

Antibiotics: PBS/RPBS utilisation

Drug utilisation sub-committee (DUSC)

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Abstract

Purpose

To assess the use of antibiotics supplied through the Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS).

Background

Antimicrobial resistance (AMR) is an ongoing public health concern. Reports on the use of antibiotics can inform policy decisions to promote quality use of antibiotics and limit AMR. In April 2014, the World Health Organization released a concerning report on antibiotic resistance.¹ The Organisation for Economic Cooperation and Development (OECD) *Health at a Glance 2011* publication showed that Australia's consumption of antibiotics was higher than the OECD average in 2011.²

In this context, DUSC considered that an analysis of the use of antibiotics through the PBS/RPBS would be timely.

Data source / methodology

The data were extracted from the Department of Human Services (DHS) Medicare pharmacy claims database and the DUSC database.

¹ Antimicrobial resistance: global report on surveillance. World Health Organization 2014 ISBN 978 92 4 156474 8 (NLM classification: QV 250)

² OECD (2011), *Health at a Glance 2011: OECD Indicators*, OECD Publishing.
http://dx.doi.org/10.1787/health_glance-2011-en; Accessed 22 August 2014.

Key Findings

For the calendar year 2013:

- 45% of the Australian population (10,441,015 unique patients) were supplied at least one antibiotic through the PBS.
- There were 26,436,021 prescriptions supplied for systemic antibiotics through the PBS.
- There were 29,227,581 prescriptions supplied for any antibiotic (including systemic and topical antibiotics) through the PBS.
- The most commonly supplied antibiotics were amoxicillin (n=5,665,810), cephalexin (n=5,413,046), and amoxicillin plus clavulanic acid (n=4,512,149).
- The defined daily dose was calculated to be 22.8 DDD/1000/day. This is higher than the 2009 OECD average of 21.1.³
- \$116.5 million in PBS/RPBS benefits was paid for antibiotics.

For commonly used systemic antibiotics (amoxicillin, cephalexin, roxithromycin and amoxicillin with clavulanic acid):

- Repeats were ordered on the majority of prescriptions for cephalexin, amoxicillin with clavulanic acid and roxithromycin. Repeats were written on 40% of amoxicillin original prescriptions.
- The majority of repeats ordered were not dispensed.
- Some original prescriptions and repeats were dispensed long after the date the prescription was written. This use may not be consistent with the original reason for the prescription.

³ OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing.
http://dx.doi.org/10.1787/health_glance-2011-en; Accessed 22 August 2014

Purpose of analysis

Background

Antimicrobial resistance (AMR) is an ongoing public health concern. Reporting of antibiotic use can inform policy decisions to promote quality use of antibiotics and contain AMR. In April 2014, the World Health Organization released a comprehensive report on antibiotic resistance, giving cause for high concern.⁴ In Australia, the Australian Commission on Safety and Quality in Healthcare is undertaking the Antimicrobial Resistance and Antimicrobial Utilisation Surveillance Project.⁵

In this context, DUSC considered that an analysis of the use of antibiotics through the PBS/RPBS would be timely. The scope of this analysis is limited to utilisation of antibiotics through the PBS/RPBS.

Pharmacology⁶

Antibiotics treat bacterial infections through one of two different mechanisms. They either act to prevent the growth of bacteria (bacteriostatic), or kill the bacteria themselves (bactericidal). Antibiotics can also be used to prevent bacterial infection in circumstances where patients are susceptible e.g. surgery. There are many different types of antibiotics available, grouped by either their mechanism of action or their chemical structure. The largest group are beta-lactam antibiotics, which includes penicillins, cephalosporins, carbapenems and monobactams. Other antibiotic groups include aminoglycosides, tetracyclines, macrolides, fluoroquinolones and glycopeptides. Some antibiotics are effective against a limited range of infectious agents (narrow spectrum); others are effective against many different pathogens (broad spectrum).

Therapeutic Goods Administration (TGA) approved indications, dosage and administration

Approved indications vary by antibiotic drug and are available from the Product Information (PI).

The current PI and Consumer Medicine Information (CMI) for antibiotics are available from [the TGA website](#).

⁴ Antimicrobial resistance: global report on surveillance. World Health Organization 2014 ISBN 978 92 4 156474 8 (NLM classification: QV 250)

⁵ <http://www.safetyandquality.gov.au/national-priorities/amr-and-au-surveillance-project/>

⁶ Shaban RZ, Cruickshank M, Christiansen K & the Antimicrobial Resistance Standing Committee (2013). National Surveillance and Reporting of Antimicrobial Resistance and Antibiotic Usage for Human Health in Australia. Antimicrobial Resistance Standing Committee, Australian Health Protection Principal Committee: Canberra.

PBS listing details (as at July 2014)

As of the July 2014 PBS Schedule, there are 137 PBS/RPBS item codes for antibiotics, representing various forms and strengths of 47 different antibiotics (including antibiotic combination products).

The antibiotics listed on the PBS have varying levels of restrictions. The majority of antibiotics are unrestricted or Restricted Benefit; with a small number listed as Authority Required (STREAMLINED) and Authority Required (Table 1). A PBS restriction requires that the medicine can only be subsidised when prescribed for specific therapeutic uses. Where a prescriber wishes to prescribe an antibiotic outside of the restriction specified by the PBS, the prescriber may choose to write a private prescription, which is not subsidised by the PBS.

Many antibiotics are permitted to be prescribed by approved non-medical prescribers (dentists, optometrists, midwives and nurse practitioners). These items are marked as such in the PBS schedule.

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

Historical PBS listings are available from the [PBS Publications Archive](#).

Table 1: Summarised item details and restrictions for Authority Required antibiotics

Drug	Item details	Restriction
Authority Required (STREAMLINED)		
Cephalexin 250mg tablet	2655R (MP)	Prophylaxis of UTI (higher quantity than unrestricted listings)
Tobramycin inhalation capsules and inhalation solution	10066T, 10074F (inhalation capsules) 5442K (solution for inhalation) (MP)	Management of a proven <i>Pseudomonas aeruginosa</i> infection in a patient with cystic fibrosis
Trimethoprim 300mg tablet	2666H (MP)	Prophylaxis of UTI (higher quantity than other listing)
Authority Required		
Cefepime Powder for injection	8315P, 8316Q (MP, NP)	Treatment of febrile neutropenia
Ciprofloxacin 250mg tablet	1208N (250mg tablet) 1209P (500mg tablet)	Respiratory tract infection proven or suspected to be caused by <i>Pseudomonas aeruginosa</i> in severely immunocompromised patients;
500mg tablet 750mg tablet	1210Q (750mg tablet) (MP, NP)	Bacterial gastroenteritis in severely immunocompromised patients;

Drug	Item details	Restriction
0.3% eye drops 0.3% ear drops		Treatment of infections proven to be due to <i>Pseudomonas aeruginosa</i> or other gram-negative bacteria resistant to all other oral antimicrobials;
		Treatment of joint and bone infections, epididymo-orchitis, prostatitis or perichondritis of the pinna, suspected or proven to be caused by gram-negative bacteria or gram-positive bacteria resistant to all other appropriate antimicrobials;
		Gonorrhoea (250 mg tablet only)
	0.3% eye drops 1217C (MP); 5564W (OP)	Bacterial keratitis
	2480M (0.3% ear drops) (MP, NP)	Treatment of chronic suppurative otitis media in: an Aboriginal or a Torres Strait Islander person aged 1 month or older a patient less than 18 years of age with perforation of the tympanic membrane a patient less than 18 years of age with a grommet in situ
Norfloxacin 400mg tablet	Authority required	Acute bacterial enterocolitis
	3010K (MP, NP)	Complicated urinary tract infection
Ofloxacin 0.3% eye drops	Authority Required: 5567B (OP); 8383F (MP)	Bacterial keratitis
Rifaximin 550mg tablet	Authority Required: 10001J (MP)	Prevention of hepatic encephalopathy
Vancomycin 125mg capsule 250mg capsule	Authority Required: 3113W, 3114X (MP)	Antibiotic associated pseudomembranous colitis due to <i>Clostridium difficile</i> which is unresponsive to metronidazole or where there is intolerance to metronidazole
S100 Highly Specialised Drugs Program		
Clarithromycin 250mg tablet 500mg tablet	6151R, 6152T (private hospital, Authority Required); 5624B, 5625C (public hospital, Authority Required (STREAMLINED)) (MP)	Treatment of <i>Mycobacterium avium</i> complex infections (higher quantity than other listings)
Azithromycin 600mg tablet	6221K (private hospital, Authority Required); 5616N (public hospital, Authority Required (STREAMLINED)) (MP)	Prophylaxis against <i>Mycobacterium avium</i> complex infections in HIV-positive patients with CD4 cell counts of less than 75 per cubic millimetre (higher quantity than other listings)

