AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

Active Ingredient Prescribing

User Guide for Australian Prescribers

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This document was last updated by the Commission in December 2022.

From 1 January 2023, the Australian Government Department of Health and Aged Care is managing the curation of Active ingredient prescribing resources. From this date, please direct all AIP enquiries to aiprescribing@health.gov.au

Summary

This user guide supports prescribers in all health care setting to adopt active ingredient prescribing. It has been developed in consultation with relevant stakeholders to assist prescribers' clinical decisions and provide best practice guidance on when prescribers should consider specifying the medicine brand name on a prescription. The user guide also provides support to clinical software vendors when making necessary changes to their products to ensure the safety of prescribing choices.

Active ingredient prescribing will:

- Improve safe and quality use of medicines with consistent and standardised descriptions of medicines
- Increase consumer health literacy around their medicines and make communication clearer and unambiguous
- Empower and equip prescribers and consumers to better understand the active ingredients in medicines
- Assist conversations between pharmacists and consumers concerning generic and biosimilar alternatives
- Promote the appropriate uptake of generic and biosimilar medicines, with a decrease of out-of-pocket expenses for some consumers
- Improve financial sustainability of the Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS)
- Enhance prescribers' stewardship role of the PBS, and encourage more sustainable prescribing practices
- Align Australian prescribing with international practices.

In October 2019 the *National Health (Pharmaceutical Benefits) Amendment (Active Ingredient Prescribing) Regulations 2019*, and the *Veterans' Affairs Pharmaceutical Benefits Schemes (Electronic Prescriptions and Active Ingredient Prescribing) Amendment Instrument 2019* mandated active ingredient prescribing. From 1 February 2021 most prescriptions generated for supply under the PBS and the RPBS must meet the revised arrangements to be eligible for subsidy.

This user guide describes principles for active ingredient prescribing and identifies situations and/or medicines where prescribers should consider if the specification of brand is clinically necessary for the treatment of their patient. In situations where formulations are not interchangeable due to variations in delivery of the active ingredient prescribers should consider specification by brand, for patient safety. These medicines and situations are listed in:

- List of Medicines for Brand Consideration (LMBC): A list of medicines prescribers should consider prescribing by brand name in addition to active ingredient name, if the inclusion of brand name is necessary for safe selection, or the clinical treatment of their patients.

- List of Excluded Medicinal Items (LEMI): A list of medicines and supplementary pharmaceuticals for prescription by brand name only. The items in this list may be safer and more practical to prescribe by brand name. For PBS items, legislation is regularly updated in line with the LEMI to allow for prescribing by brand name only. However, the active ingredient name(s) may also be included by the prescriber if practical and safe to do so.

The LMBC and LEMI assist prescribers in making good clinical prescribing decisions and meet the legislative requirements for active ingredient prescribing. The decision regarding the prescribing and supply of a particular brand of medicine remains the choice of the prescriber as part of a shared decision-making process with the patient. However, it is important to consider brand specification to ensure clarity of the medicine prescribed and prevent medication harm. Note, the LMBC and LEMI may only list a few brand names as examples for a particular medicine, rather than all brand names registered on the Australian Register of Therapeutic Goods (ARTG).

Prescribing system software providers are required to regularly update medicines included on the LMBC and LEMI. Software systems can support prescribers by alerting when a medicine on the LMBC is prescribed. Software systems will vary but for example, an alert may pop-up and link prescribers directly to the LMBC.

The LMBC and LEMI undergo regular review (see *List curation*). The medicines considered for inclusion or exclusion at each iteration of the lists is summarised in the Active Ingredient Prescribing Issues Register. This includes medicines or issues raised to the Australian Commission on Safety and Quality in Health Care (the Commission), and a review of newly registered/cancelled medicines on the ARTG.

This user guide and the associated lists have been developed through extensive consultation and feedback from stakeholders acknowledged in **Appendix A**.

Introduction

Active ingredient prescribing using standardised terminology increases consumer understanding of their medicines, assists health literacy and communication, and increases the uptake of generic and biosimilar medicines. This user guide supports prescribers to prescribe medicines by the active ingredient with best practice guidance for specification of brand.

Principles are outlined to determine when prescribers should consider brand name specification if clinically necessary. Specifying the brand name may be necessary to support safe and quality use of a medicine where consumer harm could result from switching between medicine brands or to ensure prescriber instructions are suitable for the dispensed medicine. This guidance is supported by a list of medicines where prescribers should consider prescribing by brand name in addition to the active ingredient name (List of Medicines for Brand Consideration, LMBC).The List of Excluded Medicinal Items (LEMI) lists medicines and non-medicinal items exempt from active ingredient prescribing. These items should be prescribed by brand name only for practical purposes (for example, very long active ingredient names). This does not preclude the addition of active ingredient name(s) should the prescriber deem this appropriate.

Objective

To provide guidance to prescribers regarding active ingredient prescribing.

To clarify the circumstances where prescribers should consider specifying the medicine brand name in the interests of safety, practicality, or to prevent confusion.

Scope

Active ingredient prescribing applies across all health care settings where medicines are prescribed. That is, whenever prescribing a medicine as defined under the *Therapeutic Goods Act*[1] and listed on the ARTG. This includes electronic medication charts such as the electronic National Residential Medication Chart (eNRMC).

Active ingredient prescribing legislation covers most PBS and RPBS medicines. However, the principles for active ingredient prescribing apply across all medicines. This user guide and associated resources, including provisions for software vendors, reflect the broader scope of all medicines and is not limited to medicines available for PBS and RPBS subsidy.

Situations where active ingredient prescribing is not mandated and requirements are out of scope include:

- Handwritten prescriptions
- Computer generated paper-based National Residential Medication Charts
- Prescriptions generated through a free text function within prescribing software
- Medicines containing four or more active ingredients
- Items listed under the ‘Various’ section of the General PBS schedule
- Items listed under the ‘Various’ section of the RPBS schedule
- Medicines not registered for use in Australia, which may include Special Access Scheme medicines.

Context

Medicines have a pivotal role in disease management with potential for medicine-related adverse events.[2] Medicines literacy is an important part of health literacy. All health professionals and consumers need to be able to establish a platform for shared decision-making with consistent communication around medicines. Being familiar with and implementing the active ingredient name for medicines is essential to consistent communication and optimising health outcomes.

Active ingredient prescribing is allowed in the UK, Ireland, and eighteen other countries across continental Europe. It is mandatory in France, Spain, Portugal, Italy, Greece and eight other countries in Eastern Europe.[3] Active ingredient prescribing has been implemented in the USA[4], Canada[5], New Zealand[6] and Japan.[7]

As part of the 2018–19 Budget, the Australian Government undertook to improve the uptake of generic and biosimilar medicines listed on the PBS.

