

Antibiotics Roundtable Outcomes Statement

Key points

- Antibiotics are overused at the population level in Australia. This high use, combined with the high proportion of broad- and moderate-spectrum antibiotics, is likely to be contributing to antimicrobial resistance.
- There is significant clinical variation in prescribing within antibiotic classes.
- A restrictive PBS listing sends a strong message about appropriate antibiotic use, and can be helpful guidance for both prescribers and consumers.
- PBS listings should be better aligned with recommendations in *Therapeutic Guidelines: Antibiotic*, including by altering pack sizes.
- Targeted and consistent messaging is required to educate prescribers and consumers, and also people within the health and regulatory systems.
- Repeats should not be listed as the default choice in prescribing software. Reducing the validity period of original and repeat prescriptions should be considered to prevent antibiotic misuse in the community.
- Prescribing software could be improved to integrate decision support tools on antibiotic prescribing, change default settings and make the software field for indication mandatory.
- Data quality is a critical consideration in understanding prescribing practices and evaluating education initiatives.

Background

On 18 May 2015, an Antibiotics Roundtable was held in Canberra as part of the Post-market Review of Authority Required Pharmaceutical Benefits Scheme (PBS) Listings (the Review). The Review aims to reduce the administrative burden on prescribers, improve patient care and increase the transparency of the criteria used by the Pharmaceutical Benefits Advisory Committee (PBAC) to list PBS items as Authority Required and Authority Required (STREAMLINED).

The purpose of the Antibiotics Roundtable was to seek stakeholder input on PBS-listed antibiotics, including:

- identifying options to reduce regulatory burden on health professionals associated with requests for authority to prescribe, while managing risks to the community associated with antibiotic misuse and antimicrobial resistance
- considering the role of the PBS in antibiotic stewardship, including alignment of listings with clinical guidelines.

Roundtable participants included representatives from consumer groups, industry, government and health professionals (see Appendix 1). Discussions focused on optimising the use of antibiotics through the PBS in the context of the broader strategy of managing risks to the community associated with antibiotic misuse and antimicrobial resistance.

The outcomes of the Antibiotics Roundtable will be used to assist the PBAC to form recommendations to the Minister for Health on the PBS Authority levels and restrictions for PBS-listed antibiotics.

Topics for discussion

Topics discussed included those raised during public consultation for the Review, as well as those raised by the Reference Group, the Drug Utilisation Sub-Committee (DUSC) and the PBAC, including the following:

- Some public submissions to the Review indicated that current Authority Required listings should be retained, but others felt that there is a need to change the Authority Required medicines to lower levels of restriction to reduce regulatory burden, improve patient access and allow timely treatment.
- Some PBS restrictions for antibiotics do not align with *Therapeutic Guidelines: Antibiotic*.
- The Authority system enables increased quantities and/or repeats for longer courses of treatment or prophylaxis in most situations, but there is a need to review the number of repeats for antibiotics, and the validity period of original and repeat prescriptions (currently 12 months), to ensure appropriate use.
- There should be separate listings for specific indications that require higher quantities to meet the recommended treatment course. Alternatively, increased quantities and repeats could be linked to specific prescribers for specific indications (e.g. osteomyelitis).
- Shared care models may be appropriate in some instances (i.e. prescribing ‘in consultation with’) to promote stewardship.
- Default settings on prescribing software could be reviewed to ensure that they are appropriate and help prescribers make the right decisions.
- The development of new antibiotics to address antimicrobial resistance could be incentivised.

Additional issues that participants discussed included:

- challenges to manufacturers from changes to the PBS, such as changing pack sizes or shortages of supply
- the importance of educating health professionals to successfully implement any PBS changes, and educating general practitioners (GPs) about the roles of other health professionals (such as dentists) in antibiotic prescribing
- equipping consumers with the information to discuss appropriate courses of antibiotics with their GPs, and ensuring that consumers are adequately informed, to counter antibiotic misuse in the community
- antimicrobial stewardship in hospitals and residential aged care facilities, and accounting for casemix and disease severity of hospital inpatients when examining PBS prescriptions through hospital pharmacies
- consideration of access, and differences in the types and incidence of infections in rural and remote areas, as well as in other populations, such as Aboriginal and Torres Strait Islander people
- the type of support that may be required from a range of organisations, such as the Pharmacy Guild of Australia
- how outcomes from the Review will relate to Australia’s Antimicrobial Resistance Strategy and surveillance plan
- the role of the PBAC and the PBS in guiding appropriate prescribing.

