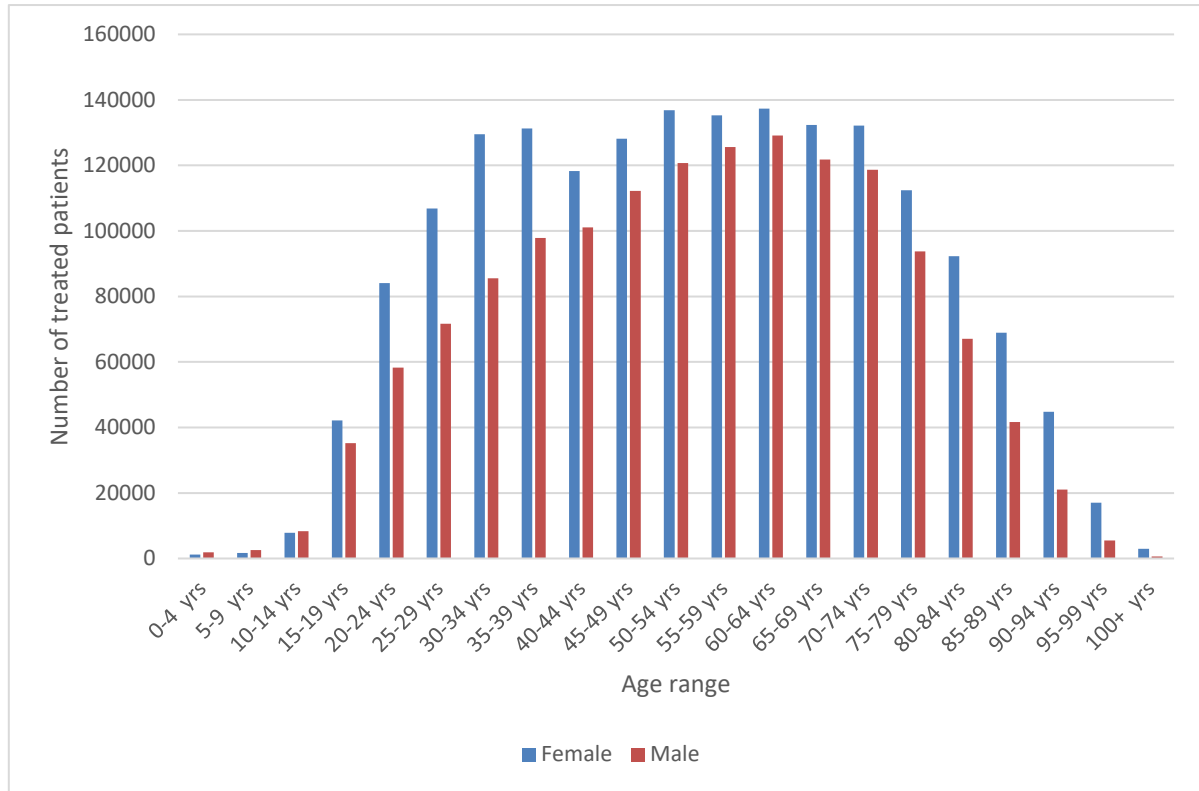


Figure 7: Age and gender of patients supplied opioids and non-opioids in 2021

The number of patients supplied opioids and non-opioids in 2021 was highest in patients aged 50-74 years old. The proportion of female patients aged 20-39 years old (approximately 60%) supplied opioids and non-opioids in 2021 was higher than male patients (approximately 40%).

Figure 8 below shows the age and gender of palliative patients supplied opioids and non-opioids in 2021. Age was determined by the last prescription the patient was supplied in 2021, if a patient was treated as a general patient for part of the year and then was supplied a prescription under the palliative care schedule they are counted as a palliative care patient. In palliative patients the proportion of females supplied opioids and non-opioids was higher across all age groups, and increases with age.

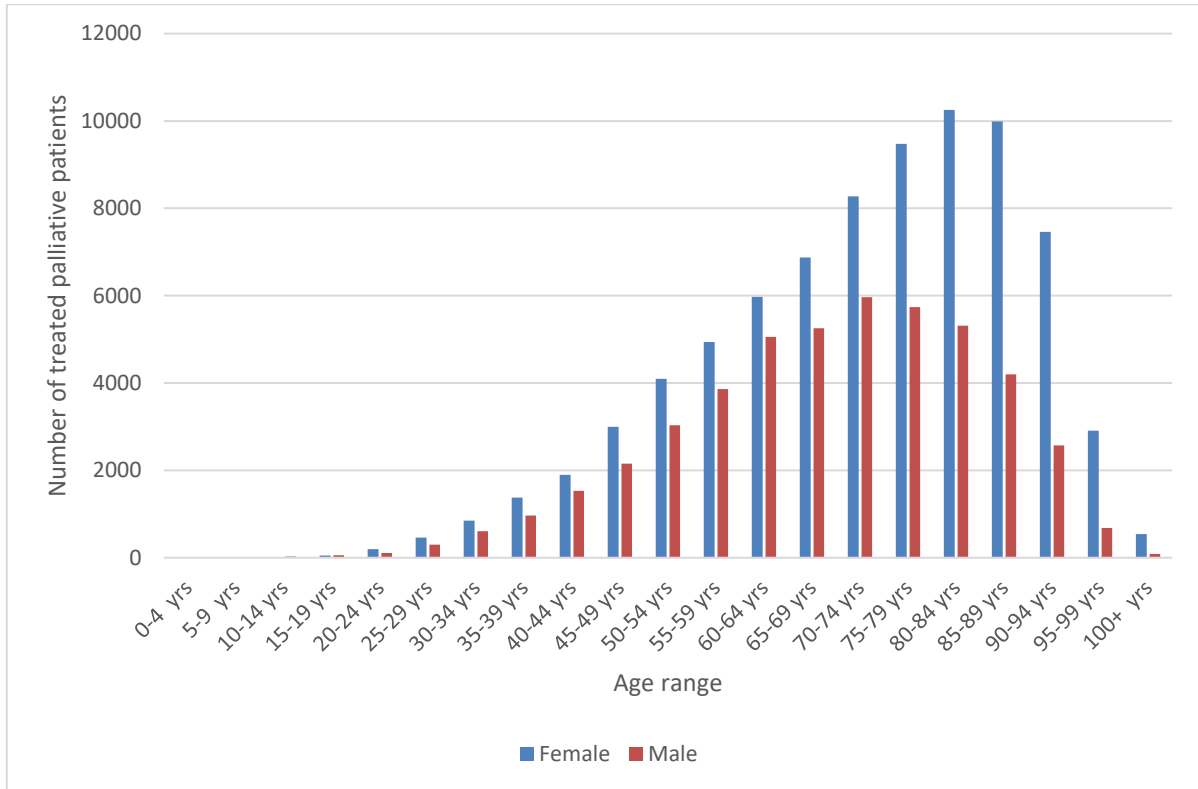


Figure 8: Age and gender of palliative care patients supplied opioids and non-opioids in 2021

Same day supply

Table 5: Same day supply of two or more opioids or non-opioids

	2019		2021	
	Number	Percent	Number	Percent
Same day supply of two or more opioid or non-opioid medicines	513,938	15%	401,574	13%
Same day supply of an opioid and non-opioid	206,959	6%	181,805	6%
Same day supply of two opioids	380,656	11%	276,110	9%
Total patients	3,387,099		3,183,838	

In 2019 there were around 3 million patients supplied an opioid through the PBS. Six percent of these patients were supplied an opioid and a non-opioid medicine on the same day, 11% were supplied two or more opioids on the same day, and 15% were supplied two or more opioids or non-opioids on the same day.

In 2021 there were around 3 million patients supplied an opioid through the PBS. Six percent of these patients were supplied an opioid and a non-opioid medicine on the same day, 9% were supplied two or more opioids on the same day, and 13% were supplied two or more opioids or non-opioids on the same day.

Repeats prescribed and supplied

Table 6: Number of supplied prescriptions by whether repeats prescribed

Year supplied	Supplied prescriptions	Supplied as original prescription	Percent supplied as original prescriptions	Supplied as repeat prescription	Percent supplied as repeat prescriptions
2016	18,917,901	14,404,010	76%	4,513,891	24%
2017	19,355,160	14,652,824	76%	4,702,336	24%
2018	19,972,873	15,151,745	76%	4,821,128	24%
2019	19,329,957	14,635,456	76%	4,694,501	24%
2020	18,403,851	14,436,467	78%	3,967,384	22%
2021	17,632,399	14,531,253	82%	3,101,146	18%
2022 (YTD September)	12,385,899	10,165,614	82%	2,220,285	18%

Table 7: Number of original prescriptions by whether repeats prescribed

Year prescribed	Number of prescribed original prescriptions	Number prescribed with no repeats ordered	Percent prescribed with no repeats	Number prescribed with repeats ordered	Percent prescribed with repeats
2016	14,375,386	12,466,657	87%	1,908,729	13%
2017	14,626,409	12,710,343	87%	1,916,066	13%
2018	15,113,298	13,186,129	87%	1,927,169	13%
2019	14,593,252	12,752,104	87%	1,841,148	13%
2020	14,387,861	12,971,767	90%	1,416,094	10%
2021	14,505,913	13,332,088	92%	1,173,825	8%
2022 (YTD September)	9,958,110	9,131,982	92%	826,128	8%

Prescriptions in the dataset that were prescribed in 2015 are not included

There was a decrease in the percent of supplied repeats from 24% in 2019 to 18% in 2021. The number of prescribed repeats also decreased from 13% in 2019 to 8% in 2021.