Strategies have been developed to increase the uptake of generic and biosimilar medicines and improve the health literacy of consumers and prescribers around the active ingredients in medicines.[8,9]

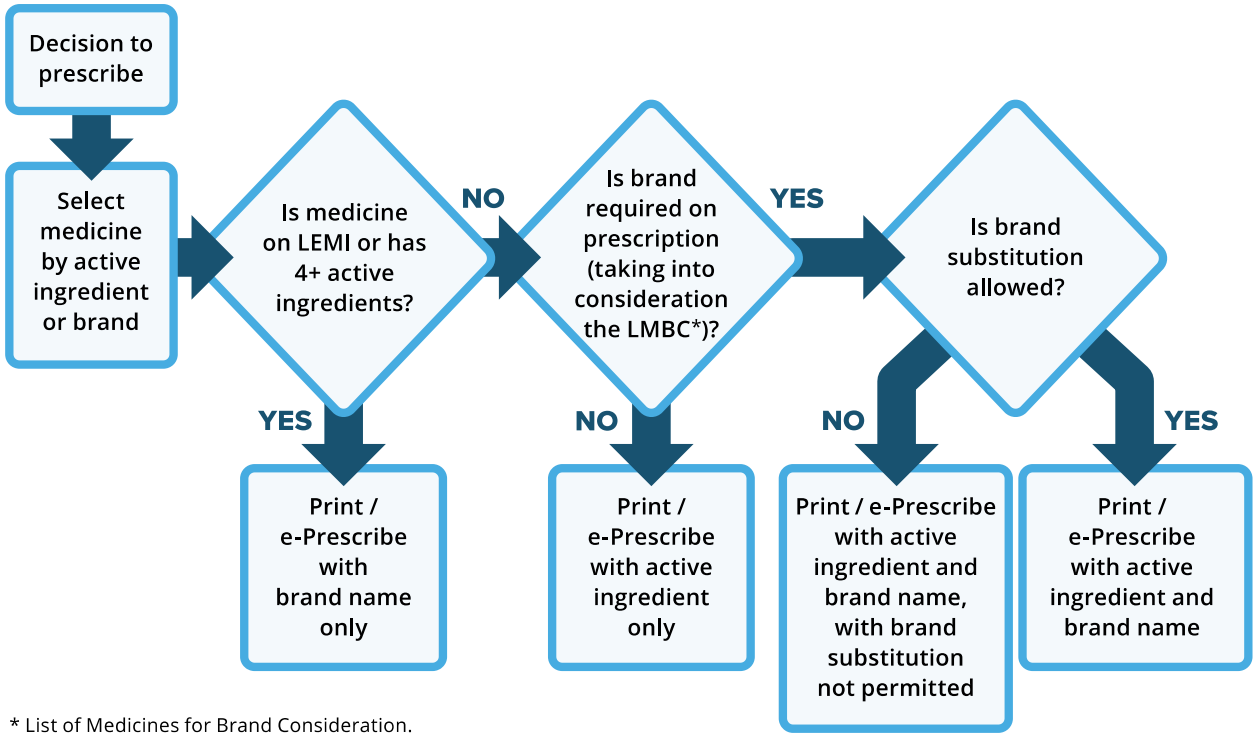
Consumer and prescriber choice of medicines remain key priorities for the Australian Government. This initiative, to prescribe the medicinal product by active ingredient rather than brand name, may further increase public awareness of generic and biosimilar medicines. Prescribers will retain choice of medicines and brands, and consumers will retain choice of brands.

Active ingredient prescribing overview

Prescribing process

Figure 1 sets out an example of a prescribing decision process under active ingredient prescribing.

Figure 1: Prescriber decision process under active ingredient prescribing



* List of Medicines for Brand Consideration.

Options for active ingredient prescribing

1. Medicines are prescribed by active ingredient with or without brand

Upon the decision to prescribe, the prescriber should search for and select the medicine according to the software in use. This may involve keying in the first few letters of the active ingredient or the originator brand, depending on how the software is configured.

Once the medicine is selected, the prescription stating the active ingredient name of the medicine can be prepared. A prescriber may also consider if it is clinically necessary to specify the brand of the medicine. In this case, 'include brand name' (or similar) is selected within the prescribing software. The prescription will then be generated to state the active ingredient and followed by the brand, if considered necessary by the prescriber.

Prescribers can also indicate if brand substitution is not permitted, taking into consideration the clinical needs of their patient.

Prescribing a medicine by brand name in addition to the active ingredient name is preferrable in some circumstances, for clinical reasons and/or patient safety[10]. This is particularly important for some high-risk medicines, such as insulins, for high-risk consumers and/or high-risk situations. There are circumstances where it may be preferable to include the brand name, to avoid miscommunication between clinicians, to prevent selection error, and to ensure accuracy when interpreting and dispensing the prescription. For example, in situations where formulations are not interchangeable due to variations in delivery of the active ingredient, prescribers should consider specifying brand name to prevent the risk of medication-related harm.

The LMBC includes medicines recommended for consideration of brand specification to prevent serious incidents and consumer harm and is annotated with notes that give detailed reasoning for inclusion in the list. Prescribers are encouraged to consider the LMBC and decide on the need for brand, based on the medicine and their patient's clinical need. Where switching between brands is not recommended, these exceptions are annotated in the LMBC. Intentional one-off switching from one brand to another for these products may be achievable under controlled situations with dose titration, close monitoring, caution, and the agreement of the consumer and/or carer.

In public and private hospital settings, prescribing choices will be derived according to local policy as determined by contract purchasing and the Drugs and Therapeutics Committee. Brand should be specified by the prescriber where clinically required in accordance with the local hospital policy.

Principles for including the medicine brand

The LMBC has been developed to support prescribing and is not prescriptive nor exhaustive. At the point of prescribing, the decision regarding the specification of a particular brand of medicine remains the choice of the prescriber as part of shared decision making with the patient. From a safety perspective, it is important to recognise that active ingredient names can be complex and may confuse some consumers. Prescribers should consider this as they assess consumers and discuss their medicines with them.

For example, prescribers may specify brand in making the decision with the consumer where:

- True allergy or intolerance to excipients is known or suspected and will have a negative clinical impact. For example, confirmed lactose intolerance or proven allergic reaction[11]
- Differences in appearance between products will cause confusion and anxiety and may impact adherence or clinical outcomes. For example, in aged care, or for consumers with learning difficulties
- Other situations where switching between medicine brands is not considered to be in the consumer's best interests
- A particular brand can only be prescribed for certain conditions, to be eligible for PBS subsidy.