Overview of antimicrobial resistance

Professor John Turnidge provided an overview of antimicrobial use and resistance in Australia. He noted that one of the most important adverse effects of antimicrobial use is the selection of antimicrobial-resistant organisms. Resistant strains of bacteria can spread within the population, and mobile genetic elements mean that resistance genes can also be transferred to other organisms. Longer and more frequent exposure to antimicrobials in an individual can lead to higher levels of resistance in that individual, and higher proportions of antimicrobial exposure in a population can lead to increased resistance at the population level. Importantly, resistance can emerge and amplify in response to antimicrobial use, and decrease in response to reduced exposure to the antimicrobial, meaning that reducing exposure to antimicrobials through shorter courses or avoiding unnecessary use will reduce levels of resistance. However, resistance is often never completely eliminated.

Professor Turnidge noted that a significant amount of antibiotic prescribing is unnecessary, meaning it has little or no benefit for the individual. Antimicrobial stewardship systems aim to improve prescribing practices and reduce selection pressure on the organisms, leading to stabilising or decreasing resistance levels. This will ensure that effective antimicrobials are preserved for those who need them most.

Antibiotic utilisation under the PBS and RPBS

Representatives from the DUSC presented data on antibiotic utilisation; a copy of the report is available on the [PBS website](http://www.pbs.gov.au) (www.pbs.gov.au).

As at July 2014, there were 137 item codes for antibiotics listed in the PBS and the Repatriation Pharmaceutical Benefits Scheme (RPBS); most of these were listed as Unrestricted or Restricted Benefit. Authority Required antibiotics are shown in Appendix 2.

In 2013, 45% of the Australian population was prescribed at least one antibiotic. More than 29 million prescriptions were supplied for any antibiotic, and more than 26 million of these were for systemic antibiotics. The most commonly supplied antibiotics in 2013 were:

- amoxicillin (5.7 million prescriptions)
- cephalexin (5.4 million prescriptions)
- amoxicillin plus clavulanic acid (4.5 million prescriptions)
- roxithromycin (1.8 million prescriptions).

GPs prescribed 75% of antibiotics in 2013; 'other medical' professionals (such as specialists) prescribed 21%; dentists prescribed 3%; and optometrists, midwives and nurse practitioners prescribed less than 1% each.

The total number of prescriptions supplied under the PBS and RPBS decreased from around 28 million in 1994 to around 22 million in 2003, but then increased to almost 30 million in 2013. The vast majority of these are for systemic antibiotics. The defined daily dose in Australia is 22.8 per 1000 population per day, which is higher than in other OECD countries (e.g. the United Kingdom has a defined daily dose of 18 per 1000 population per day, and Scandinavian countries have defined daily doses of 10–15 per 1000 population per day). In Australia, broad-spectrum and moderate-spectrum antibiotics are prescribed more commonly than narrow-spectrum antibiotics.

Many prescriptions for commonly used antibiotics are ordered with repeats. This ranges from 28% of original prescriptions for chloramphenicol to 71% of prescriptions for roxithromycin. However, only

around 20% of these repeats are dispensed. In addition, the time between the original supply and the repeat supply can be long—25% of repeats for amoxicillin were supplied 34 or more days after the original supply. The DUSC considered that this use may not be for the same course of treatment and may be inappropriate. Other issues (e.g. relating to the Medicare Safety Net) can influence a patient's decision to present a prescription. However, take-home or delayed prescriptions can reduce costs for the patient.

It was noted that PBS prescription processing data do not include the indication or reason for prescribing an antibiotic. It may be possible to use the prescription history to determine the likely reason for prescribing of some antibiotics, such as for treatment of neutropenic fever following chemotherapy.