Reduced pack sizes

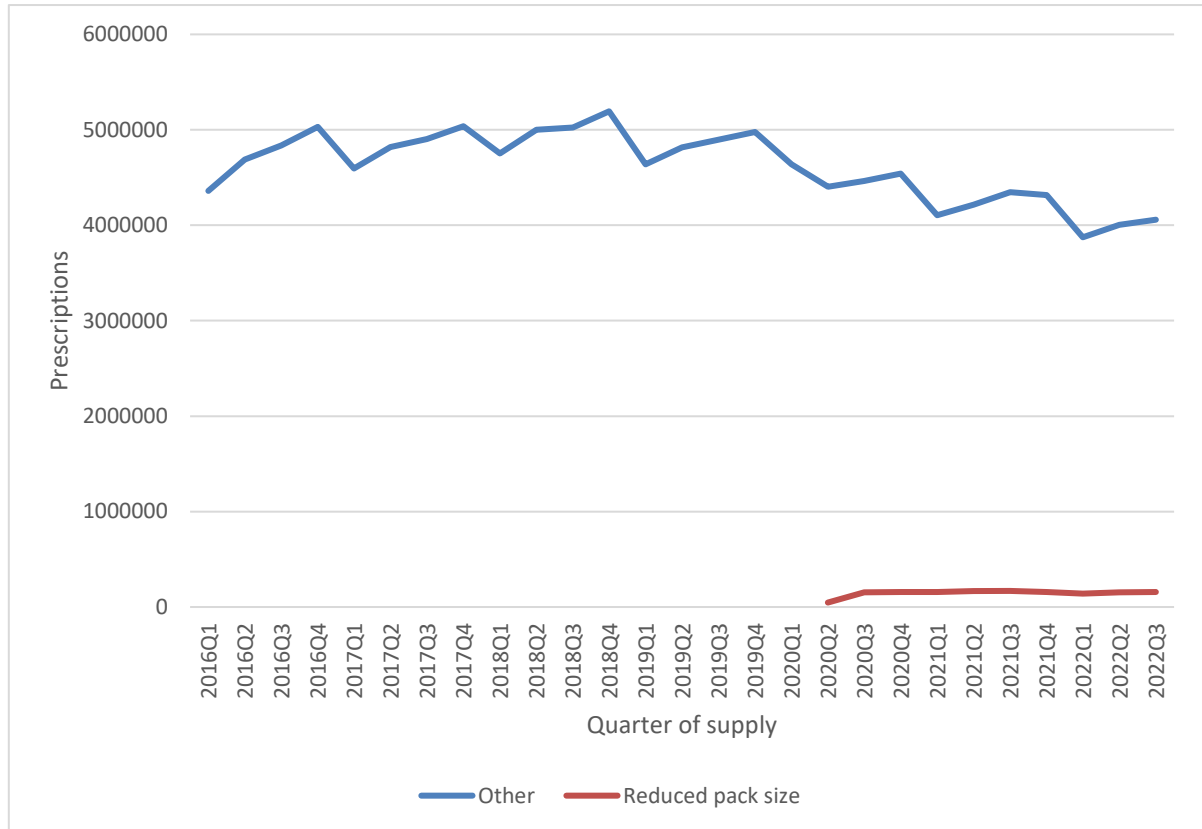


Figure 9: Prescriptions by whether the listing was for a reduced pack size

The number of supplied prescriptions with a reduced pack size is small in the context of the opioids market. In 2021 there were 649,551 prescriptions supplied with a reduced pack size.

Figure 10 below shows the number of patients supplied a reduced pack size prescription or other prescription. This also suggests the utilisation of reduced pack size prescriptions is relatively small.

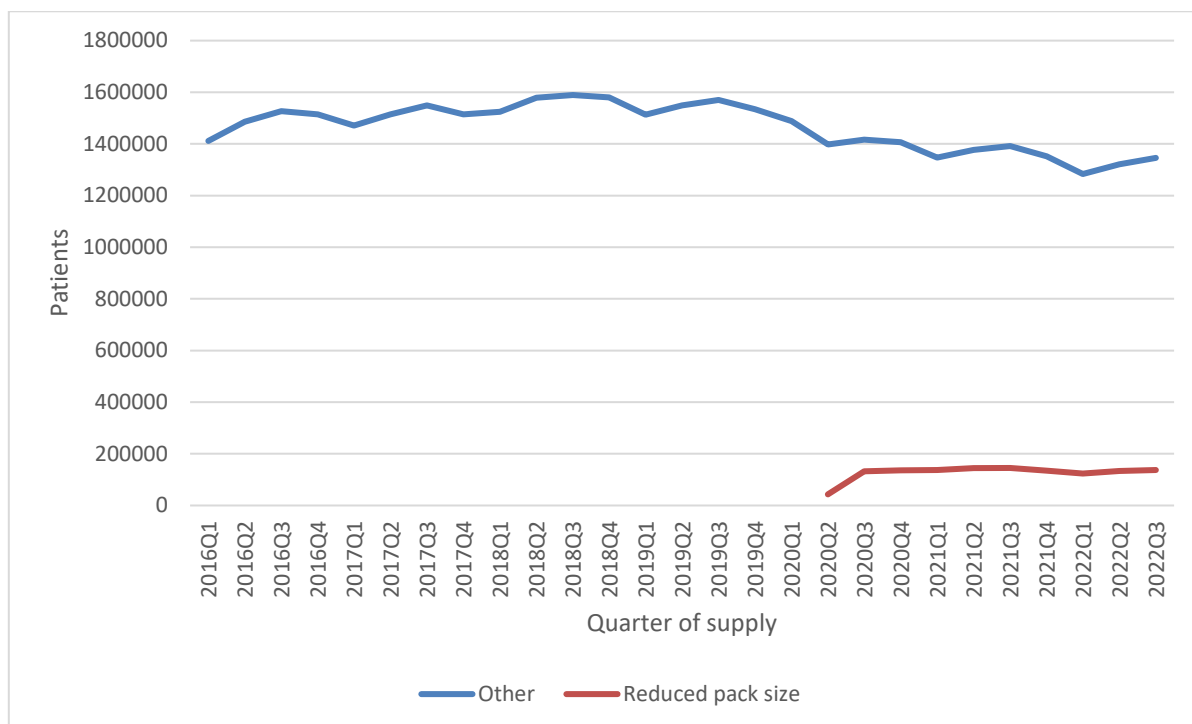


Figure 10: Number of patients by whether the listing was for a reduced pack size

Table 8 below shows the number of repeats prescribed by year, for prescriptions supplied under the reduced pack size PBS item codes and other PBS item codes. In 2021 there were 165 of 649,437 prescriptions prescribed with repeats for reduced pack size (0.03%) compared to 1,173,660 of nearly 14 million other pack sizes (8.5%).

Table 8: Number of original prescriptions by pack size and repeats prescribed

	Other			Reduced pack sizes (listed in 2020)		
	Number of prescribed original prescriptions	Number prescribed with no repeats ordered	Number prescribed with repeats ordered	Number of prescribed original prescriptions	Number prescribed with no repeats ordered	Number prescribed with repeats ordered
2015	220,943	137,028	83,915			
2016	14,375,386	12,466,657	1,908,729			
2017	14,626,409	12,710,343	1,916,066			
2018	15,113,298	13,186,129	1,927,169			
2019	14,593,252	12,752,104	1,841,148			
2020	14,026,225	12,610,331	1,415,894	361,636	361,436	200
2021	13,856,476	12,682,816	1,173,660	649,437	649,272	165
2022 (YTD September)	9,510,113	8,684,131	825,982	447,997	447,851	146

Medicine sequence

The table below shows the top 30 medicine sequences of patients who initiated in 2019, up to September 2022, and notes when patients were recorded in the date of death data. Medicines are only counted once, for example if a patient is supplied A > B > A this is counted as A > B.