Principles for prescribing by active ingredient plus brand name are described in **Box 1**.

Box 1: Prescribing by brand name in addition to active ingredient name

Prescribing by brand name in addition to active ingredient name should occur where:

1. Medicines are not therapeutically equivalent or different brands of the same active ingredient have not been assessed as being therapeutically equivalent. This includes active ingredients with multiple brand substitution groups (that is, '■a' and '▲b' groupings)
2. Medicines have a narrow therapeutic index and minor changes in bioavailability of different brands of the same active ingredient may be clinically important. That is, small changes may result in toxicity or sub-therapeutic dosing which would have a clinically significant impact on outcome
3. Different formulations of the same active ingredient and strength have different dosing and/or rates of administration
4. Different formulations of the same active ingredient and strength have different release characteristics. This includes modified release formulations
5. Different brands of the same active ingredient and strength have different dosing regimens for the same indications
6. Different brands of the same active ingredient and strength have different dosing regimens for different approved indications
7. Similarity of active ingredient names will likely cause confusion, unless differentiated by strength and/or dose form
8. Administration delivery devices have different instructions for use and consumer familiarity with one product is an important contributor to consumer compliance, medicines continuity or safety
9. Certain medicines listed as Highly Specialised Drugs (HSD) on the PBS/RPBS and require prescriptions authorised in accordance with specific Authority Required procedures.

Applying the principles for LMBC inclusion

Medicines are considered for inclusion where there is potential for misinterpretation of a prescription and the brand name is required for differentiation. The active ingredient name, strength and/or form of a medicine should be reviewed when applying the nine principles for LMBC inclusion. If relevant, medicines may be considered against more than one of the nine principles for inclusion. The examples below provide further detail on application of some principles:

- insulins are high-risk medicines which can cause significant patient harm if the wrong type, brand, strength, form or device is given. Insulins are available in multiple strengths and formulations of similar looking and sounding active ingredient names. This can cause confusion if the brand name is not qualified. Prescriptions that include the insulin brand name, in addition to the active ingredient name, support safer selection and use of insulin. Insulins are included on the LMBC in line with **principles 3, 7 and 8**.
  See the Safer insulin prescribing factsheet for more information
- betamethasone dipropionate in an 'optimised vehicle' (OV) offers a different absorption and uptake of active ingredient to the original formulations. Without the brand name, the OV formulations (available as a cream or ointment) are difficult to differentiate from the original formulations (available as a cream or ointment), as they share the same strength and form. The OV formulations are included on the LMBC in line with **principle 4**.
- two brands of C1 esterase inhibitor injection have different dosing regimens for the same indication. The two brands are not interchangeable although they share the same strength and dose form. The two brands are only distinguished by the number of vials in the pack and the container size of the diluent. They are included on the LMBC in line with **principles 1 and 5.**

- risedronate sodium tablet products have been challenged against **principles 6** for LMBC inclusion, as they are available in different brands for different approved indications. However, the different available brands can be differentiated by strength and/or form for their specific indications. For example, risedronate sodium enteric coated 35mg tablet (indicated for osteoporosis) can be differentiated from risedronate sodium 30 mg tablet (indicated for Paget's disease). Brand name is not necessary, and these products have not been included on the LMBC.
- clozapine is a Highly Specialised Drug (HSD) requiring specific authority procedures when prescribing and regular ongoing monitoring. Specific brands of clozapine have their own patient programs, for which the consumer, prescriber and pharmacist register while being treated with clozapine. Clozapine has a narrow therapeutic index and the various strengths are included on the LMBC in line with **principles 2 and 9**.

2. Medicines prescribed and specified by brand

Medicines and medicinal items excluded from active ingredient prescribing are listed in the LEMI. The prescription for these items will be prepared with the brand name only. The active ingredient name(s) may be included for these items, if deemed appropriate by the prescriber, and is practical and safe to do so. The principles for inclusion in the LEMI extend to all medicines registered on the ARTG. However, the LEMI only captures medicines that are PBS listed.

In some instances, it is both safer and more practical to prescribe by brand only. This is the case for products containing **four or more** active ingredients in line with the National Guidelines for On-Screen Display of Medicines Information.[12] The prescriber may also consider including the brand name on the prescription if there are concerns regarding medicines with three active ingredients contributing to consumer confusion.

The circumstances where prescribing should be by brand only are described in **Box 2**.

Box 2: Prescribing by brand name

Prescribe by brand name where:

- Products contain four or more active ingredients
- Vaccines have varying strains, components or immunisation regimens (See LEMI)
- Items are non-medicinal items, listed under the 'Various' section of the General PBS Schedule or the RPBS Schedule. These include items such as non-absorbed treatments, bandages tapes and dressings, allergens, diagnostic agents, oral rehydration salts, general nutrients, food supplements and vitamin supplements (See LEMI)
- Inclusion of active ingredients has been deemed impractical (for example, dermatologicals, ocular lubricants) (See LEMI)

The Medication Software Industry Association (MSIA) continues to work with prescribing software developers to embed the LMBC and LEMI into prescribing software packages to ensure prescribers have access to decision support information when prescribing decisions are being made and the prescription prepared.

Documenting the decision to specify brand

Decisions to specify a brand (either originator, branded generic or biosimilar) should be documented in the patient's record, including My Health Record, to ensure treatment continuity.

Management of the lists

List development process

The LMBC and LEMI have been developed after review of the New Zealand[6], Ireland[13] and the United Kingdom[14] documents that clarify brand prescribing and define the situations where exceptions to active ingredient prescribing should be implemented.

Medicines have been included on the lists as appropriate even if there is only one brand available in Australia. In this way, the introduction of new generic and biosimilar medicines to the market should not impact the naming and presentation of existing medicines in prescribers' software systems.

Changes to prescribing software will facilitate population of the active ingredient name on the prescription and the inclusion of brand names on prescriptions, where clinically necessary. The professional judgement of clinicians is not impacted, and prescribers can continue to select the most appropriate medicine for their patient.

Prescribing software

Computer systems which assist active ingredient prescribing with provision of generic and biosimilar alternatives, clinical advice, and consumer information leaflets, have been found to support active ingredient prescribing.[15]

The Australian Medicines Terminology (AMT) is a national, standards-based approach to the identification and naming of medicines for human use. The AMT uniquely and accurately describes medicines in a standardised format using a set of defining properties including the active ingredient.[16] An AMT reference set for medicines on the LMBC and LEMI is available from the Australian Digital Health Agency (ADHA).