MP: Medical Practitioner; OP: optometrist; NP: nurse practitioner

Relevant aspects of the PBAC consideration

The PBAC has always considered the potential for developing antibiotic resistance when listing antibiotics on the PBS and sought information from relevant bodies such as the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR), and the Expert Advisory Group on Antimicrobial Resistance (EAGAR); and more recently the Antimicrobial Resistance Standing Committee (AMRSC).

The most recent PBAC considerations are summarised in Appendix A.

Methods

Data for prescriptions, benefits and defined daily dose (DDD) per 1000 people per day were extracted from the DUSC database by date of supply for the months January 1994 to March 2014 inclusive for all antibiotic ATC codes.

Department of Human Services (DHS) Medicare Pharmacy claims data for 2013 were used to determine:

- Count of people supplied an antibiotic based on de-identified patient numbers;
- Use of antibiotics by age of patients;
- Number of antibiotics supplied per person

For a subset of commonly supplied antibiotics, DHS Medicare Pharmacy claims data were also used to determine:

- proportion of antibiotic prescriptions where repeats were prescribed; and the proportion of ordered repeats that were dispensed; and
- number of days between the original supply of an antibiotic and the first repeat supply.

The proportion of private prescriptions of total prescriptions for the last available year of the private estimate data (2011) was determined from the DUSC database.

Major specialty type of prescriber was determined from DHS Medicare pharmacy claims data.

Aboriginal health services data were accessed to determine the number of packs of antibiotics and the most commonly processed antibiotics through these services.

Results

Analysis of drug utilisation

10,441,015 unique patients (45% of the Australian population⁷) were supplied at least one antibiotic under the PBS/RPBS in 2013⁸. 18% (n=4,199,137) of the Australian population had only one antibiotic prescription supplied in 2013 and 3.5% (n=807,870) had greater than six antibiotic prescriptions dispensed (Figure 1). By way of comparison, 25% (n=5,934,693) of the Australian population were supplied with just one antibiotic medicine on one or more occasions whilst 0.1% (n=32,808) had greater than six different antibiotics supplied.

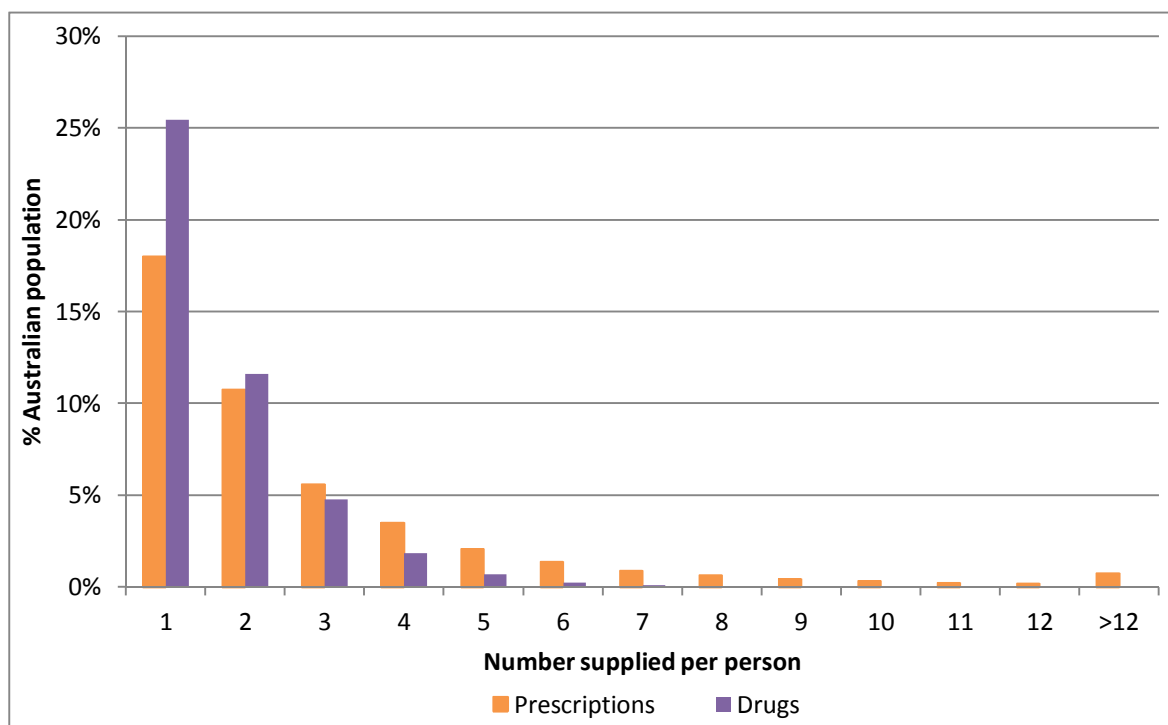


Figure 1: Number of antibiotic drugs and antibiotic prescriptions supplied per person under the PBS/RPBS in 2013 by percentage of the Australian population.

Based on December 2013 Australian population = 23,319,400 people.

Source: DHS Supplied prescriptions database, August 2014.

⁷ The preliminary estimated resident population (ERP) of Australia at 31 December 2013 was 23,319,400 people.

3101.0 - Australian Demographic Statistics Dec 2013.

<http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3101.0Main+Features1Dec%202013?OpenDocument>

⁸ The patient count may be very slightly underestimated, due to lack of capture of patient level data for S100 clarithromycin and azithromycin packs processed 'offline' through some public hospitals in the first half of 2014 (n=384).