Table 9: Medicine sequence

Sequence	Count Patients
PARACETAMOL + CODEINE	451,840
OXYCODONE	193,939
PARACETAMOL + CODEINE > OXYCODONE	66,378
TRAMADOL	61,493
OXYCODONE > PARACETAMOL + CODEINE	44,768
PREGABALIN	34,574
OXYCODONE + NALOXONE	24,802
PARACETAMOL + CODEINE > TRAMADOL	20,316
PARACETAMOL + CODEINE > PREGABALIN	15,715
TAPENTADOL	14,379
TRAMADOL > PARACETAMOL + CODEINE	13,773
OXYCODONE > OXYCODONE + NALOXONE	12,716
OXYCODONE > TRAMADOL	10,132
TRAMADOL > OXYCODONE	10,041
PREGABALIN > PARACETAMOL + CODEINE	8,640
MORPHINE > DEATH	8,159
PARACETAMOL + CODEINE > OXYCODONE + NALOXONE	5,854
OXYCODONE > PREGABALIN	5,643
OXYCODONE + NALOXONE > PARACETAMOL + CODEINE	5,325
OXYCODONE > TAPENTADOL	5,107
PARACETAMOL + CODEINE > TAPENTADOL	4,767
OXYCODONE > DEATH	4,546
PREGABALIN > OXYCODONE	4,432
TAPENTADOL > OXYCODONE	4,364
CODEINE	4,315
PARACETAMOL + CODEINE > DEATH	4,161
PARACETAMOL + CODEINE > OXYCODONE > TRAMADOL	3,866
PARACETAMOL + CODEINE > OXYCODONE > OXYCODONE + NALOXONE	3,663
PARACETAMOL + CODEINE > TRAMADOL > OXYCODONE	3,643
TRAMADOL > PREGABALIN	3,286

Mean quantity over time

Table 10: Mean quantity supplied per year by drug and form

Drug and form	2016	2017	2018	2019	2020	2021	2022
BUPRENORPHINE TRANSDERMAL PATCH	2.75	2.74	2.74	2.75	2.72	2.72	2.74
CODEINE TABLET	56.3	56.99	53.34	51.7	54.74	46.41	44
FENTANYL LOZENGE	73.94	78.02	80.45	78.64	74.83	76.49	79.08
FENTANYL TABLET	53.43	63.56	70.38	71.16	70.64	71.39	71.56
FENTANYL TRANSDERMAL PATCH	6.7	6.76	6.81	6.85	6.84	6.87	6.97
GABAPENTIN CAPSULE	112.71	115.4	115	114.01	113.01	113.77	117.03
GABAPENTIN TABLET	115.54	116.69	118.05	114.92	114.7	117.72	116.67
HYDROMORPHONE INJECTION	12.05	12.79	12.65	11.73	11.7	10.74	10.34
HYDROMORPHONE ORAL LIQUID	1.11	1.06	1.06	1.19	1.22	1.32	1.03
HYDROMORPHONE ORAL SOLUTION						1.23	145.81
HYDROMORPHONE TABLET	26.08	27.26	27.37	27.5	27.18	28.7	28.59
METHADONE INJECTION	22.21	18.59	24.3	18.78	22.45	24.99	24.75
METHADONE ORAL LIQUID	2.23	6.35	2.46	1.89	4.42	10.99	2.7
METHADONE TABLET	82.03	80.62	79.14	77.63	76.73	77.94	78.27
MORPHINE CAPSULE	45.33	45.58	45.48	45.39	45.25	44.81	45.38
MORPHINE GRANULES FOR ORAL SUSPENSION	40.38	39.02	39.16	38.49	37.8	38.18	34.89
MORPHINE INJECTION	8.11	7.73	7.68	7.97	7.87	7.88	8.07
MORPHINE ORAL SOLUTION	1.15	1.14	1.14	1.14	1.23	1.12	1.13
MORPHINE TABLET	43.38	43.26	42.78	42.17	41.53	41.36	40.99
OXYCODONE + NALOXONE TABLET	33.33	33.07	33.2	33.55	33.94	34.12	34.92
OXYCODONE CAPSULE	36.11	36.94	36.94	37.92	37.48	36.28	36.03
OXYCODONE ORAL SOLUTION	1.33	1.31	1.34	1.35	1.32	1.3	1.33
OXYCODONE SUPPOSITORY	34.47	32.81	35.35	37.13	35.78	29.45	30.02
OXYCODONE TABLET	30.14	29.58	28.8	28.29	27.07	25.82	26.32
PARACETAMOL + CODEINE TABLET	51.3	51.58	47.79	47.93	45.01	40.12	39.73
PREGABALIN CAPSULE	56.47	56.43	56.42	56.43	56.39	56.35	56.32
TAPENTADOL TABLET	35.5	34.95	34.75	34.48	34.97	35.05	34.94
TRAMADOL CAPSULE	20.15	20.11	20.02	19.93	20.52	21.98	22.45
TRAMADOL INJECTION	4.81	4.85	4.88	4.89	5.18	5.5	6.19
TRAMADOL ORAL DROPS	2.02	2.12	2.04	1.76	1.64	1.55	1.64
TRAMADOL TABLET	40.37	40.59	40.29	40.47	38.83	35.82	35.85

Note: For units of the mean quantity supplied refer to the units specified in the maximum quantity.

The average supplied quantity of hydromorphone oral solution increased from 1.03 in 2021 to 145.81 in 2022 (January to September). This is due to the amendments made from 1 August 2022 to the PBS listings of hydromorphone oral solutions to allow pharmacists to dispense volumes smaller than a whole bottle at PBS subsidised prices.

Fentanyl patches

The PBAC recommended narrower indications for fentanyl patches. The intent was to reduce the number of new patients rather than to require patients who are currently reliant on the patches to move to other pain relief medications. However, there was an expectation that prescribers would identify patients who are currently prescribed fentanyl patches outside of the cancer pain and the palliative care setting to consider weaning patients where it is appropriate and safe to do so. The figure below shows initiating and treated patients for fentanyl patches only, and counts initiating patients as their first supply of a fentanyl patch.

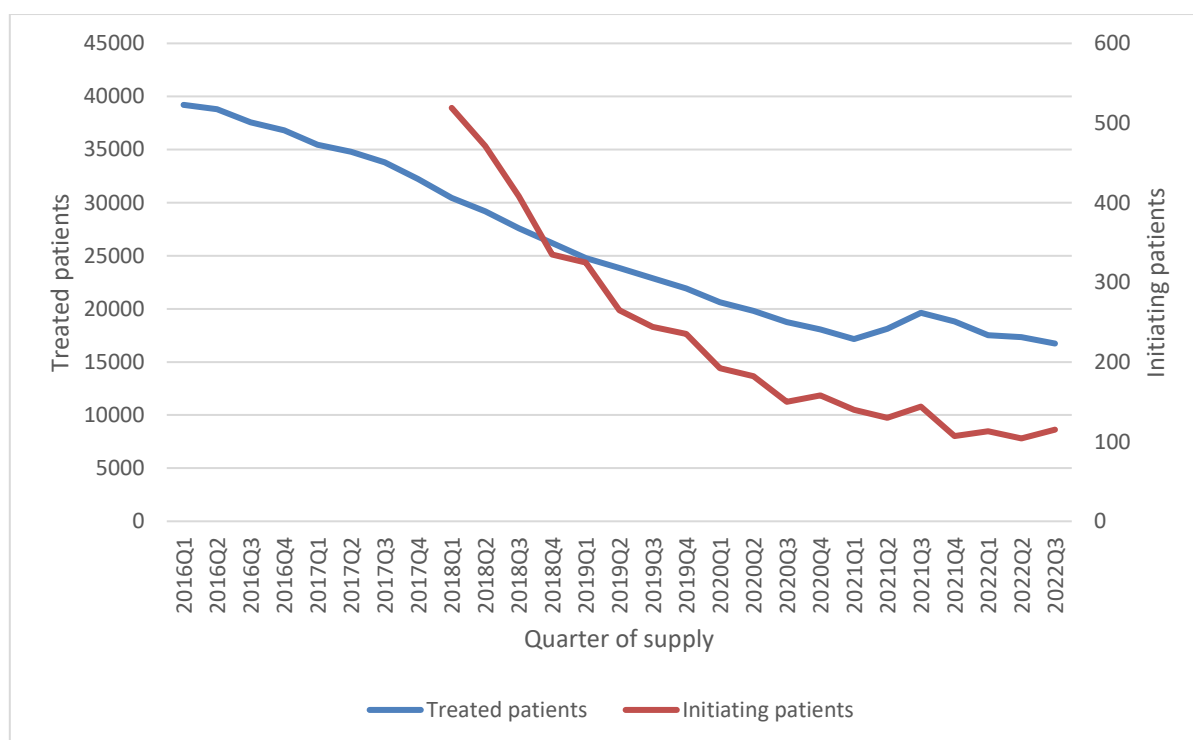


Figure 11: Number of treated and initiating patients on fentanyl patches

Table 10 shows that the average quantity of supplied fentanyl patches has not changed. The number of initiating patients has been decreasing over time, although this may be exaggerated due to the method of determining an initiating patient. Overall it appears that the number of new and treated patients may have stabilised.

It is likely that the increase in treated patients is due to the changes made to the palliative care schedule on 1 June 2021, which were intended to further reduce barriers to the prescribing and timely supply of opioid analgesic medications for palliative care patients.