Roundtable participants considered that a further breakdown of prescriber type (e.g. vocationally or non-vocationally registered GP) may be useful to explore any differences in prescribing practices by type of health professional.

Antibiotic prescribing practices in Australia

Margaret Williamson presented background on the MedicineInsight project, a general practice data platform that collects clinical and service delivery data. Data were presented on reasons for prescribing commonly used antibiotics and commonly treated infections. Participants noted that a relevant condition could not be identified in the specified data field for around 40% of antibiotic prescriptions.

A comparison of rates of prescribing in Australian practice and benchmarks set by the European Surveillance of Antimicrobial Consumption Project Group (ESAC) was presented. Participants noted that the proportion of Australian patients who were prescribed an antibiotic for specified conditions was well above the acceptable range set by ESAC for most conditions. An acceptable range has not been developed for Australia, but this would be a useful addition to analyses. It was suggested that the data could be analysed in terms of practice size and type to explore any differences relating to after-hours care or patients who do not present to their regular GP. Participants felt that these issues can affect the level of consumer involvement in decision making.

Participants discussed the potential to use data on variation across practices as an education tool for GPs to help to set a benchmark for reducing antibiotic prescribing. The reasons behind these variations need to be understood and addressed—for example, it may be sufficient to educate GPs about how to help patients manage their symptoms, instead of prescribing antibiotics. Partnerships across health care professions will be important to provide consistent messaging, and change the culture relating to antibiotics in terms of what consumers and health professionals expect.

Quality use of antibiotics

Professor Turnidge presented information about *Therapeutic Guidelines: Antibiotic* (currently in its 15th edition). This is a benchmark publication that is rigorously reviewed and updated, and widely used among prescribers. Several programs and standards from other organisations also cover antimicrobial stewardship, such as the National Safety and Quality Health Service Standards, the Antimicrobial Stewardship Clinical Care Standard, the National Antimicrobial Prescribing Survey, the National Antimicrobial Utilisation Surveillance Program, and *Antimicrobial stewardship in Australian hospitals*.

The Clinical Care Standard specifies that antibiotics should be prescribed in accordance with the current version of *Therapeutic Guidelines: Antibiotic*. However, data from MedicineInsight indicate

that the proportions of patients who are prescribed systemic antibiotics are far above the acceptable range (set by ESAC) for most selected conditions. Other elements of the Clinical Care Standard, such as whether a patient was provided with information about their antibiotic, and whether patients who are prescribed broad-spectrum antibiotics have their treatment reviewed and switched to a narrow-spectrum antibiotic (where appropriate), are difficult to gather data on.

Participants noted that the Australian Commission on Safety and Quality in Health Care is developing an atlas of health care variation. This will inform strategies, resources and tools to identify and reduce unwarranted health care variation—including for antibiotics—and will drive further investigation of variation at the local area level.

Participants agreed that the PBS has a strong role in antimicrobial stewardship. Currently, common antimicrobials are cheap and subsidised for around half the population. An Authority Required listing provides a significant disincentive to prescribe, which can drive down inappropriate use. Professor Turnidge noted that regulation of fluoroquinolones in Australia illustrates this point—strong regulation through the PBS as Restricted Benefit or Authority Required, and little use in the field of animal health, led to Australia having one of the lowest rates of fluoroquinolone use in the world and the lowest proportion of *E. coli* strains that were resistant to fluoroquinolones.

Optimising PBS listings

Participants discussed the following issues with reference to several case studies, including high-volume antibiotics (amoxicillin, amoxicillin and clavulanic acid, cephalexin), where a small change in listing could have a large effect on total antibiotic use, and examples where the current PBS restrictions (azithromycin) or quantities (clindamycin) do not align with current guidelines.

Addressing regulatory burden

Participants noted the regulatory burden of Authority Required listings, and also that the streamlined authority was introduced to reduce this burden. Listing antibiotics as Authority Required (STREAMLINED) allows the streamlined code relating to indication to be captured, and also sends a signal to the prescriber that the item is restricted under the PBS. It was suggested that some antibiotics (such as amoxicillin) could be listed as Authority Required (STREAMLINED) without repeats, but a higher maximum quantity would be listed as Authority Required. Since repeats are only dispensed around 20% of the time, it may not be a significant additional administrative burden to list increased quantities as Authority Required. However, it was noted that greater granularity would be required for the restrictions to provide informative and detailed data, but that the increase should not be so great that it leads to too many restricted items.