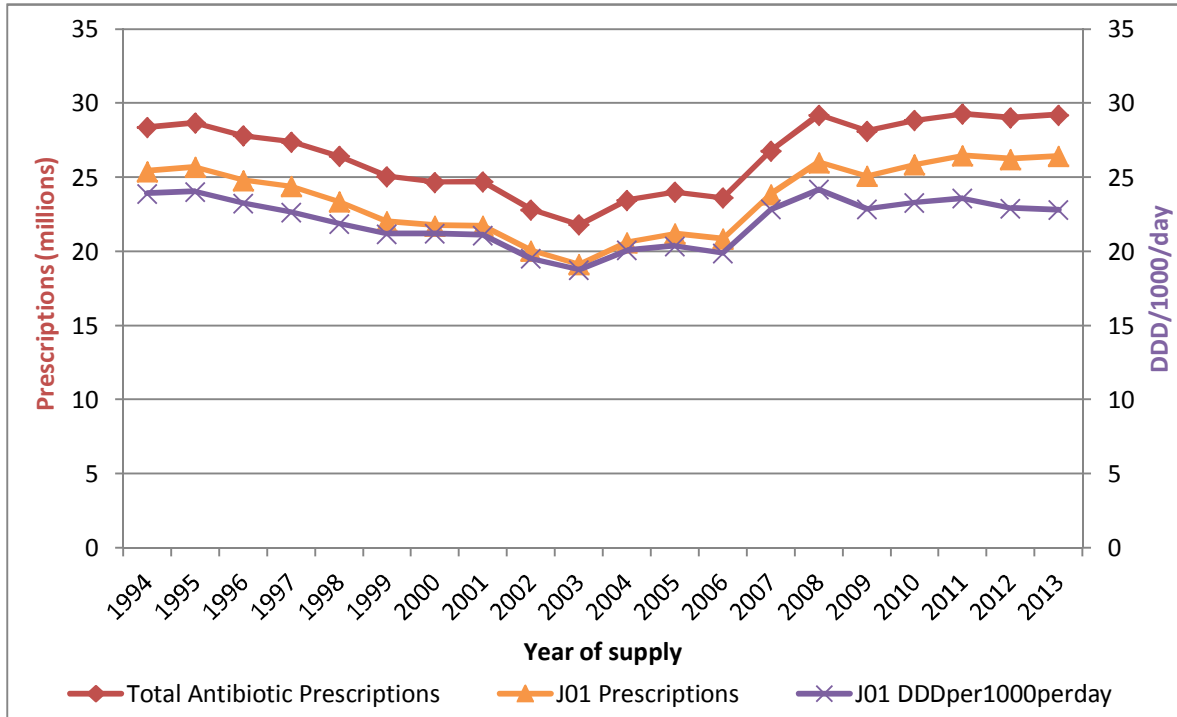


Figure 2: Quantity of antibiotics dispensed under the PBS/RPBS per year from 1994-2013 expressed as prescriptions and DDDs per 1000 people per day.

Excludes private estimate. Includes under co-payment estimate and actual. The DDDs/1000/day are almost identical for systemic antibiotics (J01) and all antibiotic ATC, therefore only the total is depicted.

DDD/1000/Day excludes some items for which there is no DDD defined. Source: DUSC database, August 2014.

In 2013, the use of PBS/RPBS systemic antibiotics (J01) was 26,436,021 prescriptions and 22.8 DDD/1000/day (Figure 2). Over the same year, 29,227,581 prescriptions were supplied for any PBS/RPBS antibiotic, also accounting for 22.8 DDD/1000/day, noting that some non-systemic antibiotics do not have a DDD assigned by the World Health Organization.

The ten most commonly supplied antibiotics by number of prescriptions supplied in 2013 are shown in Table 3. The number of prescriptions is inclusive of all forms and strengths applicable to the listed ATC code.

Table 3: Ten most commonly supplied antibiotics by number of prescriptions in 2013.

	ATC	Drug Name	Prescriptions 2013
1	J01CA04	AMOXYCILLIN	5,665,810
2	J01DB01	CEPHALEXIN	5,413,046
3	J01CR02	AMOXYCILLIN + CLAVULANIC ACID	4,512,149
4	J01FA06	ROXITHROMYCIN	1,826,038
5	J01AA02	DOXYCYCLINE	1,804,790
6	S01AA01	CHLORAMPHENICOL	1,353,514
7	J01FA09	CLARITHROMYCIN	932,640
8	J01EA01	TRIMETHOPRIM	899,007
9	J01FA01	ERYTHROMYCIN	856,504
10	J01DC04	CEFACLOR	674,772

Includes actual under co-payment prescriptions. Private prescription estimate not available for 2013. Source: DUSC database, August 2014.

In 2013, 98% of community antibiotic prescriptions (i.e. not including public hospital admitted patients) were supplied from a community pharmacy (including 4% from friendly society pharmacies). 1% of antibiotic prescriptions were supplied from a private hospital pharmacy and 1% of antibiotic prescriptions were supplied from a public hospital to inpatients on discharge or public hospital outpatients. A previous analysis from the DUSC Database presented to the AMRSC in 2013 showed that the percentage of total PBS antibiotic use by DDD/1000 population/day from hospital dispensaries was 2.16% in 2005.

Under co-payment prescriptions accounted for 52% of antibiotics supplied in 2013.

Utilisation by age

The proportion of people in each age group who were supplied an antibiotic under the PBS/RPBS in 2013 is shown in Figure 3.

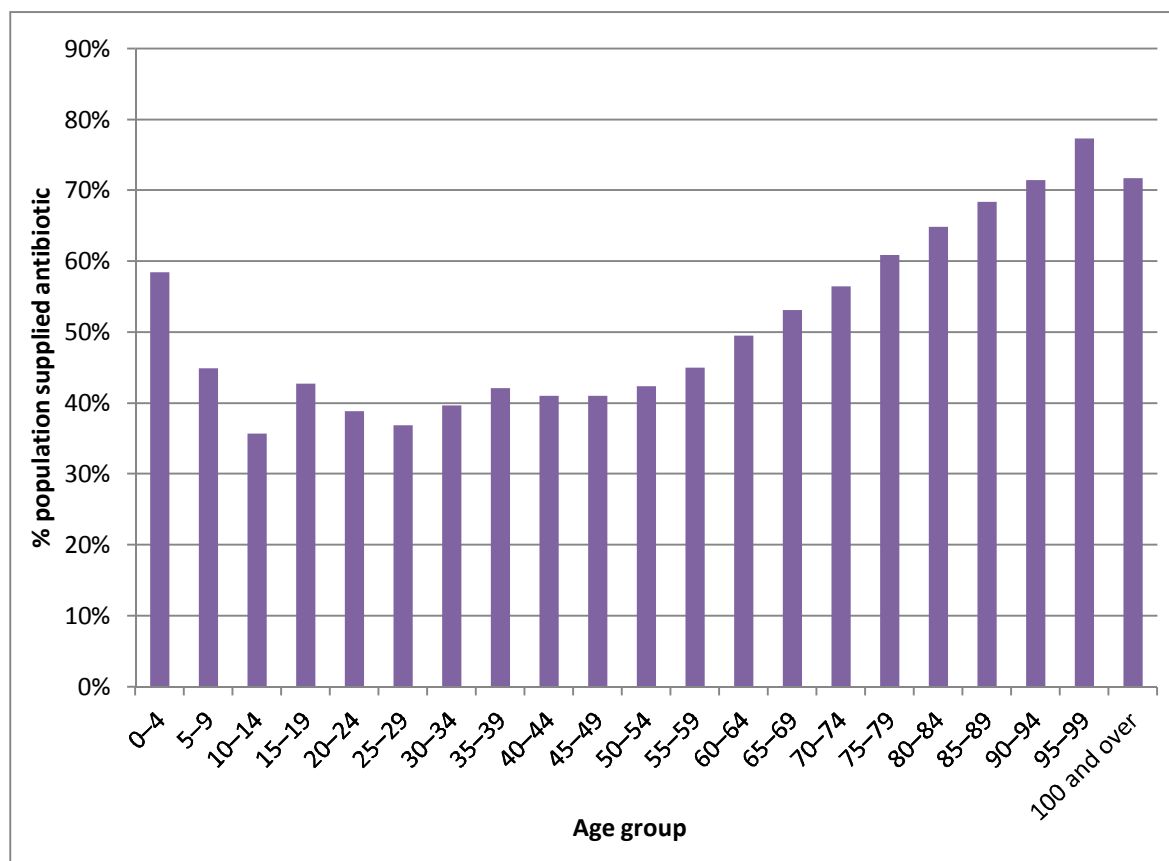


Figure 3: Use of antibiotics by age group in 2013.

Percentage of people in each age bracket who were supplied at least one PBS/RPBS antibiotic in 2013. Age standardised based on the estimated resident population by age at 30 June 2013.

Source: DHS Supplied prescriptions database, August 2014.

The use of antibiotics was more common in the youngest and oldest age groups. 58% of persons aged 0-4 years and 59% of persons aged 65 years and over were supplied at least one antibiotic in 2013; compared with an overall population figure of 45%. In 2013, 70% of people aged 85 years and over were supplied at least one antibiotic.

Utilisation by antibiotic class

Figure 4 shows the number of systemic antibiotic prescriptions per year by ATC level 3.