Tapentadol

Table 11: Prescriber type of treated patients for tapentadol by year

Prescriber type	2016	2017	2018	2019	2020	2021	2022
VRGP	62,631	93,808	118,145	147,166	161,204	166,676	157,154
Non-VRGP	16,786	22,908	27,400	24,753	19,478	24,052	20,803
(blank)	353	3,642	12,689	32,862	46,613	22,175	11,706
GP Trainee	6,577	11,184	15,529	17,106	14,702	20,980	25,691
Surgery	5,955	13,428	21,023	26,430	16,335	9,867	8,381
Anaesthetics	6,082	12,395	16,248	21,552	10,079	4,244	3,090
Palliative Medicine	5,340	5,203	5,066	5,608	4,356	3,607	3,265
GP Unclassified	6,889	14,458	10,052	951		<5	10
Rehabilitation Medicine	2,196	3,186	4,251	5,697	3,981	3,386	2,757
Internal Medicine	1,127	1,535	2,055	2,676	2,408	2,159	1,805
Rheumatology	1,653	1,723	2,111	2,349	1,885	1,790	1,325
Geriatric Medicine	646	1,217	1,782	2,298	1,793	1,445	1,092
Medical Oncology	461	692	859	1,138	1,208	1,409	1,412
Intensive Care	613	868	1,059	1,518	1,022	1,080	992
Obstetrics and Gynaecology	362	792	1,504	1,610	959	433	352

Note: Patients may be counted under more than one prescriber type

VRGP: Vocationally registered general practitioner, Non-VRGP: Non-vocationally registered general practitioner

The majority of prescribers for tapentadol across all calendar years was GPs. In 2021 there were 215,145 patients supplied tapentadol, including 187,091 (87%) patients supplied tapentadol which was prescribed by a VRGP, non-VRGP or trainee GP.

Table 12: Medicine sequence for patients supplied tapentadol

Sequence	Count Patients	Percent
TAPENTADOL	14,379	17.9%
OXYCODONE>TAPENTADOL	5,107	6.3%
PARACETAMOL + CODEINE>TAPENTADOL	4,767	5.9%
TAPENTADOL>OXYCODONE	4,364	5.4%
TAPENTADOL>PARACETAMOL + CODEINE	2,796	3.5%
TRAMADOL>TAPENTADOL	1,910	2.4%
PARACETAMOL + CODEINE>OXYCODONE>TAPENTADOL	1,743	2.2%
PREGABALIN>TAPENTADOL	1,462	1.8%
TAPENTADOL>TRAMADOL	1,380	1.7%
TAPENTADOL>PREGABALIN	1,280	1.6%
OXYCODONE + NALOXONE>TAPENTADOL	1,134	1.4%
PARACETAMOL + CODEINE>TAPENTADOL>OXYCODONE	1,130	1.4%
OXYCODONE>TAPENTADOL>PARACETAMOL + CODEINE	1,011	1.3%
TAPENTADOL>OXYCODONE>PARACETAMOL + CODEINE	863	1.1%
OXYCODONE>PARACETAMOL + CODEINE>TAPENTADOL	721	0.9%
PARACETAMOL + CODEINE>TRAMADOL>TAPENTADOL	720	0.9%
PARACETAMOL + CODEINE>PREGABALIN>TAPENTADOL	686	0.9%
OXYCODONE>OXYCODONE + NALOXONE>TAPENTADOL	604	0.8%
TAPENTADOL>OXYCODONE + NALOXONE	585	0.7%
PARACETAMOL + CODEINE>TAPENTADOL>PREGABALIN	513	0.6%
TRAMADOL>OXYCODONE>TAPENTADOL	434	0.5%
OXYCODONE>TAPENTADOL>PREGABALIN	431	0.5%
TAPENTADOL > DEATH	401	0.5%
PARACETAMOL + CODEINE>OXYCODONE + NALOXONE>TAPENTADOL	398	0.5%
TRAMADOL>TAPENTADOL>OXYCODONE	380	0.5%
TAPENTADOL>PARACETAMOL + CODEINE>OXYCODONE	374	0.5%
PARACETAMOL + CODEINE>TAPENTADOL>TRAMADOL	370	0.5%
PREGABALIN>OXYCODONE>TAPENTADOL	351	0.4%
OXYCODONE>TRAMADOL>TAPENTADOL	349	0.4%

The medicine sequence includes patients who initiated during 2019, and patients were followed until 30 September 2022, with no duplicate medicines included. In total 80,254 patients who initiated treatment in 2019 have been supplied tapentadol, and approximately 18% of these were only supplied tapentadol through the PBS, noting that private prescriptions and over the counter medicines were not included in the data.

Analysis of expenditure

Table 13: Cost to Government by calendar year

	2016	2017	2018	2019	2020	2021	2022 (YTD September)
BUPRENORPHINE	\$64,403,137	\$65,381,290	\$60,210,263	\$55,208,881	\$56,496,826	\$56,049,580	\$37,526,013
CODEINE	\$1,950,161	\$1,856,015	\$1,759,525	\$1,649,674	\$1,415,729	\$1,387,936	\$993,974
FENTANYL	\$25,198,684	\$20,337,381	\$17,788,485	\$15,405,840	\$13,451,389	\$12,368,062	\$7,855,851
GABAPENTIN	\$144,379	\$93,221	\$82,633	\$86,216	\$103,129	\$99,479	\$58,961
HYDROMORPHONE	\$10,224,028	\$9,976,657	\$9,165,012	\$8,101,218	\$8,039,311	\$7,474,916	\$5,210,082
METHADONE	\$3,544,654	\$3,471,443	\$3,404,220	\$3,221,020	\$3,209,834	\$3,118,688	\$2,004,313
MORPHINE	\$21,601,435	\$19,997,592	\$18,437,751	\$16,814,522	\$16,187,953	\$15,471,791	\$10,776,582
OXYCODONE	\$63,083,676	\$60,190,363	\$54,714,892	\$47,268,306	\$48,015,771	\$48,575,111	\$35,380,002
OXYCODONE + NALOXONE	\$66,208,229	\$71,313,468	\$72,268,271	\$67,945,433	\$66,714,712	\$64,770,446	\$34,942,430
PARACETAMOL + CODEINE	\$23,001,396	\$26,706,993	\$28,814,560	\$28,039,121	\$35,459,515	\$38,031,933	\$25,754,980
PREGABALIN	\$153,417,805	\$151,940,627	\$126,404,161	\$98,113,993	\$82,964,933	\$62,956,405	\$38,420,248
TAPENTADOL	\$12,263,070	\$18,128,578	\$23,062,790	\$27,124,057	\$31,442,298	\$34,636,441	\$27,154,588
TRAMADOL	\$23,507,424	\$23,902,154	\$24,054,502	\$23,171,474	\$20,947,869	\$18,426,741	\$12,182,612
Total	\$468,548,077	\$473,295,785	\$440,167,062	\$392,149,756	\$384,449,268	\$363,367,530	\$238,260,637

The cost to Government based on the published prices for opioids and non-opioids has decreased each year, from \$470 million in 2016 to \$360 million in 2021.

Discussion

The 1 June 2020 regulatory reforms to PBS listed opioids were implemented with the intention of complementing the TGA's efforts to support the safe and clinically appropriate use of opioids while recognising the important role they play in providing pain relief for many people.

The utilisation of opioids does appear to be decreasing according to PBS data, however this decline in use and the number of patients treated was not sudden and may have been a continuing trend from before the regulatory reforms were implemented.

At the time of its recommendation (December 2019), the PBAC noted that the regulatory changes and recommended changes to PBS listings would be implemented as part of a broader suite of measures intended to support appropriate use of opioids, including education and awareness campaigns, changes to clinical guidelines and ongoing prescription and compliance monitoring. It is therefore difficult to determine the proportion of the reduction use that was directly attributable to the reforms.

The reduction in the number of prescribed repeats when 2021 is compared to 2019, and the number of prescriptions for reduced pack sizes suggests that the reforms may have led to less wastage or stored opioids in the community.

The number of patients initiating and supplied fentanyl patches appears to have decreased over time, but may have stabilised. The number of patients treated with fentanyl patches appeared to increase in the second and third quarters of 2021, likely because of changes to the palliative schedule intended to reduce barriers to the prescribing and timely supply of opioid analgesic medications for palliative care patients.

The use of tapentadol, which is available as modified release tablets, appears to be increasing. Tapentadol was increased to Authority Required (STREAMLINED) for daily, continuous, long term management of pain due to cancer or in patients who have not responded to, are intolerant to or who experience inadequate pain management at maximum doses of non-opioid or other opioid analgesics. The majority of prescribers for tapentadol across all calendar years were GPs, with 87% of the 215,145 patients supplied tapentadol in 2021 prescribed at least one prescription written by a GP.

DUSC consideration

DUSC noted the report showed the number of PBS supplied prescriptions of opioids medicines had decreased. DUSC noted the report showed no therapeutic shift to gabapentinoids listed on the PBS. DUSC noted the number of treated patients had decreased, and it appeared that the number of initiating patients had decreased but commented that as the method only allowed one initiation per patient, the number of initiating patients may not be continuing to fall.

DUSC noted additional analyses of defined daily doses (DDDs) based on a 10% sample. DUSC noted that although DDDs are based on cancer pain the analysis of use by DDDs shows the volume of drug over time, and commented that the reduction in supplied opioids was much higher than the number of prescriptions and better reflects the impact of the change in pack sizes.

DUSC noted the number of prescriptions of oxycodone + naloxone reduced in quarter 2 of 2022, with a corresponding increase in oxycodone. DUSC noted that this was likely due to a medicine shortage.

DUSC noted the report showed the use of tapentadol was rising. Noting that patients may be being discharged post operatively from hospital on tapentadol, which may be contributing to its increasing use. DUSC noted that tapentadol had been marketed as being useful for treating neuropathic pain. DUSC noted that tapentadol has a higher potency than some other opioids and the modified release formulation may or may not be harm minimising.

DUSC noted that more women than men are treated with opioids in every age group on the general and palliative care schedules.