The MSIA, at the request of the Australian Government Department of Health and Aged Care, provides a software vendor resource document aligning with this user guide. This supports prescribing software vendors to enable prescribing by active ingredient, with or without the inclusion of brand name, as deemed appropriate by the prescriber.[17]

Prescribing software should be consistent with the National guidelines for on-screen display of medicines information[12]. These guidelines describe consistent, unambiguous terms and processes for on-screen display of medicines information, including medicine names.

From 1 January 2023, curation of active ingredient prescribing resources will transition to the Australian Government Department of Health and Aged Care. This includes curation of the LMBC and LEMI.

List curation

The LMBC and LEMI are derived according to the principles in these guidelines (**Box 1** and **Box 2**). Medicines are reviewed for LMBC and LEMI inclusion or exclusion to reflect changes in best practice, or in response to safety concerns. Medicines newly registered or cancelled from the ARTG are also regularly reviewed. For medicines on the LMBC or LEMI where a brand is identified as no longer registered on the ARTG, the following is applied:

- Medicine with more than one brand registered on the ARTG: the brand no longer registered will be removed from the LMBC/LEMI entry with other brand(s) remaining
- Medicine with only one brand registered on the ARTG: the month and year of cancellation will be noted on the LMBC/LEMI entry

The outcomes of these reviews and medicines under consideration for inclusion or exclusion to the lists are summarised in the Active Ingredient Prescribing Issues Register.

Active ingredient prescribing background

Medicines naming

The active ingredient of a medicine is the therapeutically active component in the medicine's final formulation that is responsible for its physiological or pharmacological action. The brand or trade name of a medicine is the name given to the medicine by the manufacturer. The same active ingredient may be marketed under a range of different brand names.

The approved nomenclature for active ingredients in the pharmaceutical domain in Australia and across the world is defined using International Non-proprietary Names (INN). Active ingredient prescribing is the use of the INN when prescribing.[18]

The standardised nomenclature used by the INN includes use of a common 'stem' which indicates the activity of the substance and the pharmacological group to which it belongs. For example, substances having *adol* as the stem indicates an analgesic (for example, tramadol); *mab* indicates a monoclonal antibody (for example, denosumab); *vir* indicates an antiviral (for example, aciclovir). The agreed system to naming biologic medicines was subject to a review by experts in the field, the INN Expert Group and the INN Secretariat of the World Health Organization in 2019.[19]

For medicines available in different salts and where the salt confers a clinically significant difference in potency, the full active ingredient name should be displayed (base followed by salt). For further details and examples, see National Guidelines for On-Screen Display of Medicines Information[7]

Familiarity with the active ingredient name aids clinician and consumer recognition of the substance and the family of similar pharmacological substances to which it belongs.

For many medicines there may be a wide range of generic brands.[20] An overview of practice in different countries concluded that prescribing by active ingredient is likely to improve consumer safety by assuring that the prescribed medicine is in fact what is dispensed.[21]

Medicines literacy and safer communication

Communicating by the active ingredient name should lead to increased health literacy in relation to medicines and medicine-related information. Medicines literacy is the degree to which individuals obtain, comprehend, communicate, calculate, and process information about their medicines. This helps consumers to make informed decisions on the safe and effective use of their medicines. Active ingredient prescribing is expected to improve clarity and knowledge about medicines, leading to improved shared decision-making. Medication errors from brand name confusion would reasonably be expected to decline. For example, double dosing due to not recognising two brands with the same active ingredient.

Active ingredient prescribing has been implemented in Australian public hospitals for a number of years. Even though this is well accepted in clinical practice, a prospective survey of hospital doctors and senior medical students at a 650 bed Australian teaching hospital demonstrated that when a medicine was described by its brand name, the ability to name a medicine and its actions was poor, even for common and high-risk medicines. The authors support calls to mandate prescribing using active ingredient rather than brand names of medicines in hospitals.[22]

The broadening of active ingredient prescribing to primary care is expected to improve understanding and communication in the community. Amongst older Australians, increased education is required to develop medicines knowledge, which may improve health literacy, optimise medicine use, and minimise harm.[23] Communication of medicines information across the transition between acute and primary care is important for continuity of care. This transition is a well-recognised point for medication error and consumer harm.[24] Improving communication between health professionals supports medication safety by reducing misinterpretation and is supported by consistent and standardised use of terminology including medicine names. The prescription may need to be supported by other communication. For example, a discharge summary or a My Health Record document to convey information regarding brand specification on admission to hospital and at discharge. Importantly, hospital pharmacy medicines stocked are dependent on local policies and contracts. Therefore, at discharge the brand supplied should not necessarily be interpreted as the brand for the consumer to continue in the community.

Medicines approval in Australia

Before a new medicine can be commercially supplied in Australia, the Therapeutic Goods Administration (TGA) must assess it for quality, safety, and efficacy with approval for inclusion on the ARTG. Applications for inclusion of a new medicine on the ARTG must include biopharmaceutical evidence including bioavailability.[25]

In Australia, the PBS[26] lists all medicines available to be dispensed to consumers at a price subsidised by the Australian Government. Generic/biosimilar and originator/reference products which are considered bioequivalent, and which would be expected to be able to be interchanged without differences in clinical effect, are annotated using the symbol '■a' located immediately before the brand names of a particular strength. This indicates that the sponsors of these brands have submitted evidence that they have been demonstrated to be bioequivalent or therapeutically equivalent, or that justification for not needing bioequivalence or therapeutic equivalence data has been provided to and accepted by the TGA. '▲b' attached to brand names indicates that these brands are also equivalent, but that it is not known if there is equivalence between brands marked '■a' and brands marked '▲b'. In some cases, '■a' flagged generics and biosimilars have proven therapeutic equivalence associated with specific indications. This should not be extrapolated across other indications.

For other brands of an item, that is, those not indicated as above, it is unknown whether they are equivalent. There may be several reasons for this, such as bioequivalence data not being considered necessary when the products were approved for marketing, or that advice or data have not been forthcoming from sponsors. This does not necessarily suggest a lack of safety or efficacy, but in these circumstances, caution should be taken if brands are interchanged.

This brand equivalence information is also included in the *Australian Medicines Handbook*[27], which states that substitution may be considered if the brands are bioequivalent (indicated by an 'a' or 'b' next to the brand name in the PBS).

Medicine affordability

The PBS is an Australian Government program that benefits all Australians by subsidising the cost of a wide range of medicines to make them more affordable. The *National Health Act 1953* governs the PBS. The RPBS provides a range of pharmaceutical benefits to veterans, members (including former members) of the Defence Force, or their dependants at a concessional rate and is governed by the *Veterans' Entitlements Act 1986*.