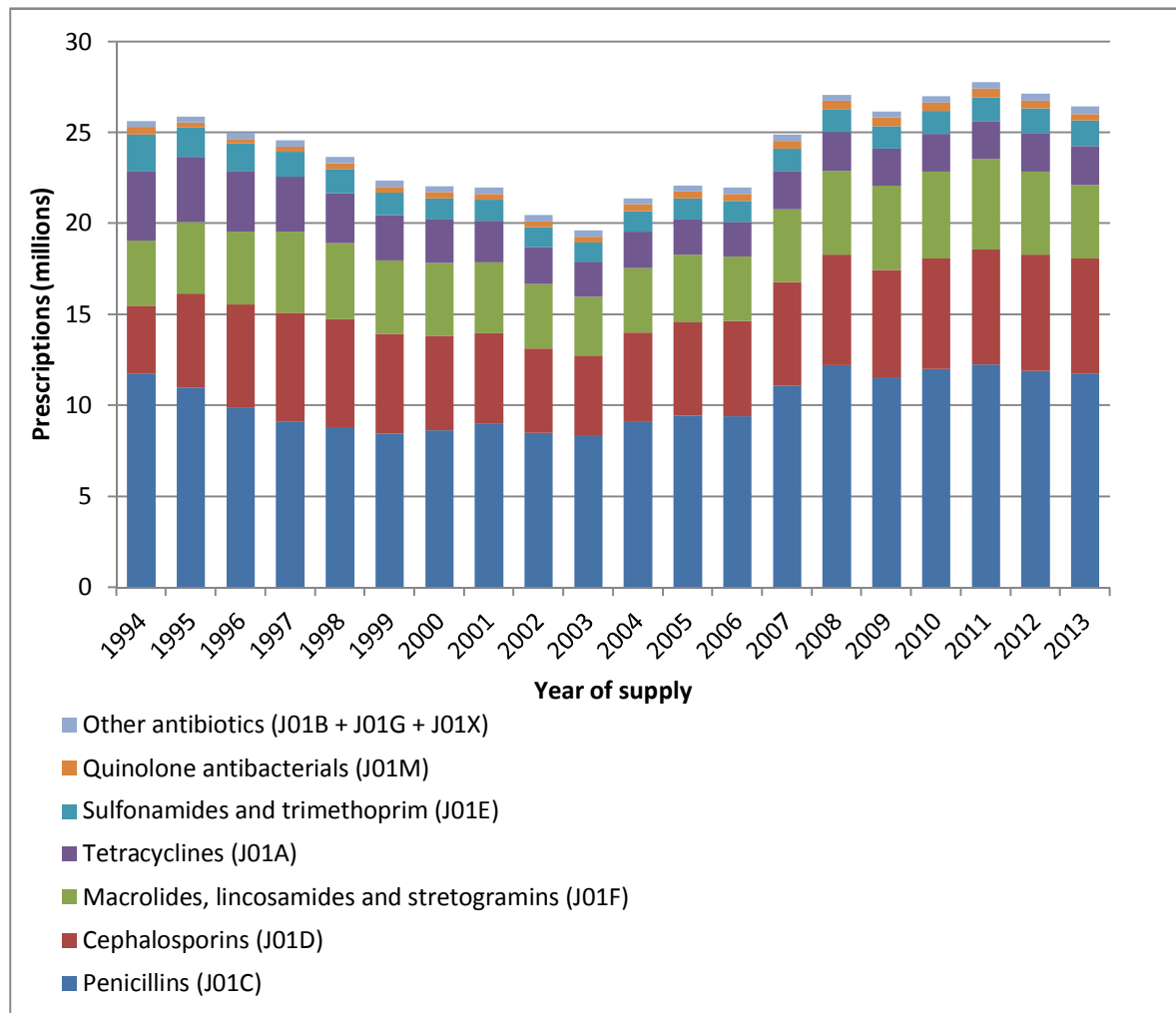


Figure 4: Contribution to prescriptions per year by ATC 3 for systemic antibiotics (J01).

'Other antibiotics' includes amphenicols (J01B), aminoglycoside antibacterials (J01G) and other antibacterials (J01X). Private estimate included; under co-payment estimate and actual included.

Source: DUSC database, August 2014.

In 2013, there were 11,756,220 prescriptions supplied for penicillins; and 6,341,961 prescriptions for cephalosporins (Figure 4).

Penicillins have been the largest contributor in each year over the period from 1994 (46%) to 2013 (44%). The relative contribution of each antibiotic group has not changed markedly over the study period.

Figure 5 depicts use of ophthalmological and otological antibiotics by prescriptions per year from 1994 to 2013.

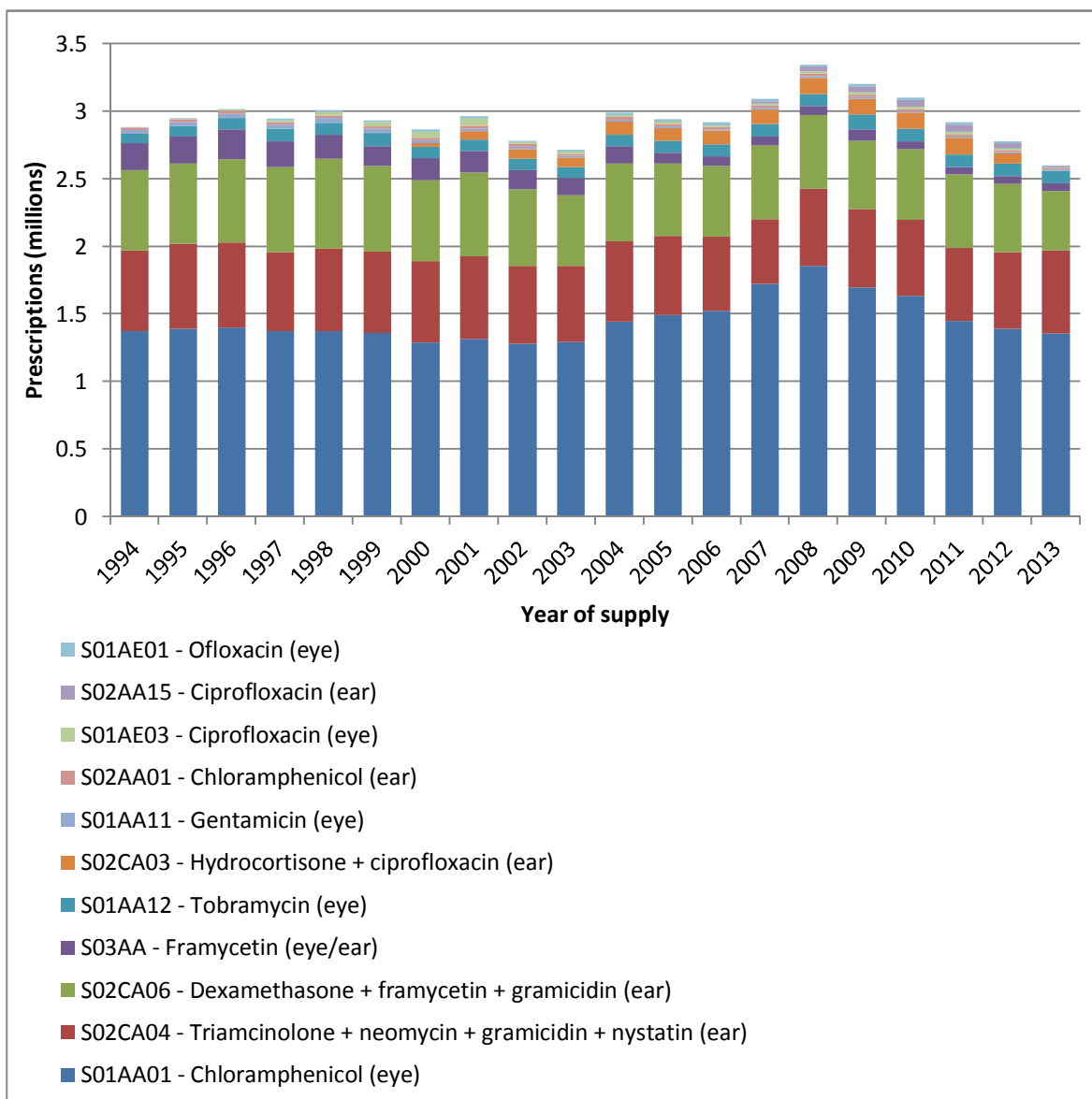


Figure 5: Contribution to prescriptions per year by ATC for ophthalmological and otological antibiotics (S01AA, S01AE, S02AA, S02CA, S03AA).