DUSC noted that the PBS opioid reforms intended to move the use of fentanyl patches more towards cancer pain, and that the use of fentanyl patches was decreasing. DUSC commented that the decrease in use of fentanyl patches started prior to the restriction changes.

DUSC noted that since the reforms, fewer patients were supplied two or more treatments on the same day and the number of prescriptions written without repeats had reduced. DUSC noted that reduced pack sizes only applied to a few of the medicines, and accounted for 4% of the prescriptions and 10% of patients. DUSC suggested that the proportion of prescriptions written for reduced pack sizes may have been higher in initiating patients, and considered a further analysis stratified by new and existing users may be informative.

DUSC noted the sponsor responses to the utilisation analysis, and the responses from The National Aboriginal Community Controlled Health Organisation and Painaustralia.

DUSC noted the sponsor response from Janssen stated, "The present DUSC analysis suggests that regulatory reforms and associated PBS changes to opioid analgesics since 1 June 2020 have contributed to the continued decline in their utilisation and government expenditure on this class of medicines. Meanwhile, growth in prescriptions under the Palliative Care Schedule show that recent palliative care schedule changes have met their intended purpose of improving opioid access to palliative care patients. Utilisation and government expenditure on fentanyl and hydromorphone (including Janssen marketed forms and brands) during the analysis period was lower than for most other opioids and show declining trends. In summary, Janssen supported DUSC's conclusion that there is continuing downward trend of opioid use from before the regulatory reforms were implemented."

DUSC noted the sponsor response from TEVA, which is the sponsor of fentanyl orally disintegrating tablets and lozenges. The response noted the use of fentanyl lozenges has been declining and the volumes may become commercially unviable, as it is extremely difficult to anticipate where and when there will be a demand for low volume items.

DUSC noted the long term use of opioids for non-cancer pain in existing patients which represents a large volume of use is likely to be among complex patients where changes in opioid use are more likely to be realised over a longer time frame. DUSC noted that a publication from 2015⁴ found 51% of Australian patients using opioids chronically for non-cancer pain were unemployed because of pain, 60% were also diagnosed with depression and 32% were diagnosed with generalised anxiety. The report also noted 40% had an alcohol use disorder and 47% were smokers. DUSC noted that these are patients with complex medical problems and they need other types of support outside the scope of the PBS listings.

DUSC noted that it is difficult to measure the impact of the opioid reforms on overdoses or fatalities. DUSC considered that there are still many PBS listings for chronic pain, and that although patients may need to visit their doctor more often, they should still be able to access appropriate subsidised treatment. DUSC noted that more frequent visits to the doctor could be viewed as a positive change as it has created more opportunities for discussions with the patient regarding their pain and care.

DUSC requested additional information be presented to the committee, including:

- Use over time by DDDs
- Use over time in 2022 by jurisdiction (by state and regional/remote) and age
- The proportion of reduced pack size use in initiating patients versus chronic patients and the proportion of initiating patients who become chronic users (more than 90 days' supply) stratified by whether they initiate on small or standard pack sizes.
- An analysis to determine if there has been a shift to private prescriptions (if possible)
- An analysis to determine if there has been a disproportionate effect on Aboriginal and Torres Strait Islander people (if possible)
- An analysis by volume of use per person per year (Lorenz curves) to determine the proportion of the population each year who get less than 30 days' supply.

Additional analyses were presented to the June 2023 DUSC meeting and are included in the addendum.

⁴ Campbell G, Nielsen S, Bruno R, Lintzeris N, Cohen M, Hall W, Larance B, Mattick RP, Degenhardt L. The Pain and Opioids IN Treatment study: characteristics of a cohort using opioids to manage chronic non-cancer pain. *Pain*. 2015 Feb;156(2):231-242. doi: 10.1097/01.j.pain.0000460303.63948.8e. PMID: 25599444.

Addendum: Impact of regulatory reforms on utilisation of opioids

Purpose

At its February 2023 meeting, DUSC considered a review of the utilisation of Pharmaceutical Benefits Scheme (PBS)-listed opioid analgesics to examine the impact of the 1 June 2020 regulatory reforms and associated PBS listing changes for opioid analgesics.

DUSC requested additional information be presented to the committee, including:

- Use over time by defined daily doses (DDDs)
- Use in 2022 by jurisdiction (by state and regional/remote) and age
- The proportion of reduced pack size use in initiating patients versus chronic patients and the proportion of initiating patients who become chronic users (more than 90 days' supply) stratified by whether they initiate on small or standard pack sizes.
- An analysis to determine if there has been a shift to private prescriptions (if possible)
- An analysis to determine if there has been a disproportionate effect on Aboriginal and Torres Strait Islander people (if possible)
- An analysis by volume of use per person per year (Lorenz curves) to determine the proportion of the population each year who get less than 30 days' supply.

Methods and sources

Data extracted from the PBS claims database maintained by the Department of Health and Aged Care and processed by Services Australia were used for the analyses of:

- Initiating and treated patients over time using a two year lookback for initiating patients.
- Use over time by DDDs
- Use in 2022 by jurisdiction (by state and regional/remote) and age.
- Further analysis of the proportion of reduced pack sizes.
- Volume of use per person per year from 2018 to 2022.

Prescription data were extracted from 1 January 2016 up to and including 31 December 2022 based on the date of supply.

Data were extracted for:

- N02A (analgesics – opioids).
- N02BG (Other analgesics and antipyretics) – pregabalin and gabapentin.
- Where the PBS restriction included 'pain'.

- Data extracted from the PBS data maintained by Department of Health and Aged Care, processed by Services Australia, was used for the analyses. The data was extracted from 1 January 2016 to 31 December 2022 based on the date of supply.

Initiating and treated patients over time

Data were extracted from 1 January 2016, initiating patients were determined using a two year lookback and presented from 1 January 2018.

Use in 2022 by jurisdiction (by state and regional/remote) and age

The number of patients by age and sex were standardised using the estimated resident population at 30 June 2022 (31010do002_202209 National, state and territory population, Sep 2022, <https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/sep-2022#national>).

The number of patients by State and Territory and remoteness level were standardised using the estimated population at 30 September 2022 (<https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/latest-release#states-and-territories>).

Further analysis of the proportion of reduced pack sizes

Reduced size packs were identified by the phrase “short term therapy” in the PBS restriction. Initiating patients were determined using a two year lookback, and one year of prescription data was examined to determine in the patient received 90 days continuous supply. The mode refill time by form and strength were used to determine the number of days supply for each supplied prescription, and 3 times the mode refill time were used to test for breaks.

Volume of use per person per year from 2018 to 2022

Presented as Lorenz curves using code provided by Professor Nicole Pratt.

Use of private prescriptions

It was not possible to complete an analysis to determine if there has been a shift to private prescriptions in the PBS data or other data available to the Secretariat.

Use for Aboriginal and Torres Strait Islander people

The PBS prescription data contains a variable named ‘CTG_CD’ which is an indicator of whether the patient is eligible for a Closing the Gap (CTG) co-payment, as represented by a code. The CTG co-payment was established to reduce the cost of PBS medicines for eligible Aboriginal and Torres Strait Islander people either living with or at risk of chronic disease. This variable is generally underreported as patients must register for the CTG co-payment, and may be blank although a patient is an Aboriginal or Torres Strait Islander person. In the opioids data, 2.3% of patients were indicated as being eligible for the CTG co-payment.

Results

Use over time

At the February 2023 DUSC meeting, DUSC commented that the decrease in the number of initiating patients may appear higher as the analysis only counted first time initiators. Figure 12 below shows patients initiating with a two year lookback and for the first time with a lookback to 1 January 2016.