Any changes in restrictions and pack sizes would also increase the regulatory burden on manufacturers and the Therapeutic Goods Administration, as manufacturers would need to update their Product Information (PI) and Consumer Medicines Information (CMI), which can take time. Participants discussed the need for the PI and CMI to reflect current practice so that consumers receive the same information from the CMI and their prescriber.

Aligning the PBS with *Therapeutic Guidelines: Antibiotic*

Pack sizes could be adjusted to better reflect *Therapeutic Guidelines: Antibiotic*. For cephalexin, a pack size of 20 is adequate for the majority of indications and does not require a change; however, roxithromycin is recommended as a 10-day course for almost all indications, and this should be reflected in the PBS-listed pack sizes. The PBS-listed pack size for clindamycin is insufficient for the

usual length of treatment. Amoxicillin also presents issues with non-alignment between PBS-listed indications, duration and quantity, and the same information in *Therapeutic Guidelines: Antibiotic*.

Participants noted that off-label prescribing for azithromycin is common as a result of misalignment between the PBS-listed indications and the recommendations in *Therapeutic Guidelines: Antibiotic*. In addition, some antibiotics that are available and recommended under *Therapeutic Guidelines: Antibiotic* are not PBS-listed, and this can affect access, particularly in private hospitals.

It was suggested that the PBS listing and restrictions for antibiotics could include a requirement for prescribing in accordance with *Therapeutic Guidelines: Antibiotic*. It would also be useful to develop a mechanism to ensure that prescribers are using the latest edition of *Therapeutic Guidelines: Antibiotic*, as prescribers are not always willing to pay to update their version.

Using PBS restrictions to limit antibiotic use

Participants discussed the potential for a return to bulk packs—that is, where the pharmacist would not be restricted by the pack size and could dispense a short course, which could then be reviewed on receiving the patient’s microbiology results. However, this would mean that practices would need to order more tests than they do currently, which would affect budgets. It was also noted that some antibiotics (such as amoxicillin and clavulanic acid) are hygroscopic, which presents difficulties for breaking packs. It would be preferable to avoid the inconvenience of breaking packs by setting up a system in which pack sizes are matched to listings. Changing pack sizes would also present challenges for manufacturers, particularly those who supply to many countries.

Strategies to optimise use of antibiotics

Antimicrobial stewardship through the PBS

Participants noted that the PBS has a role in restricting, and encouraging compliance with, antibiotic prescribing by discouraging inappropriate prescribing practices, and that this approach is appropriate because mechanisms exist in other areas of health to provide incentives for appropriate prescribing. A restrictive PBS listing sends a strong message about appropriate antibiotic use, and can be helpful guidance for both prescribers and consumers. As a result, more restrictive PBS listings would be unlikely to drive an increase in private prescriptions. However, it was noted that agencies and programs other than the PBS also have a role in these decisions, and that it would be necessary to have options outside the PBS in certain situations.

One of the key roles of the PBS is education, and participants discussed the need for targeted and consistent messaging for prescribers and consumers, and also for people within the system itself. This was considered particularly important at the transition from hospital to community care, as current antimicrobial stewardship standards focus on hospitals.

High-quality data on prescribing practices are critical to ensure an appropriate response. The potential for data linkage and sharing through personal electronic health records was discussed, with participants agreeing that solutions should be future focused and include consideration of the greater role of e-health records in the future.

The PBS subsidy itself is a driver of antibiotic use—participants noted the situation in Iceland, where antibiotic use decreased substantially when subsidies were removed. It was also noted that the PBS should not be used to subsidise treatments where the risk outweighs the benefit, and this should be considered in the global context of increasing antimicrobial resistance.