After marketing approval by TGA, the sponsor may seek to have a product listed for reimbursement under the PBS. The cost of a wide range of prescription medicines is subsidised through the PBS. To be listed on the PBS an application is made to the Pharmaceutical Benefits Advisory Committee (PBAC) by the sponsor. The PBAC considers cost effectiveness, efficacy, and safety issues to make recommendations to the Minister for Health about listings of new medicines or changes to current listings of medicines.

Generic and biosimilar medicines

Generic medicines are defined by the World Health Organization (WHO) as a pharmaceutical product usually intended to be interchangeable with the originator brand (or product), manufactured without a licence from the originator manufacturer and marketed after the expiry of patent or other exclusivity rights.[28]

The TGA define a generic medicine as an additional brand of an existing medicine.[29] It contains the same 'active ingredient' as the existing medicine. The TGA requires generic brands to be 'bioequivalent' to the originator brand. Active ingredients can be manufactured and sold by other sponsors once the patent for the existing brand medicine has expired. Products listed on PBS/RPBS for which adequate evidence of therapeutic equivalence is provided are deemed to be interchangeable.

Generic and biosimilar medicines are not required to provide extensive pre-clinical and clinical studies for registration application in Australia.[29] As such their investment and development costs are greatly reduced when compared to the originator product, where research and development costs are to be recuperated. Generic and biosimilar medicines provide the opportunity for major savings in healthcare, community, and consumer expenditure.

Bioequivalence

In Australia, bioequivalence is usually assessed by single dose *in vivo* studies in healthy volunteers to determine whether the products are similar in both extent and rate of absorption. The regulatory limits applied are that the 90% confidence intervals for the ratios of the areas under the drug concentration versus time curves (AUC ratio) and the maximum plasma drug concentration (Cmax ratio) must fall between 80% and 125%. The times to maximum plasma concentration (Tmax) for both products should also be similar. Bioequivalence means that two medicines are pharmaceutically equivalent and their bioavailability of each (rate and extent of availability) in the same dose after administration is similar. With respect to both efficacy and safety the generic medicine can be expected to be essentially the same as the reference product. To be determined to be pharmaceutically equivalent and interchangeable with the originator brand or other generic brands a product must:

- Have proven bioequivalence
- Have the same quantity of active substance(s)
- Be in the same dosage form
- Have the same route of administration
- Have consistency and quality of the manufacturing process
- Have quality of the ingredients and the final product.[30]

In 2015, a systematic review examined the attitudes towards generic medicines held by lay people, doctors, and pharmacists. Colgan et al[31] identified concerns about the efficacy, safety, and quality of generic medicines, recommending further work on interventions to increase the acceptability of generic prescribing. In a study published in 2019, Yu et al[32] focused on potential explanations for differences which are occasionally observed or suspected in individual consumers upon switching from an originator brand of medicine to a generic brand of medicine. They also assessed clinician and consumer concerns about generic–generic medicine interchangeability. The authors concluded that differences in exposure to the drug were considered negligible in the investigated bioequivalence studies. Any differences in concentration were mainly due to the intra-subject pharmacokinetic variability of the active ingredient.

In a study investigating 12 years of bioequivalence data submitted to the Food and Drug Administration (FDA) in the United States of America (USA) it was shown that the average difference in absorption into the body between generic and originator brand formulations was 3.5%, which is comparable to differences between two different batches of an originator brand medicine.[33]

These studies demonstrate the small differences in bioequivalence between originator brand medicines and generic brand medicines.

Biological / biosimilar medicines

Biological medicines, including biosimilar medicines, contain one or more active substances that are derived from living cells or organisms.[34]

The TGA define a biological[35] as:

- A thing made from, or that contains, human cells or human tissues, and that is used to
    - treat or prevent disease, ailment, defect or injury
    - diagnose a condition of a person
    - alter the physiological processes of a person
    - test the susceptibility of a person to disease
    - replace or modify a person's body parts
- Faecal microbiota transplant products

- A thing that comprises or contains live animal cells, tissues or organs.

For the purposes of this user guide and the list of medicines to be specified by brand in addition to active ingredient (LMBC), biological medicines are those defined and regulated by the TGA as biological medicines:

- Human cell or tissue-based products
- Products that comprise or contain live animal cells, tissues or organs
- Combination products (for example, cell therapy and medical device).

This definition specifically excludes for example, vaccines, plasma derivatives, and recombinant products, which are regulated by the TGA as therapeutic goods.[36]

A biosimilar medicine is a version of an already registered biological medicine (the reference medicine). Both the biosimilar and its reference medicine have the following similar core characteristics (demonstrated using comprehensive comparability studies):

- Physicochemical
- Biological
- Immunological
- Efficacy and safety.[37]

Most biosimilar medicines are likely to contain biotechnology-derived proteins as the active ingredient.

Minor natural variations in the molecular structure of biologicals (or micro heterogeneity) infers molecular composition can never be exactly replicated, even between different batches of the same brand. For biosimilar medicines that have been assessed by the TGA to be bio-equivalent, these variations have been deemed not to affect therapeutic equivalence.[38] For guidance overseeing biosimilar use in Australian hospitals refer to the Council of Australian Therapeutic Advisory groups' publication.[38] For practitioners in primary care the *Australian Medicines Handbook* provides guidance on prescribing biosimilar products.[39] A biosimilar should not be substituted for another brand of biological medicine unless therapeutic equivalence has been proven.

TGA assess the reference and biosimilar brands of biological medicines for therapeutic equivalence. The PBAC makes recommendations about the substitutability of brands on the PBS based on TGA advice on therapeutic equivalence. Therefore, when a biological is first prescribed it is entirely appropriate to select the therapeutically equivalent biosimilar.

Special considerations

Cytotoxic chemotherapy should be prescribed by active ingredient consistent with PBS legislation. In addition, dose-specific prescriptions must be prepared with the amount of active ingredient(s) needed for a single infusion or injection using milligrams or other relevant units of measure. This is in line with guidance on the Efficient Funding of Chemotherapy (EFC) arrangements.[40,41] Whilst brand may be specified, PBS claims will be calculated based on the most efficient combination of vial sizes offered across all brands.

This is particularly important if the biosimilar is a more cost-effective choice. However, there is no evidence to support uncontrolled switching between brands once treatment is established. Therefore, the biologicals and biosimilars should be described by brand in addition to active ingredient to support consistency and monitoring of care.