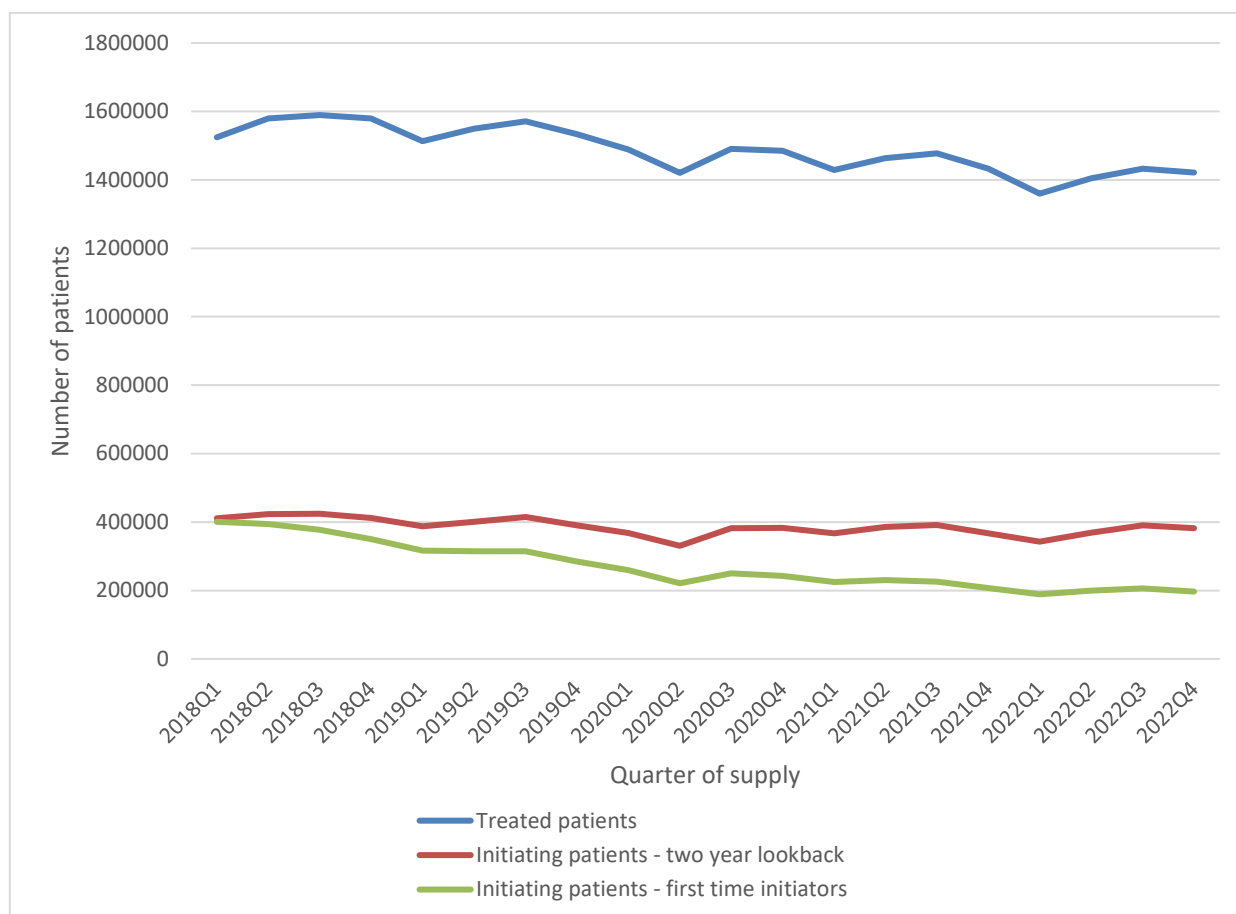


Figure 12: Initiating and treated patients over time

Use over time by drug using DDDs is shown in Figure 13.

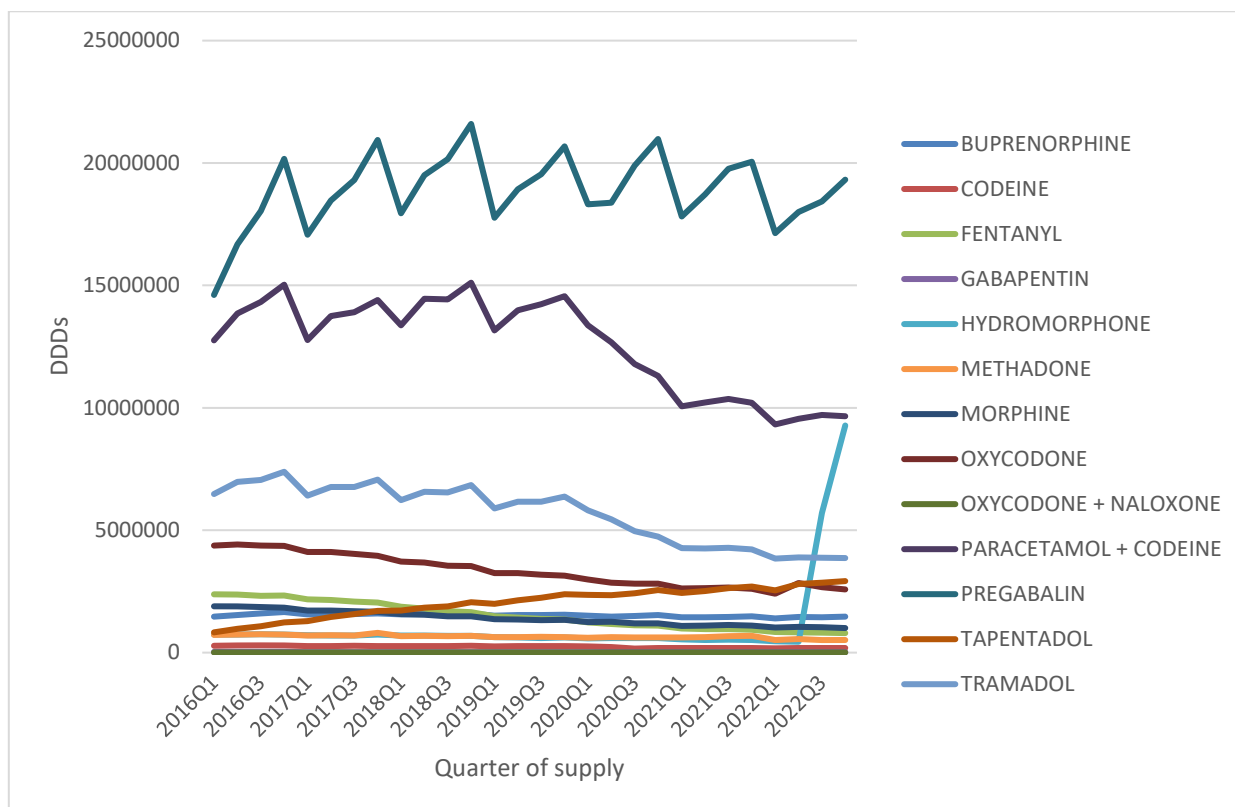


Figure 13: Use over time using DDDs

The increase in hydromorphone from the third quarter of 2022 is likely due to amendments to the PBS listings of hydromorphone oral solutions to allow pharmacists to dispense volumes smaller than a whole bottle at PBS subsidised prices, from 1 August 2022.⁵

Table 14: Amendments to hydromorphone oral solution effective 1 August 2022

Change	Previous listing	Amendments from 1 August 2022
Legislative Instrument form descriptions	Oral solution containing hydromorphone hydrochloride 1 mg per mL, 473 mL	Oral solution containing hydromorphone hydrochloride 1 mg per mL, 1 mL
Pharmaceutical Item value	1 unit (i.e. bottle)	473 units (i.e. millilitres)
Pack Qty	1	473
Pricing Qty	1	473
Max Qty Units	1	473

⁵ PBS website, Changes to PBS listing of hydromorphone oral solution
<https://www.pbs.gov.au/info/news/2022/08/changes-to-pbs-listing-of-hydromorphone-oral-solution>