Private estimate included; under co-payment estimate and actual included.

Source: DUSC database, August 2014.

Chloramphenicol eye drops dominate supply in each year of the study period; although combination corticosteroid and anti-infective ear drops also contribute a large proportion. Chloramphenicol eye drops and eye ointment are also available without a prescription as pharmacist only supply (since May 2010⁹); this use is not included in the analysis.

⁹ <http://www.tga.gov.au/newsroom/consult-otc-chloramphenicol-131122.htm> Accessed: 1 September 2014.

Narrow versus broad spectrum

Figure 6 shows the number of prescriptions supplied in 2013 for penicillins (J01C) and cephalosporins (J01D) by spectrum of activity. The classification of antibiotics by spectrum of activity varies between sources. For appropriate application to the Australian context, the classification for Figure 6 was referenced from the Therapeutic Guidelines.¹⁰

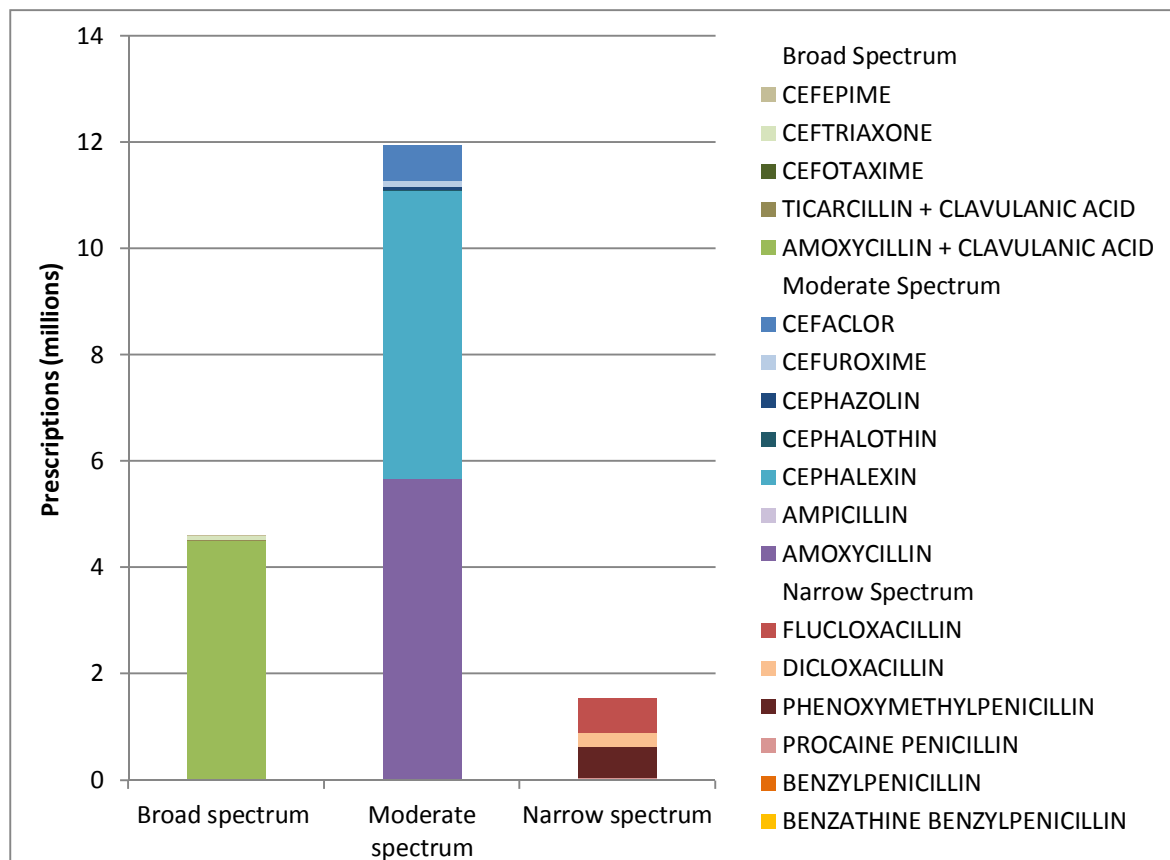


Figure 6: Penicillin and cephalosporin prescriptions supplied in 2013 classified by spectrum of activity.

Includes actual under co-payment prescriptions. Private prescription estimate not available for 2013. Source: DUSC database, August 2014.

Of penicillin and cephalosporin prescriptions supplied in 2013, narrow spectrum antibiotics accounted for 9% of use, moderate spectrum accounted for 66% of use, and broad spectrum for 25% of use (Figure 6).

¹⁰ Cephalosporins [revised June 2010; amended June 2013]. In eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2014 Mar. Accessed 2014 Aug 28 <<http://online.tg.org.au/complete/desktop/index.htm>>.

Penicillins [revised June 2010; amended February 2011, June 2013]. In eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2014 Mar. Accessed 2014 Aug 28 <<http://online.tg.org.au/complete/desktop/index.htm>>.

Analysis of prior amoxicillin use in patients supplied amoxicillin + clavulanic acid

Of patients supplied amoxicillin with clavulanic acid in 2013, 6% had amoxicillin supplied in the preceding month. The restriction for amoxicillin with clavulanic acid requires that resistance to amoxicillin is suspected or proven. The patient having completed a course of amoxicillin is one way of determining whether the infection is amoxicillin-resistant; however resistance may be suspected or proven by other means.

Time to supply analysis

Prescriptions for most medicines, including antibiotics, are valid for one year from the date of prescribing. The PBS prescription claim data does not provide information on the proportion of prescriptions written that are never dispensed. For those that are supplied the time between prescribing and supply can be determined.

In the majority of cases, prescriptions for antibiotics are supplied within one day of when they are written. For amoxicillin 500mg capsules for example, 81% of original prescriptions were dispensed on the day the prescription was written, and 92% were supplied by the third day after prescribing (Table 4). However, the distribution (not shown) has a long tail, which shows that some original prescriptions were supplied many weeks or months after the date of prescribing. For example, 2% (n=46,285) of original prescriptions supplied for amoxicillin 500mg capsules were supplied more than 60 days after the prescription was written.

Table 4: Time from date of prescribing to original supply for commonly used antibiotics

Drug	Form and Strength	Item number	% originals supplied on day of prescribing	% originals supplied <4days after date of prescribing
Amoxicillin	Capsule 500 mg	01889K	81%	92%
Cephalexin	Capsule 500 mg	03119E	79%	92%
Amoxicillin/ Clavulanic acid	875 mg/125 mg tablet	08254K	80%	92%
Roxithromycin	300mg tablet	08016X	81%	93%
Doxycycline	Tablet 50 mg (as monohydrate)	09106G	56%	73%
Doxycycline	Capsule 100 mg (as hydrochloride) (containing enteric coated pellets)	02708M	79%	91%
Chloramphenicol	Eye drops 5 mg per mL, 10 mL	02360F	73%	84%
Clarithromycin	Tablet 250 mg	08318T	83%	93%
Trimethoprim	Tablet 300 mg	02922T	78%	91%
Erythromycin	Tablet 400 mg (as ethyl succinate)	02750R	83%	93%
Cefaclor	Tablet (sustained release) 375 mg (as monohydrate)	01169M	83%	93%

Repeat prescription analysis

Table 5 shows the proportion of antibiotic prescriptions where repeats were prescribed; and the proportion of ordered repeats that were dispensed.