Policies on medicines interchangeability

International perspective

An overview of practice in different countries published in Norway in 2006 concluded that active ingredient prescribing is likely to contribute to increased consumer safety because there will be a correlation between the medicine name on the prescription and the name of the active ingredient in the medicine that the pharmacy dispenses.[42]

Interchangeable or medicines substitution resources already exist in a number of countries. The extent to which active ingredient prescribing is obligatory or mandatory varies. For example, in Europe active ingredient prescribing is not allowed in Austria, Denmark, Sweden or Serbia, but is obligatory in Albania, Armenia, Azerbaijan, Estonia, France, Greece, Italy, Lithuania, Malta, Portugal, Moldova, Romania, Russia, Slovakia, Spain, and Ukraine. In the UK, Ireland, and eighteen other countries across continental Europe, active ingredient prescribing is allowed but is not mandatory.[3]

A principal factor in stimulating generic medicines use in the UK has been teaching medical students to prescribe by INN in British medical schools. In 2017, 83.7% of all prescription items were prescribed by INN in England.[43] The UK NHS developed generic prescribing guidelines in 2013, and were updated in 2019, to include when medicines should be prescribed by brand name.[44] The Health Products Regulatory Authority in Ireland published an updated Guide to Interchangeable Medicines in 2018.[45]

In the USA, the FDA publishes the *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book) that contains therapeutic equivalence evaluations for approved multisource prescription medicines. This serves as public information and advice to state health agencies, prescribers and pharmacists to promote education in appropriate medicine selection and to foster containment of health care costs.[46] The companion publication, *Background Information: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations* (Purple Book)[47], lists biosimilar and interchangeable biological products by the reference product for which biosimilarity or interchangeability has been demonstrated.

In Ontario, Canada the Ontario Drug Benefit Formulary/Comparative Drug Index includes a guide to medicine interchangeability.[48]

In New Zealand, the Health Quality & Safety Commission publishes guidelines for the application of Specific Brand Advice within prescribing software packages.[49]

Negative perceptions held by doctors and pharmacists are likely to be barriers to wider acceptance of generic and biosimilar medicines, as health professionals have a strong influence on consumers' decisions to use generic medicines. Researchers in the Netherlands identified that a significant proportion of lay people, doctors and pharmacists held negative perceptions of generic medicines, perceiving generics as less effective, less safe, inferior in quality and more likely to cause side effects compared to the reference medicine.[50] In a Belgian study exploring the options of Dutch-speaking general practitioners and pharmacists, participants accepted the concept of INN prescribing, but 88% stressed the importance of guaranteed treatment continuity, especially in the older, population with chronic health conditions, to prevent consumer confusion, medication non-adherence and erroneous use.[51]

Australian perspective

The Australian Government is committed to increasing the uptake of generic and biosimilar medicines. This is to decrease out of pocket expenditure for consumers, to improve the financial sustainability of the PBS, maintain prescriber and consumer choices regarding medicines and to support medicine accessibility without compromising safety and efficacy. Active ingredient prescribing increases the understanding and knowledge of the active ingredients in medicines and assists to educate and familiarise prescribers, pharmacists, and the community regarding the availability and acceptability of lower cost medicines.

In the 2018–19 Federal budget, the Australian Government pledged to improve access to medicines by further encouraging greater use of generic and biosimilar products. Support for generic and biosimilar education and uptake will deliver cheaper medicines through faster and greater price reductions to medicines subsidised through the PBS, because of the price disclosure policy.[10] Measures are being implemented to continue the biosimilar medicines awareness campaign established as part of the PBS Access and Sustainability Package announced in 2015.[6] These measures include education and training for health providers to increase clinician, pharmacist, and consumer support for generic and biosimilar medicines. It is expected that increased uptake of generic and biosimilar medicines will provide increased incentives for applications of these products for TGA approval, which will support a more robust supply of medicines.

Consumers have been offered and have been able to select between different brands for a range of medicines through the PBS and RPBS for many years in Australia. Under Australia's Brand Substitution Policy (1994), pharmacists are able to substitute generic or biosimilar medicines, determined by the TGA to be therapeutically equivalent, to the originator/reference brand without seeking further advice from prescribers. Prescribers can determine if a particular brand is clinically indicated by annotating the prescription 'brand substitution not permitted', as part of shared decision making with the patient. At the time of dispensing, the consumer retains the right to choose the brand they receive.

Where there are two or more brands of the same medicine on the PBS or RPBS, the Australian Government subsidises each brand to the same amount. In some instances, a pharmaceutical company will charge an additional fee to patients for their brand of medicine. If a more expensive brand is supplied the price difference is paid by the consumer at the request of the drug company and is paid to the supplier not to the Australian Government.[52] This cost is in addition to the patient's co-payment, increasing the patient's out of pocket expenses for medicines and potentially impacting affordability of prescribed treatment regimens. This cost is known as the brand price premium.

Conclusions

Best practice guidance for active ingredient prescribing is provided to support safe and quality use of medicines.

Prescribing using the active ingredient name is safe in the majority of prescribing situations where the branded or unbranded originator and generic or biosimilar medicines are considered therapeutically equivalent. The exceptions to this approach are limited but important.

Recommendations

For prescribers

Recommend that prescribers:

- Adopt the guidelines for active ingredient prescribing into their practice
- Become familiar with the active ingredient prescribing principles and List of Medicines for Brand Consideration to understand when prescribers should consider specifying the brand name on a prescription, depending on the clinical need of their patient
- Advise and counsel patients about the use of active ingredient terminology to enhance communication and health literacy
- Encourage the uptake of generic and biosimilar medicines when appropriate by providing assurances and information regarding their bioequivalence and suitability
- Implement clinical prescribing software which conforms with PBS/RPBS requirements

For pharmacists

Recommend that pharmacists:

- Embrace active ingredient prescribing principles
- Become familiar with the active ingredient prescribing principles and List of Medicines for Brand Consideration to understand when prescribers should consider specifying the brand name on a prescription, depending on the clinical need of their patient
- Actively educate and counsel patients and the community about the use of active ingredient terminology to enhance communication and the health literacy of all
- Confirm with patients when substituting a generic or biosimilar medicine
- Encourage the uptake of generic and biosimilar medicines when appropriate by providing assurances and information regarding their bioequivalence and suitability
- Ensure patients and the community are informed regarding when it is important to use the same brand of medicine

For Australian Government

Recommend that the Australian Government:

- Reviews and updates the List of Medicines for Brand Consideration and List of Excluded Medicinal Items regularly (at least twice yearly)
- Ensure consumer and prescriber information relating to generic and biosimilar use are easily available and are kept up to date
- Maintain prescriber and patient choice principles

Appendices

Appendix A: Acknowledgements

Extensive stakeholder review of this user guide and associated lists (the List of Medicines for Brand Consideration and the List of Excluded Medicinal Items) addresses a range of issues relating to introduction of active ingredient prescribing.