Use in 2022

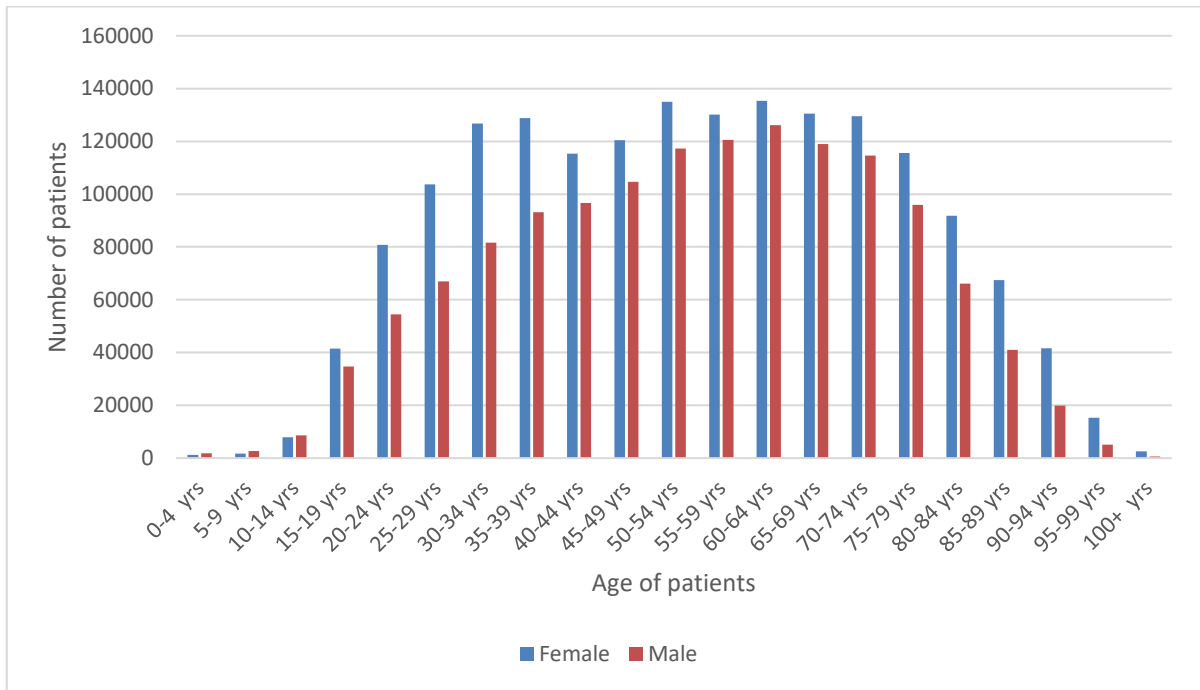


Figure 14: Age and gender of patients supplied opioids in 2022

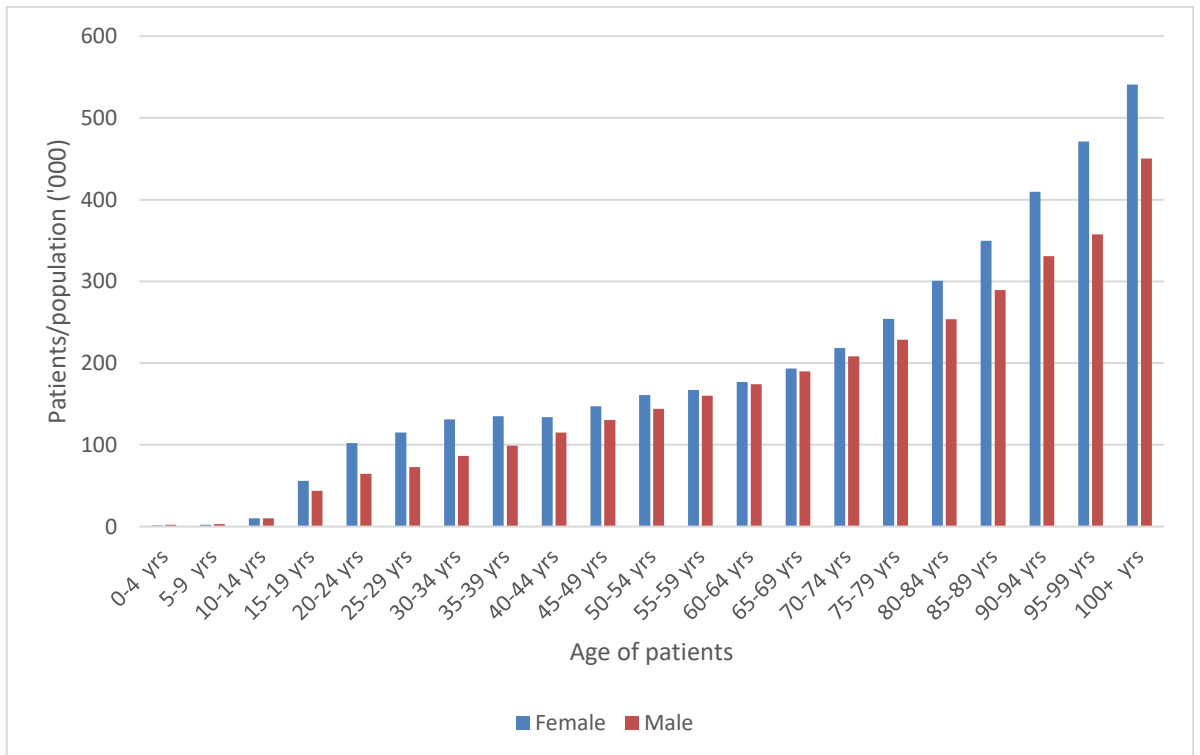


Figure 15: Age and gender of patients supplied opioids in 2022 (standardised)

Figure 15 shows that when patients supplied opioids in 2022 were standardised by age and gender, use of opioids increased with age, and was higher in female patients across every age group.

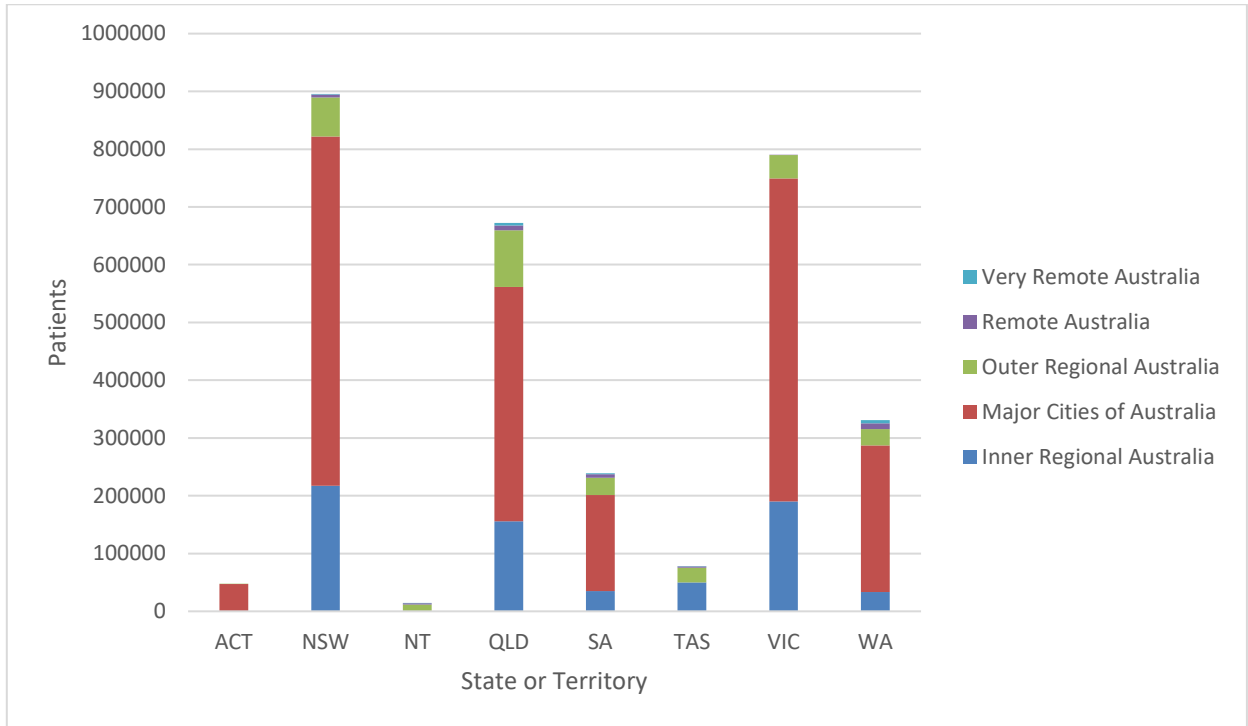


Figure 16: Patients supplied opioids in 2022 by state and remoteness level

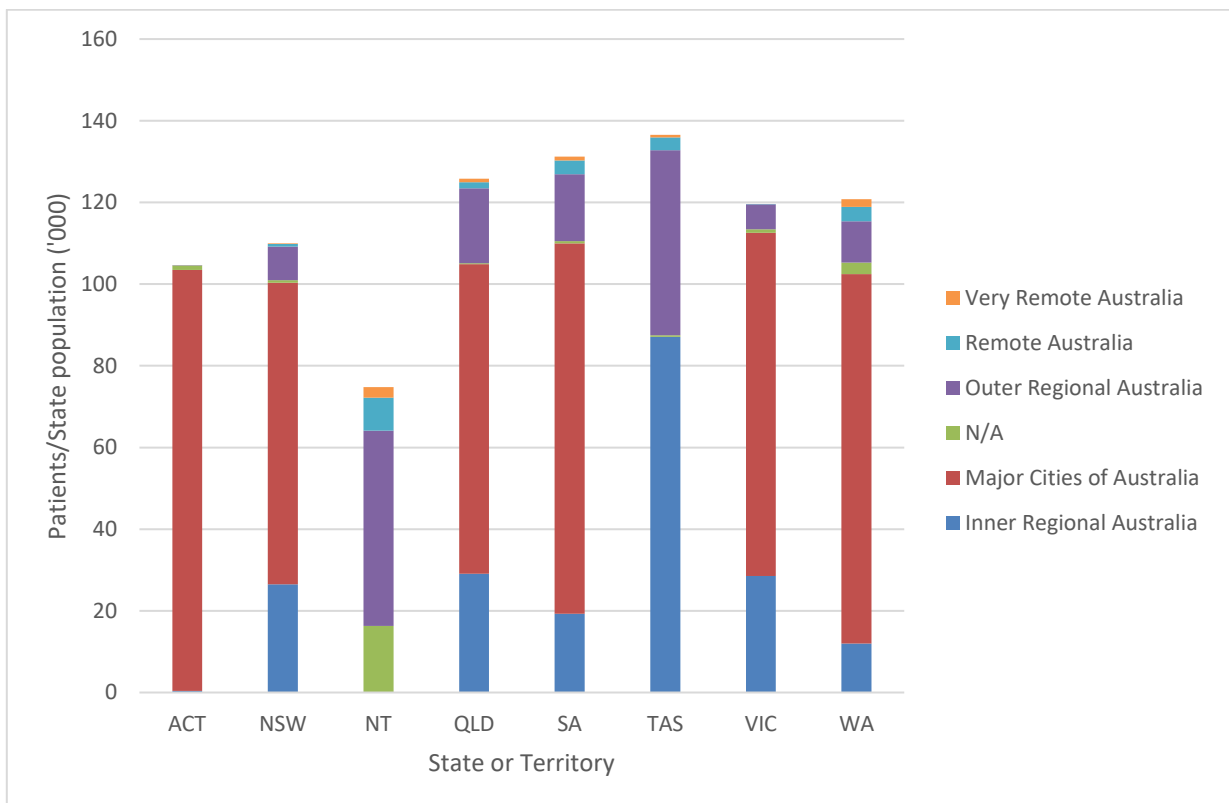


Figure 17: Patients supplied opioids in 2022 by state and remoteness level (standardised)

Figure 17 shows that the standardised number of patients supplied opioids in 2022 was highest in South Australia and Tasmania.