Table 5: Repeats ordered on original prescriptions for commonly used antibiotics

Antibiotic	Number of original prescriptions with no repeat ordered	Number of original prescriptions with repeats ordered	Number of original prescriptions	Original prescriptions with repeats ordered as a proportion of original prescriptions
Amoxicillin	2,270,614	1,521,208	3,791,822	40%
Amoxicillin + Clavulanic Acid	950,129	2,064,644	3,014,773	68%
Cephalexin	1,677,748	1,908,106	3,585,854	53%
Chloramphenicol	462,805	181,681	644,486	28%
Roxithromycin	436,087	1,046,601	1,482,688	71%

Source: DHS Medicare Pharmacy Claims database based on the date of supply. Includes original prescriptions supplied in the 2012-13 financial year.

The ordering of repeats on an original prescription was variable across the five medicines (Table 5). Only 28% of chloramphenicol original prescriptions had repeats ordered. Contrastingly, 71% of roxithromycin original prescriptions had repeats ordered.

Where repeats were ordered on the original prescription, the proportion of these repeats dispensed was fairly constant across the five medicines, at around 20% for oral preparations and 25% for chloramphenicol (Table 6).

Table 6: Repeats filled for commonly used antibiotics

Antibiotic	Number of original prescriptions with repeats ordered	Number of repeats filled	Filled repeats as a proportion of ordered repeats
Amoxicillin	1,521,208	288,448	19%
Amoxicillin + Clavulanic Acid	2,064,644	420,693	20%
Cephalexin	1,908,106	375,650	20%
Chloramphenicol	181,681	45,846	25%
Roxithromycin	1,046,601	210,173	20%

Source: DHS Medicare Pharmacy Claims database based on the date of supply. Includes original prescriptions supplied in the 2012-13 financial year.

Table 7 compares the days elapsed from original prescription to repeat prescription for the ten most supplied antibiotics by number of prescriptions in 2013.

Table 7: Time from original supply to first repeat supply for commonly used antibiotics

Drug	Form and Strength	Item number	Quantity per prescription	Mode: days to first repeat	Mode % of total 1st repeats for item	% 1st repeats for item supplied <10 days post original	% 1st repeats for item supplied > 60 days post original
Amoxicillin	Capsule 500 mg	01889K	20	7	12%	51%	19%
Cephalexin	Capsule 500 mg	03119E	20	5	13%	57%	15%
Amoxicillin/ Clavulanic acid	875 mg/125 mg tablet	08254K	10	5	20%	67%	12%
Roxithromycin	300mg tablet	08016X	5	4	21%	75%	9%
Doxycycline	Tablet 50 mg (as monohydrate)	09106G	25	25	5%	7%	12%
Doxycycline	Capsule 100 mg (as hydrochloride) (containing enteric coated pellets)	02708M	7	5	14%	67%	10%
Chloramphenicol	Eye drops 5 mg per mL, 10 mL	02360F	-	7	3%	18%	13%
Clarithromycin	Tablet 250 mg	08318T	14	7	16%	61%	12%
Trimethoprim	Tablet 300 mg	02922T	7	7	12%	47%	20%
Erythromycin	Tablet 400 mg (as ethyl succinate)	02750R	25	6	12%	47%	14%
Cefaclor	Tablet (sustained release) 375 mg (as monohydrate)	01169M	10	5	22%	72%	10%

Source: DHS Supplied prescriptions database, August 2014.

The distribution patterns (not shown) for the time elapsed between the original prescription and supply of the first repeat differ from the time to original supply distributions. The pattern for amoxicillin 500mg capsule is typical of systemic antibiotics where one course is approximately one week's treatment, with the mode being supply of the first repeat 7 days after the original prescription (Table 7).

For systemic antibiotics for acute therapy, most people who have a first repeat dispensed have it dispensed within 10 days of the original prescription being supplied (Table 7). However, like the time to original supply analysis, the distribution (not shown) has a long tail, which shows that some repeat prescriptions were supplied many weeks or months after the original prescription was dispensed. In these cases, it is unlikely that the same infection is being treated by the repeat dispensing. For the antibiotic items in Table 7, 10-20% of first repeats were supplied more than 60 days after the original prescription was dispensed. In the case of a high use item, such as amoxicillin 500mg capsules, 70,355 repeat prescriptions were supplied more than 60 days after the original prescription was dispensed.

Two of the doxycycline item codes had similar numbers of repeat prescriptions dispensed in 2013: both are shown in Table 7 for comparison. Doxycycline item 2708M is an unrestricted listing for 7 capsules of 100mg doxycycline, while item 9106G is a restricted benefit listing for 25 tablets of 50mg doxycycline for the treatment of bronchiectasis, chronic bronchitis or severe acne. In the case of chronic therapy for an ongoing condition, it may be reasonable that a patient has their prescription dispensed after more time has elapsed.

The distribution for chloramphenicol eye drops (not shown) displays a broader peak than for the systemic antibiotics. This may be due to more variable dosage regimens for chloramphenicol eye drops. However, the distribution also shows that the first repeat is sometimes supplied months after the original prescription.

Prescribers can request an increased quantity or increased number of repeats by telephone authority. Although, this is not likely to account fully for the supply of first repeats more than 60 days after the original prescription. For example, 19% of amoxicillin first repeats were supplied more than 60 days after the original prescription was supplied, but less than 1% of amoxicillin prescriptions are for increased quantities or repeats.

For all antibiotic prescriptions where the first repeat was supplied in 2013, the number of days between the original supply and the first repeat was determined. Results are presented as *x% of first repeats supplied y days after the original prescription was supplied* (Table 8).

Table 8: Days from original to repeat supply by proportion of first repeats filled

% 1 st repeats filled	Amoxycillin	Cephalexin	Amoxycillin + Clavulanic acid	Roxithromycin	Chloramphenicol
25%	6	5	4	4	12
50%	9	8	6	5	24
75%	34	25	16	10	42
80%	50	35	25	16	49
90%	122	91	74	52	67

Source: DHS Supplied Prescriptions database, August 2014.

For all of the antibiotics considered in Table 8, a number of repeats were filled well beyond the number of days covered by the original supply for a standard treatment course. For example, in most cases, the quantity of amoxycillin supplied would provide 7 days' treatment. 25% of repeats filled for amoxycillin were supplied 6 days after the original dispensing and 50% were supplied within 9 days of dispensing. These time periods are close to the expected 7 days' supply. However, Table 8 shows that 25% of the repeats were filled 34 days or more after the original dispensing.

The time to supply analysis should be interpreted in the context that for many antibiotics the dosage varies depending on the infection being treated. For example, the adult dosage of amoxycillin for lower respiratory tract infections is 500mg three times per day, meaning a 20 capsule pack will be finished on day 7. However, a single dose of 3g amoxycillin is indicated for urinary tract infection, gonorrhoea, and as prophylaxis in some dental procedures.¹¹ Additionally, a limitation of the analysis is that it doesn't assess whether patients had multiple original prescriptions prescribed within what could conceivably be one episode of care.

¹¹ Amoxil® Product Information. <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-01071-1> Accessed: 3 September 2014.

Prescriber type

Table 9 shows that prescribing by approved non-medical prescribers (dentists, optometrists, midwives and nurse practitioners) represented a small proportion of the total prescriptions supplied for antibiotics in 2013.

Table 9: Major specialty type of prescriber for prescriptions supplied in 2013

Major specialty of prescriber	Prescriptions supplied	Percentage of total prescriptions
GP	21,705,360	75%
Other Medical	6,209,423	21%
Dentist	946,540	3%
Optometrist	17,379	<1%
Midwife	69	<1%
Nurse practitioner	16,997	<1%
Total prescriptions supplied	28,895,768	100%

Source: DHS Supplied prescriptions database, August 2014.