Prescribing software as a tool to improve prescribing practices

Participants felt that there was scope for improvement of prescribing software to integrate decision support tools on antibiotic prescribing. For example, it would be possible to integrate *Therapeutic Guidelines: Antibiotic* recommendations with the software, so that selecting an antibiotic would automatically trigger the relevant recommendations to appear on the screen. Practice software could also provide a prompt to print patient information on alternative care where antibiotics are not indicated (e.g. for a cold) as a positive redirection away from the antibiotic option.

Many participants felt that the default settings should be changed to order a single course rather than repeats (e.g. so the course with no repeats is the first option in a drop-down list). This could be instigated by the prescribers (who could approach the software vendors to change the software) or through regulation. However, some participants felt that this was insufficient, and that the PBS listing should be changed so the software could automatically follow the appropriate prescribing practices.

In addition, it was suggested that the software field for indication should be mandatory. This would allow capture of high-quality data on prescribing, although potential privacy issues would need to be considered. This could be implemented across the board, or some antibiotics could be classified to allow an alternative data field in electronic systems (or an alternative prescribing pad) where an indication is required for the prescription to be valid.

It was also noted that prescribers need to pay to receive training in the software packages. This probably results in various levels of fluency with the programs, depending on the amount of training received, which may contribute to variation in prescribing practices.

Participants also noted the need to support the development of software for dental practices that can link to pharmacy dispensing systems. Until infrastructure is sufficient to allow dentists to participate in e-prescribing, there will continue to be a lack of data on prescribing practices in this area, and a missed opportunity to influence these practices through improvements in prescribing software.

Validity period of antibiotic prescriptions

PBS prescriptions are currently valid for 12 months. The time between supply of the original prescription and supply of repeats can be long, suggesting that the repeat may not be used for the original indication. The role of the pharmacist is important in these situations—there is an opportunity to educate consumers about quality use of medicines. Having the original indication or the prescriber's intention recorded on every prescription would also help pharmacists make informed decisions in these situations; however, this would require consideration of privacy issues.

Participants discussed the potential to reduce the validity period for antibiotic prescriptions (e.g. to 2 weeks, 4 weeks or 3 months). However, some exceptions were noted, such as patients with chronic obstructive pulmonary disease, emphysema or cystic fibrosis, who require antibiotics as needed or for prophylaxis. These exceptions may lead to an unnecessarily complex system.

Developing new antibiotics to address resistance

Creating links between manufacturers of antibiotics and manufacturers of oncology medicines may help to drive the development of new antibiotics, as oncology patients require antibiotics after aggressive chemotherapy; potential partnerships across these areas could be explored. The potential to use older antibiotics that had not been registered in Australia was also discussed, although it was noted that data packages for these antibiotics may not be of sufficiently high quality for the

Therapeutic Goods Administration's registration processes, and there is no incentive for sponsors to pay cost-recovery fees to register new indications for older and inexpensive antibiotics. It was also noted that development of new antibiotics is a lengthy and expensive process.

Next steps

Participants were advised that the draft Outcomes Statement would be circulated for comment. The final statement would be presented to the Review Group and the PBAC, who would then make a recommendation to the Minister for Health if any changes are required to PBS Authority and restrictions for antibiotics.

Appendix 1 Roundtable participants

Name	Organisation, committee or specialty
Dr Tony Hobbs (Chair)	Acting Australian Government Chief Medical Officer
Dr David Abbott	National Health and Medical Research Council
Patrice Cafferky	Australian Primary Health Care Nurses Association
Zoe Croker	Medicines Australia
Prof Chris DelMar	Royal Australian College of General Practitioners (via teleconference)
Peter Fowler	Society of Hospital Pharmacists of Australia
Cathie Hilton	Generic Medicines Industry Association
Eithne Irving	Australian Dental Association
Dr Ian Kamerman	Rural Doctors Association of Australia
A/Prof David Looke	Australasian Society for Infectious Diseases
Grainne Lowe	Australian College of Nurse Practitioners
Dr Elizabeth Marles	Pharmaceutical Benefits Advisory Committee
Cater Moore	Consumers Health Forum of Australia
A/Prof David Newby	Pharmaceutical Benefits Advisory Committee
A/Prof Mary O'Reilly	Council of Australian Therapeutic Advisory Groups
Dr Rashmi Sharma	Pharmaceutical Benefits Advisory Committee Drug Utilisation Sub-Committee
Suzanne Shultz	Pharmacy Guild of Australia
Dr Tom Snelling	Pharmaceutical Benefits Advisory Committee
Dr Rhonda Stuart	Infectious diseases physician
Prof John Turnidge	Australian Commission on Safety and Quality in Health Care
Jo Watson	Pharmaceutical Benefits Advisory Committee
Dr Lynn Weekes	NPS MedicineWise
Margaret Williamson	NPS MedicineWise