Reduced pack sizes

Table 15: Chronic use in initiating patients stratified by whether they initiate on small or standard pack sizes

Year	Initiation type	Did not receive chronic treatment	Chronic treatment	Number of patients
2018	Initiated on a standard size pack	95.2% (1,669,565)	4.8% (83,718)	1,753,283
2019	Initiated on a standard size pack	95.6% (1,592,722)	4.4% (73,400)	1,666,122
2020	Initiated on a standard size pack	95.1% (1,339,132)	4.9% (68,516)	1,407,648
	Initiated on a reduced size pack	98% (124,422)	2% (2,496)	126,918
2021	Initiated on a standard size pack	95.2% (1,274,269)	4.8% (63,575)	1,337,844
	Initiated on a reduced size pack	98.2% (237,079)	1.8% (4,415)	241,494

Table 15 above suggests that the percentage of patients who received more than 90 days supply of opioids in the first year following initiation was lower in patients who initiated on reduced size pack.

Volume of use per person per year from 2018 to 2022

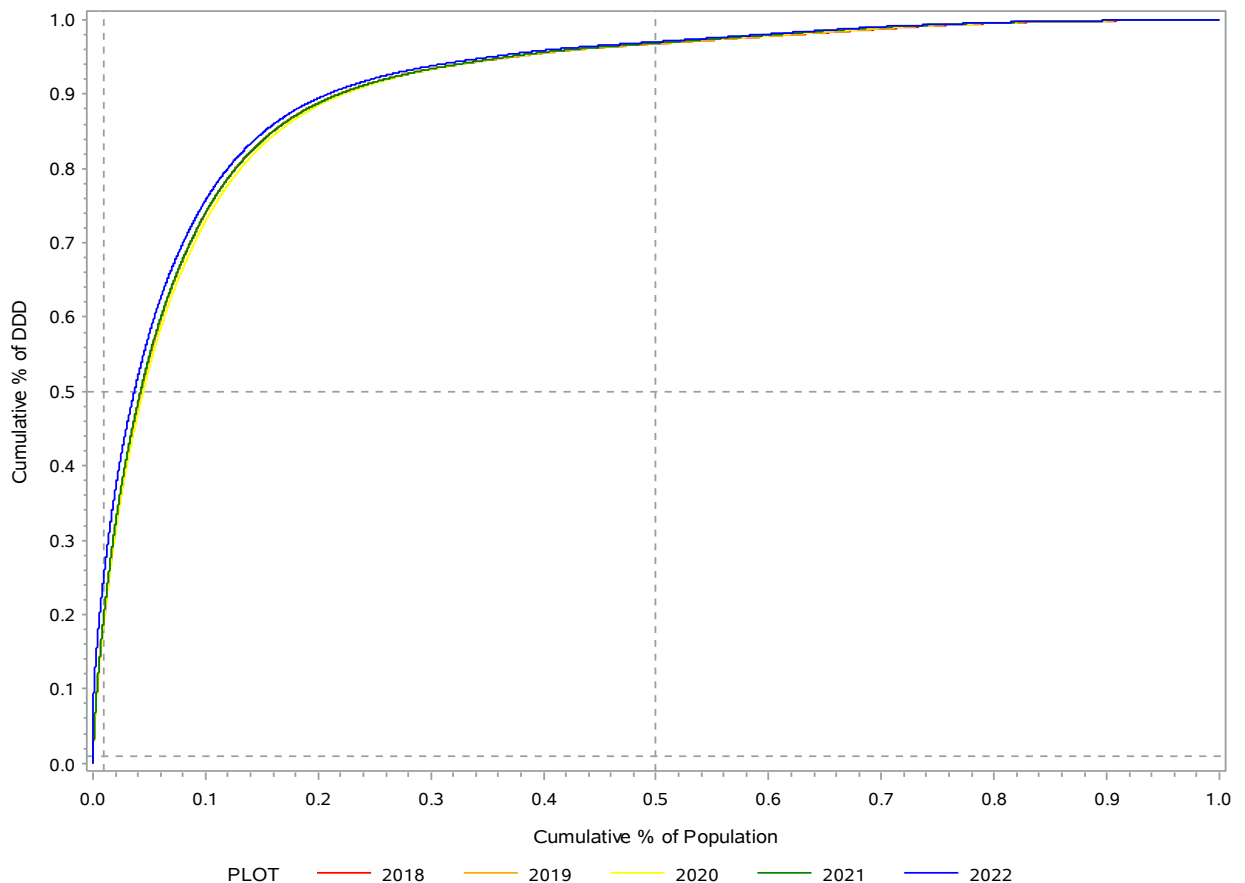


Figure 18: Volume use per person per year from 2018 to 2022

Figure 18 suggests that approximately 10% of the population were supplied 70% of the opioids supplied in each year from 2018 to 2022.

DUSC consideration

At the June 2023 DUSC meeting, the committee was presented an addendum to the February 2023 review of the utilisation of Pharmaceutical Benefits Scheme (PBS)-listed opioid analgesics to examine the impact of the 1 June 2020 regulatory reforms and associated PBS listing changes for opioid analgesics.

At its February 2023 meeting, DUSC requested additional information be presented to the committee, including:

- Use over time by defined daily doses (DDDs)
- Use in 2022 by jurisdiction (by state and regional/remote) and age
- The proportion of reduced pack size use in initiating patients versus chronic patients and the proportion of initiating patients who become chronic users (more than 90 days' supply) stratified by whether they initiate on small or standard pack sizes
- An analysis to determine if there has been a shift to private prescriptions (if possible)
- An analysis to determine if there has been a disproportionate effect on Aboriginal and Torres Strait Islander people (if possible)
- An analysis by volume of use per person per year (Lorenz curves) to determine the proportion of the population each year who are dispensed less than 30 days' supply

DUSC noted that it was not possible to complete an analysis to determine if there had been a shift to private prescriptions in the PBS data or other data available to the Secretariat. DUSC noted that in the opioids data, 2.3% of patients were indicated as being eligible for the Closing the Gap (CTG) co-payment, and that this variable is generally underreported as patients must register for the CTG co-payment, and may be blank although a patient is an Aboriginal or Torres Strait Islander person.

At the February 2023 DUSC meeting, DUSC commented that it appeared the number of initiating patients had decreased but commented that as the method only allowed one initiation per patient, the number of initiating patients may not be continuing to fall. DUSC noted the number of initiating patients using a two year lookback appeared stable. DUSC commented that this analysis demonstrated that the regulatory reforms did not reduce access to opioids to initiating patients, but that the number of treated patients is decreasing.

DUSC noted the analysis of use over time by DDDs, and commented that the majority of the decrease in use is for codeine with paracetamol and tramadol. DUSC commented that the reduction in supplied codeine with paracetamol was largely due to the pack size changing from 60 to 20. DUSC considered this reduction suggested that prior to the reforms a proportion of the larger packs were wasted, shared with other people or used for other purposes.

DUSC noted the standardised analysis of age and sex of patients supplied opioids in 2022 showed that use is highest in older people, and that use is higher in women than men across all age groups. DUSC noted that the analysis by state and remoteness showed that use was lowest in NT and highest in Tasmania. DUSC noted that utilisation according to remoteness appeared to reflect the known demographic differences between jurisdictions and not necessarily the patients supplied opioids.

DUSC noted the analysis of the volume of use person per year from 2018 to 2022 using a Lorenz curve. DUSC noted this analysis did include aged care patients, palliative patients and patients treated for cancer. DUSC commented this analysis showed that in each year the majority of patients use opioids short term, that 10% of the population account for 75% of the use and that 1% of the patients account for 20% of the use.

DUSC noted the further analysis of reduced pack sizes, and chronic use in initiating patients, stratified by initiation of small or standard pack sizes. DUSC commented that the number of patients initiated on small pack sizes was in relative terms modest, but those patients who were initiated on a reduced pack size were less likely to receive subsequent chronic treatment. DUSC commented that the reforms were intended to have an effect on the use of opioids into the future and considered this analysis suggested reduced packs are being prescribed and supplied to the appropriate patients.

DUSC commented on a research manuscript led by members of NHMRC Medicines Intelligence Centre of Research Excellence investigating changes in the supply of opioids to the PBS and private market after the 1 June 2020 regulatory reforms and PBS listing changes. DUSC noted preliminary findings from this study, showing that PBS dispensing and sales declined after June 2020, but total opioid sales (including the private market) declined to a lesser extent. This likely indicates there was a small shift to the private market in those opioids that were supplied on the PBS prior to the reforms.

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 PBAC. The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist

consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Sponsors with medications mentioned in the report were contacted for comment.

CSL Seqirus: To assist with interpretation, CSL Seqirus would like to note that, in comparison to other opioids tapentadol SR was PBS listed relatively recently in 2013 with utilisation growing prior to the reforms. Since the reforms, the increase in utilisation has slowed significantly, with the increase from previous years reduced from 2019 (20.9%) through 2020 (9.93%) to 2021 (7.72%), with tapentadol only representing 6.65% of total prescriptions in 2021 as shown in the report.

Other sponsors had no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health and Aged Care has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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