Aboriginal health services supply

Table 10 shows the number of antibiotic packs provided by aboriginal health services (AHS) per year from 1999-2013.

Table 10: Packs of antibiotics provided by aboriginal health services (AHS)

Year	Antibiotic packs
1999	51,206
2000	99,526
2001	198,021
2002	239,944
2003	277,926
2004	314,236
2005	282,803
2006	288,052
2007	302,975
2008	295,394
2009	297,326
2010	286,818
2011	306,160
2012	285,491
2013	281,351

AHS data: August 2014. AHS data is at item level by date of processing.

The number of packs processed through AHS in 2013 was 281,351; which is 1% of the number of antibiotic prescriptions supplied through the PBS over the same year (n=28,156,700).

Table 11 shows which antibiotics were most commonly processed through AHS in 2013.

Table 11: Ten antibiotics most commonly processed by aboriginal health services in 2013

ATC	Antibiotic	Sum of packs supplied
J01CA04	AMOXYCILLIN	53,325
J01FA10	AZITHROMYCIN	33,731
S01AA01	CHLORAMPHENICOL (EYE)	29,778
J01CR02	AMOXYCILLIN + CLAVULANIC ACID	29,227
J01DB01	CEPHALEXIN	21,002
J01CF05	FLUCLOXACILLIN	18,966
S02AA15	CIPROFLOXACIN (EAR)	17,064
J01FA06	ROXITHROMYCIN	9,801
J01CF01	DICLOXACILLIN	8,991
J01EE01	TRIMETHOPRIM + SULFAMETHOXAZOLE	7,523

AHS data: August 2014. AHS data is at item level by date of processing

Like the general population, amoxycillin was the most supplied antibiotic through AHS in 2013. Some of the differences in commonly supplied antibiotics in AHS versus the wider community are due to the prevalence of different infections in Indigenous communities. For example, azithromycin is PBS listed for the treatment of trachoma and uncomplicated urethritis due to *Chlamydia trachomatis*. Trachoma continues to be a public health problem in Aboriginal and Torres Strait Islander communities in many rural and remote areas of the NT, SA and WA; and is no longer found in Australia outside of these communities.¹² The Northern Territory Emergency Response Child Health Check trachoma screening found trachoma at endemic rates (more than 5%) in the majority of regions.¹³ Australia is a signatory to the World Health Organization (WHO) Global Elimination of Trachoma (GET 2020) resolution. Additionally, ciprofloxacin ear drops are PBS listed for the treatment of chronic suppurative otitis media in an Aboriginal or a Torres Strait Islander person aged 1 month or older. Nearly 12% of children examined through the Northern Territory Emergency Response Child Health Check initiative had chronic suppurative otitis media.¹⁵

¹² Communicable Disease Network Australia (CDNA) National Guidelines for the Public Health Management of Trachoma. <http://www.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-trachoma.htm> Accessed: 1 September 2014.

¹³ Australian Institute of Health and Welfare 2011. The health and welfare of Australia's Aboriginal and Torres Strait Islander people 2011, an overview. Cat. no. IHW42. Canberra: AIHW.

Private prescriptions

The DUSC database provided an estimate of private prescriptions until August 2012. Using data extracted from the DUSC database, the proportion of private prescriptions for calendar year 2011 is shown in Table 12. It is estimated that private prescriptions accounted for 7% of all antibiotic prescriptions supplied in 2011. The proportion of systemic antibiotics estimated as being supplied by private prescription in 2011 was 5%. For non-systemic (e.g. otological, optometrical) antibiotics, a higher proportion (26%) was estimated as being supplied by private prescription.

Table 12: estimated proportion of private prescriptions supplied for antibiotics in 2011

	PBS/RPBS including under co-payment estimate	Private estimate	Total prescriptions supplied (including private and under co-payment estimates)
All	29,287,172	2,278,985	31,566,157
	93%	7%	
Systemic (J01)	26,475,068	1,298,435	27,773,503
	95%	5%	
Non-systemic	2,812,104	980,550	3,792,654
	74%	26%	

Analysis of expenditure

In 2013, \$116.5 million in PBS/RPBS benefits was paid for antibiotics.

Discussion

The DUSC acknowledged that the PBS data are limited by not including the indication for which the antibiotic is prescribed, and cannot provide direct information on the appropriateness of prescribing or on the contribution to antimicrobial resistance. However, the DUSC considered that community antibiotic supply is extensive, high relative to other OECD nations, and increasing in recent years.

The DUSC considered that a DDD of 22.8/1000/day was particularly high given that in-patient hospital use of antibiotics and private community prescriptions were excluded from the analysis, and therefore that the true extent of use in Australia would be higher than this. The DUSC considered that the high use of broad and moderate spectrum penicillins and cephalosporins, in the context of overall high use of antibiotics, may be a factor contributing to the development of antimicrobial resistance.

The DUSC noted the trend in antibiotic use over the time period 1994 to 2013; and noted the slow decline in use to 2003, followed by an increase in use in 2007-2008, with little to no change in levels of use since 2009. While the DUSC did not have an immediate explanation for this trend, the DUSC considered that antibiotic utilisation may be influenced by peak influenza years, national surveillance programs, national education programs and changes to the therapeutic guidelines.

Repeats were ordered on the majority of prescriptions for cephalexin, amoxicillin with clavulanic acid and roxithromycin. Repeats were written on 40% of amoxicillin original prescriptions. However, where repeats were ordered for the selected oral antibiotics, the repeat was filled on approximately 20% of occasions. It is unknown whether this is due to patient non-compliance with the prescriber's instructions or whether the prescriber intended the repeat only to be filled under specific circumstances communicated to the patient; e.g. only get the repeat if you are not feeling better after seven days.

One of the primary concerns identified by the DUSC is the repeat dispensing of antibiotics beyond what is considered a reasonable time to be the same course of treatment. The DUSC acknowledge that while the 10-20% of first repeats being supplied more than 60 days after the original prescription may be indicative of inappropriate use, the reason for repeat supply cannot be confirmed from the data.

Given that doses and durations vary across (and sometimes within) indications, it is difficult to align the PBS maximum quantity and repeats with recommended clinical practice for appropriate antibiotic prescribing. For example, there are a number of indications for which repeat prescriptions of amoxicillin, cephalexin and roxithromycin would be required in order to fulfil the recommended treatment course. The Therapeutic Guidelines¹⁴ show the variability in treatment duration for some indications, which mean repeats would be required in some but not all cases even within the same indication; e.g. for the treatment of cellulitis, 500 mg of cephalexin may be given orally four times a day for five to 10 days, indicating that a range of 20 to 40 capsules may be required depending on the duration of therapy in each particular case. The DUSC discussed whether there should be a separate listing for specific indications where therapeutic guidelines recommend longer treatment.

The DUSC suggested seeking changes to medical prescribing software such that the default for antibiotics is zero repeats. However, the DUSC noted research which shows an education intervention advising doctors about changing their default computer settings did

¹⁴ eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2014 Mar. Accessed 2014 Aug 28 <<http://online.tg.org.au/complete/desktop/index.htm>>.

not significantly alter the proportion of repeats ordered on computerised versus written prescriptions.¹⁵

The DUSC discussed an alternate approach of removing repeats from the listings for all oral antibiotics. In considering whether repeats are required on antibiotic prescriptions, the DUSC considered that regard should be given to those indications for which the current maximum quantity is not sufficient to fulfil the recommended course of treatment. The DUSC acknowledged that repeats could still be ordered by a clinician through the authority process. The DUSC noted the potential impact on the DHS administrative burden associated with changing antibiotics to authority listings. The DUSC suggested performing an analysis of the quantitative impact of removing repeats on oral antibiotics.