The Commission acknowledges the contribution of the following stakeholders in providing feedback to inform these resources:

- Australian College of Midwives
- Australian College of Rural and Remote Medicine
- Australian Dental Association
- Australian Digital Health Agency
- Australian Medical Association
- Australian Nursing and Midwifery Federation
- Australian Primary Health Care Nurses Association
- Consumers Health Forum of Australia
- Department of Veterans' Affairs
- Generic Biosimilar Medicines Association
- Medical Software Industry Association
- Medicines Australia
- NPS MedicineWise
- Optometry Australia
- Pharmacy Guild of Australia
- Pharmaceutical Society of Australia
- Royal Australian College of General Practitioners
- Society of Hospital Pharmacists of Australia
- State and territory health departments
- Therapeutic Goods Administration

Glossary

Term	Definition
Active ingredient	The approved pharmaceutical ingredient in a product, substance or compound that produces its biological effect in the body. The active ingredient in the originator brand, Zyloprim, is allopurinol. The same active ingredient is present in the generic products Allosig, Progout, APO-Allopurinol etc. The active ingredient in the reference biological medicine Remicade, is infliximab. The same active ingredient is present in the biosimilar brands Inflectra and Renflexis.
'a' flagged PBS items	Denotes that brand substitution for these PBS items may be undertaken by pharmacists at the point of dispensing, with the patient's consent, without differences in clinical effect.
AMT reference set	Reference sets serve as a mechanism for creating subsets of content from AMT. Each of these reference sets is used to represent a set of AMT components for a specific purpose within a defined scope. For example, a reference set could contain the AMT concept IDs applying to medicinal items for brand inclusion identifying medicines for which prescribers should consider including the brand name on the prescription.
'b' flagged PBS items	Denotes that brand substitution with the originator brand for these PBS items may be undertaken by pharmacists at the point of dispensing without differences in clinical effect. However, it is not known if there is equivalence with the 'a' flagged PBS item.
Bioavailability	The rate and extent of absorption of the medicine.
Bioequivalence	Two medicines are bioequivalent if there is no clinically significant difference in their bioavailability.
Biological	A medicine whose active substance is made from, or contains, human cells or human tissues, or live animal cells, tissues or organs. This definition specifically excludes vaccines, recombinant products, plasma derived products, blood and blood components, haematopoietic progenitor cells used for haematopoietic reconstitution, in vitro diagnostic devices, and samples of human cell or tissue that are solely for diagnostic purposes in the same individual. Also known as biologic medicine.
Biopharmaceutics	The study of the ways that the physical and chemical properties of drug substances, drug products and routes of administration affect bioavailability. Biopharmaceutic studies of new medicines typically include the investigation of bioavailability, relative bioavailability and bioequivalence of different dosage forms or formulations, and the effect of food or antacids on their bioavailability.

Term	Definition
Biosimilar	A biosimilar medicine is a highly similar, but not identical version of an already registered reference biological medicine. A biosimilar medicine has a demonstrable similarity in physicochemical, biological and immunological characteristics, efficacy and safety, based on comprehensive comparability studies as evaluated by the Therapeutic Goods Administration (TGA). The reference biological medicine and the biosimilar medicine are marketed under different brand names. Biosimilar medicines are generally marketed once the patent on the reference biological medicines has expired. Also known as similar biological medicinal products (European Union); similar biotherapeutic products (World Health Organization); subsequent entry products (Canada); follow-on products.
Brand name	The name given to a medicinal product by the manufacturer. The use of the name is reserved exclusively for its owner. May also be referred to as the trade name.
Drug	A drug is any substance that causes a change in an organism's physiology or psychology when consumed. All medicines are drugs, but not all drugs are medicines.
Generic brand / generic medicine	A generic brand is an additional brand of an originator or existing medicine. It contains the same active ingredient as the originator brand or existing medicine. A generic brand has its dosage form, strength, route of administration, quality and performance characteristics, and intended use, therapeutically identical to the originator brand medicine.
Immunogenicity	The ability of a molecule or substance to provoke an immune response in the body, such as hypersensitivity or an allergic reaction.
Interchangeability	If two or more medicines are considered interchangeable, the prescriber may choose to prescribe either of the medicines for a consumer to treat the same condition. However, the pharmacist must dispense as prescribed. This generally occurs between two different medicines, rather than brands or biosimilars of the same medicine.
Medicines	Drugs within the scope of this initiative excluding bandages, dressings, diagnostic tools, food supplements and vitamin supplements. Also known as medications, medicinal products.
Microheterogeneity	Small variation in the chemical structure of a substance (as the amino acid sequence of a protein) that does not produce a major change in its properties.
Narrow therapeutic index	A narrow therapeutic index is where the range between effective dose and the dose at which adverse toxic effects are produced is narrow, and small variations in plasma concentrations can result in an insufficient therapeutic response or toxicity.[52]

Term	Definition
Pharmaceutically equivalent	Medicine that contains the same active ingredient(s), in the same dosage form and route of administration, in identical strength or concentration, and meets the same or comparable standards as the originator/reference brand.
Pharmacist	A person who is registered as a pharmacist under the Australian Health Practitioner Regulation Agency (Ahpra), which in association with the Pharmacy Board of Australia has deemed that person to be a pharmacist.
PBS prescriber	Doctors, dentists, optometrists, midwives, and nurse practitioners who are approved to prescribe PBS medicines under the *National Health Act 1953*.
Reference brand	The biological or generic medicine that was the first brand to market.
Substitution	The practice of dispensing one brand of a medicine instead of another brand of the same medicine at the pharmacy level without needing to go back to the prescriber, but in consultation with the patient. Substitutable brands include reference brands (sometimes referred to as the originator or innovator brand), generic brands and biosimilar brands. Substitutable brands have been tested and shown to be as safe and work as well as each other, and to produce the same health outcomes. If two or more medicines are considered substitutable, the pharmacist may dispense either of these medicines from the script, provided the prescriber has not indicated 'brand substitution not permitted', and they have permission from the patient. Substitutable medicines are marked in the PBS with an 'a' (a-flagged).
Switching	Decision by the treating medical practitioner to change between branded (reference) medications and their corresponding generic products, between generic products, or from a generic product to a branded medication during treatment.
Therapeutic equivalence	Medicines are therapeutically equivalent only if they are pharmaceutically equivalent and can be expected to have the same clinical effect and safety profile when administered to consumers under the conditions specified in the labelling.