Australian Government Department of Health representatives

Name	Position
Dr Anna Colwell	Medical Officer, Office of Health Protection
Julie Cutts	Director, Post-market Review Section
Dr Alexandra Greig	Medical Officer, Office of Health Protection
Jacinta Holdway	Director, Health Protection Policy Section
Anne Jackson	Assistant Director, Post-market Review Section
Vanessa McMahon	Assistant Director, Drug Utilisation Sub-Committee Secretariat
Greg O'Toole	Director, Health Technology Assessment
Dr Alicia Segrave	Director, Drug Utilisation Sub-Committee Secretariat
Shaiyena Williams	Secretariat, Post-market Review Section

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Appendix 2 Summarised item details and restrictions for Authority Required antibiotics

Authority Required (STREAMLINED)

Drug	Item details	Restriction
Cephalexin, 250 mg tablet	2655R (MP)	Prophylaxis of urinary tract infections (higher quantity than unrestricted listings)
Tobramycin, inhalation capsules and inhalation solution	<ul style="list-style-type: none"> 10066T, 10074F (inhalation capsules) (MP) 5442K (solution for inhalation) (MP) 	Management of a proven <i>Pseudomonas aeruginosa</i> infection in a patient with cystic fibrosis
Trimethoprim, 300 mg tablet	2666H (MP)	Prophylaxis of urinary tract infections (higher quantity than other listings)

MP: medical practitioner

Authority Required

Drug	Item details	Restriction
Cefepime, powder for injection	8315P, 8316Q (MP, NP)	Treatment of febrile neutropenia
Ciprofloxacin, 250 mg tablet, 500 mg tablet, 750 mg tablet	<ul style="list-style-type: none"> 1208N (250 mg tablet) (MP, NP) 1209P (500 mg tablet) (MP, NP) 1210Q (750 mg tablet) (MP, NP) 	<ul style="list-style-type: none"> Respiratory tract infection proven or suspected to be caused by <i>Pseudomonas aeruginosa</i> in severely immunocompromised patients Bacterial gastroenteritis in severely immunocompromised patients 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)
Ciprofloxacin, 0.3% eye drops	1217C (MP), 5564W (OP)	Bacterial keratitis

Drug	Item details	Restriction
Ciprofloxacin, 0.3% ear drops	2480M (MP, NP)	Treatment of chronic suppurative otitis media in: <ul style="list-style-type: none"> • 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, 400 mg tablet	3010K (MP, NP)	<ul style="list-style-type: none"> • Acute bacterial enterocolitis • Complicated urinary tract infection
Ofloxacin, 0.3% eye drops	5567B (OP), 8383F (MP)	Bacterial keratitis
Rifaximin, 550 mg tablet	10001J (MP)	Prevention of hepatic encephalopathy
Vancomycin, 125 mg capsule, 250 mg capsule	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

MP: medical practitioner; NP: nurse practitioner; OP: optometrist

S100 Highly Specialised Drugs Program

Drug	Item details	Restriction
Clarithromycin, 250 mg tablet, 500 mg tablet	<ul style="list-style-type: none"> • 6151R, 6152T (private hospital, Authority Required) (MP) • 5624B, 5625C (public hospital, Authority Required (STREAMLINED) (MP) 	Treatment of <i>Mycobacterium avium</i> complex infections (higher quantity than other listings)
Azithromycin, 600 mg tablet	<ul style="list-style-type: none"> • 6221K (private hospital, Authority Required) (MP) • 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