The DUSC also considered that reducing the number of months that a prescription for an antibiotic remains valid might be a way of reducing inappropriate use. However, the DUSC noted that changes to the life of a PBS prescription would influence the expiry for subsidy only; and prescriptions would still be considered valid under state and territory law. Therefore, the DUSC noted that any changes would require consultation with these jurisdictions.

The DUSC considered that there was high, and therefore some potentially inappropriate, use of amoxicillin plus clavulanic acid, particularly since the restriction limits use to patients where resistance to amoxicillin is suspected or proven. The DUSC noted that of the patients supplied with amoxicillin plus clavulanic acid, that in the year 2013 only 6% had been supplied with a prior script for amoxicillin in the previous month, but noted that resistance can be suspected or proven by other means. The DUSC discussed whether requesting the PBAC to consider further restricting amoxicillin plus clavulanic acid to an authority required listing would help to reduce inappropriate use; but noted that previous action targeting clinician prescribing behaviour for amoxicillin with clavulanic acid resulted in unintended consequences of a shift away from best-practice prescribing, increased costs to the government and a trend toward poorer patient outcomes.¹⁶

The DUSC requested an analysis of the impact of biological disease modifying anti-rheumatic drugs (bDMARDs) on the prescription of antibiotics. This would quantify if infections from bDMARDs are contributing to the increasing use of antibiotics.

¹⁵ Newby DA, Robertson J. Computerised prescribing: assessing the impact on prescription repeats and on generic substitution of some commonly used antibiotics. *Med J Aust* 2010; 192: 192-195.

¹⁶ Beilby J, Marley J, Walker D, Chamberlain N, Burke M. Effect of changes in antibiotic prescribing on patient outcomes in a community setting: a natural experiment in Australia. *Clinical Infectious Diseases* 2002; 34:55-64.

DUSC actions

- The DUSC requested that the report be provided to the PBAC. The DUSC recommended that the PBAC consider options for reducing inappropriate delays in the dispensing of repeat prescriptions for antibiotics, including the following:
 - Investigating changes to medical prescribing software defaults for the number of repeats on antibiotic prescriptions.
 - Removing repeats from oral antibiotic listings.
 - Reducing the validity of oral antibiotic prescriptions to less than 12 months.
 - Introducing separate listings for specific indications that require higher quantities to meet the recommended treatment course.
- The DUSC requested that the report be forwarded to the Secretariat of the post-market review of Authority Required PBS listings.
- The DUSC recommended superimposing peak influenza years, national surveillance programs and national education programs onto an overall utilisation graph and looking for any trends or points of impact that may have affected the utilisation of antibiotics over time. The DUSC also requested an analysis of the impact of bDMARDs on the prescription of antibiotics to quantify if infections from bDMARDs are contributing to the increasing use of antibiotics.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

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

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

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

Sponsors' comments

Abbott Australasia Pty Ltd, Actavis Pty Ltd, AFT Pharmaceuticals Pty Ltd, Alcon Laboratories (Australia) Pty Ltd, Allergan Australia Pty Limited, Alphapharm Pty Ltd, Apotex Pty Ltd, Aspen Pharma Pty Ltd, Aspen Pharmacare Australia Pty Limited, AstraZeneca Pty Ltd, Aurobindo Pharma (Australia) Pty Limited, Baxter Healthcare Pty Limited, Bayer Australia Ltd, bioCSL (Australia) Pty Ltd, Dr Reddy's Laboratories (Australia) Pty Ltd, Fawns and McAllan Proprietary Limited, Generic Health Pty Ltd, GlaxoSmithKline Australia Pty Ltd, Hospira Pty Limited, iNova Pharmaceuticals (Australia) Pty Limited, Link Medical Products Pty Ltd, Mayne Pharma International Pty Ltd, Mayne Products Pty Ltd, Norac Pharma Australia Pty Ltd, Norgine Pty Limited, Novartis Pharmaceuticals Australia Pty Limited, Omegapharm Pty Ltd, Petrus Pharmaceuticals Pty Ltd, Pfizer Australia Pty Ltd, Pharmacor Pty Limited, Ranbaxy Australia Pty Limited, Roche Products Pty Ltd, Sandoz Pty Ltd, sanofi-aventis Australia Pty Ltd, Smith & Nephew Pty Limited, The Trustee for Virgo Unit Trust (trading as Phebra), Valeant Pharmaceuticals Australasia Pty Limited:

No comment received.

Appendices

Appendix A

Relevant aspects of the PBAC consideration

The most recent PBAC consideration of a major submission for the PBS listing of an antibiotic was at the November 2013 meeting, when the PBAC recommended the listing of tobramycin powder for inhalation as an Authority Required (STREAMLINED) benefit for the treatment of *Pseudomonas aeruginosa* infection in a patient aged 6 years or older with cystic fibrosis. While tobramycin was already listed for management of a proven *Pseudomonas aeruginosa* infection in a patient with cystic fibrosis, the recommendation related to a new form (i.e. powder for inhalation).

A copy of the Public Summary Document from the November 2013 PBAC meeting is available on the [PBS website](#).

In another recent consideration, the PBAC rejected the PBS listing of linezolid at its July 2013 meeting on the basis of incorrect comparator, and consequent lack of comparative data against the therapies most likely to be replaced.

The PBAC expressed concern about the potential for antibiotic resistance. The PBAC were also concerned about potential for toxicity with use of linezolid, particularly in long term use.

The PBAC expressed concern about the current lack of effective means to monitor emergence and trends of antimicrobial resistance, despite wide acknowledgement in all healthcare sectors of the importance of these data.

The PBAC considered that the current framework of the PBS did not easily accommodate new antibiotics intended for use against resistant microorganisms. The PBAC considered that it may be appropriate to explore whether a suitable policy construct could be identified which would recognise both the value of development of new antibiotics and the risks of emerging resistance to antimicrobial agents.

A copy of the Public Summary Document from the July 2013 PBAC meeting is available on the [PBS website](#).

Rifaximin was PBS-listed on 1 December 2013 for prevention of hepatic encephalopathy (HE) in combination with lactulose, if tolerated, in a patient who has had prior episodes of HE; after consideration at the July 2012, November 2012, March 2013 and April 2013 PBAC meetings.

Throughout the consideration, the PBAC remained concerned that there is potential for development of antibiotic resistance with use of rifaximin. The PBAC recommended listing of rifaximin on the basis of high clinical need, improved clinical benefit over the existing treatments and acceptable cost effectiveness.

A copy of the Public Summary Document for these considerations is available on the [PBS website](#).

Ciprofloxacin ear drops were considered at the July 2006 PBAC meeting for treatment of chronic suppurative otitis media (CSOM). The product is identical to the PBS-listed eye drop formulation.

The Committee noted that the use of fluoroquinolones in other indications has previously been restricted on advice from the EAGAR. This has been done in an attempt to limit the potential for the development of resistant strains which could limit the usefulness of these agents. EAGAR's advice to the Committee for ciprofloxacin ear drops was that that group remains reluctant to support widespread use of fluoroquinolones to treat ear infections. The EAGAR advice concluded that if the PBAC is inclined to list, use be restricted to the Aboriginal and Torres Strait Islander (ATSI) population.

The PBAC recommended the listing for treatment of chronic suppurative otitis media in an Aboriginal or a Torres Strait Islander person aged one year and older; which was PBS listed on 1 February 2007.

A copy of the Public Summary Document for these considerations is available on the [PBS website](#).

The PBAC considered a minor submission from the Optometrists Association Australia at its November 2012 meeting, seeking to change the current Authority Required listing under the Optometric schedule to remove the current requirement for optometrists to be under the supervision and direction of an ophthalmologist when prescribing ciprofloxacin and ofloxacin eye drops for bacterial keratitis. The PBAC recommended that the listings in the general and optometric schedules for these two eye drops be made consistent by requiring the involvement of an ophthalmologist for both drugs in both the general and optometric schedule restrictions.

A Public Summary Document is not available for this consideration. The PBAC outcome is available on the [PBS website](#).

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 (DoH) 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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