Abbreviations and acronyms

ACSQHC	Australian Commission on Safety and Quality in Health Care
AIP	Active Ingredient Prescribing
AMA	Australian Medical Association
AMT	Australian Medicines Terminology
ARTG	Australian Register of Therapeutic Goods
Cmax	Maximum plasma drug concentration
CMI	Consumer Medicines Information
FDA	Food and Drug Administration (US)
INN	International Non-proprietary Name
LEMI	List of Excluded Medicinal Items
LMBC	List of Medicines for Brand Consideration
MA	Medicines Australia
MSIA	Medical Software Industry Association
NHS	National Health Service (UK)
NPS MedicineWise	National Prescribing Service MedicineWise
PBS	Pharmaceutical Benefits Scheme
PI	Product Information
RACGP	Royal Australian College of General Practitioners
RPBS	Repatriation Pharmaceutical Benefits Scheme
TGA	Therapeutic Goods Administration
Tmax	Time to maximum plasma concentration
TSH	Thyroid stimulating hormone
VRD	Vendor resource document
WHO	World Health Organization

References

1. Australian Government. Therapeutic Goods Act 1989. Latest 22 January 2019. Available from www.legislation.gov.au/Series/C2004A03952 [Accessed 2022 Nov 25].
2. FIP Foundation for Education and Research. Health Literacy – Medication literacy definition, 2017. Available from www.fipfoundation.org/health-literacy/medication-literacy-definition/ [Accessed 2022 Nov 25].
3. World Health Organization Medicines reimbursement policies in Europe, 2018. WHO Regional Office for Europe.
4. Gottlieb S. 2018: A year of Advancing generic products and policies, laying the foundation for 2019. Available from www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/2018-year-advancing-generic-products-and-policies-laying-foundation-2019 [Accessed 2022 Nov 25].
5. Generics360: Generic Drugs in Canada, 2016, Patented Medicine Prices Review Board February 2018. Available from www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/NPDUIS_Generics_360_2016_Report_E.pdf [Accessed 2022 Nov 25].
6. Health Quality and safety Commission New Zealand. Guidelines for the application of Specific Brand Advices within Electronic Systems. Available from www.hqsc.govt.nz/assets/Our-work/System-safety/Reducing-harm/Medicines/Publications-resources/Specify-Brand-Advice-Guidance-May-2019.pdf [Accessed 2022 Nov 25].
7. Japan Health Policy NOW. 6.2 Generic Drugs. Available from http://japanhpn.org/en/section-6-2/ [Accessed 2022 Nov 25].
8. NPS MedicineWise. Medicines and brand names, explained, 19 January 2017. Available from www.nps.org.au/consumers/medicines-and-brand-names-explained [Accessed 2022 Nov 25].
9. Therapeutic Goods Administration. Generic prescription medicines – Information for patients: Fact sheet. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/community-qa/generic-prescription-medicines-fact-sheet [Accessed 2022 Nov 25].
10. Straka RJ, Keohane DJ, Liu LZ. Potential clinical and economic impact of switching branded medications to generics. American J Therapeutics (2017); 24(3):e278–e289.
11. Dunne S, Shannon B, Dunne C, Cullen W. A review of the differences and similarities between generic drugs and their originator counterparts, including economic benefits associated with usage of generic medicines, using Ireland as a case study. BMC Pharmacology and Toxicology (2013);14:1.
12. Australian Commission on Safety and Quality in Health Care. National guidelines for on-screen display of medicines information. Sydney: ACSQHC; 2017. Available from www.safetyandquality.gov.au/our-work/e-health-safety/national-guidelines-screen-display-medicines-information [Accessed 2022 Nov 25].
13. Health Products Regulatory Authority. Guide to Interchangeable Medicines 1 June 2018. Available from www.hpra.ie/docs/default-source/publications-forms/guidance-documents/aut-g0115-guide-to-interchangeable-medicines-v5.pdf?sfvrsn=8 [Accessed 2022 Nov 25].
14. Specialist Pharmacy Service. Which medicines should be considered for brand-name prescribing in primary care? UK Medicines Information, November 2017. NHS England. Available from www.sps.nhs.uk/wp-content/uploads/2017/12/UKMi_QA_Brand-name_prescribing_Update_Nov2017.pdf [Accessed 2022 Nov 25].

15. Moe-Byrne T, Chambers D, Harden M, McDaid C. Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review. BMJ Open (2014);4:e004623.
16. Australian Digital Health Agency. Australian Medicines Terminology Fact Sheet. Available from https://www.healthterminologies.gov.au/library/amt-australian-medicines-terminology-fact-sheet.pdf [Accessed 2022 Nov 25].
17. Medical Software Industry Association Inc. PBS/RPBS Active Ingredient Prescribing Vendor Resource Document for Prescribing Software Developers, V 1.4 2019 Dec 6.
18. Van Bever E, Elseviers M, Plovie M, Vandeputte L, Van Bortel L, Vander Stichele R. Attitudes of physicians and pharmacists towards International Non-proprietary Name prescribing in Belgium. Basic Clin Pharmacol Toxicol (2015);116(3):264–72.
19. World Health Organization. International Nonproprietary Names (INN) for biological and biotechnical substances (a review). International Nonproprietary Names (INN) Programme, 2019.
20. Hassali A, Stewart K, Kong D. Quality use of generic medicines. Aust Prescr (2004);27:80–1.
21. Nelson S, Slordal L, Spigset O. Generic prescribing of drugs: Long overdue. Journal of Norwegian Medical Association (2006) Feb 9; 12694):441–3 (Article in Norwegian).
22. Davis JS, Barrett T, Harris L. Knowledge of proprietary and generic drug names among hospital prescribers; time to mandate generic prescribing? Internal Medicine Journal (2017);47:959–62.
23. Corre LJ, Hotham E, Tsimbinos J, Todd I, Scarlett G, Suppiah V. Assessment of patient understanding of their medicines: interviews with community dwelling older Australians. Inter J Pharm Prac (2018):26:568–72.
24. Wheeler AJ, Scahill S, Hopcroft D, Stapleton H. Reducing medication errors at transitions of care is everyone's business. Aust Prescr (2018);42:73–7.
25. Therapeutic Goods Administration. Mandatory requirement for an effective application, Version 4.1 June 2022. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/sites/default/files/mandatory-requirements-effective-application-prescription-medicines-180215.pdf [Accessed 2022 Nov 25].
26. Pharmaceutical Benefits Scheme. Symbols used in the schedule, 1 July 2019. Australian Government Department of Health and Aged Care. Available from www.pbs.gov.au/info/healthpro/explanatory-notes/section2/section-2-symbols [Accessed 2022 Nov 25].
27. The Australian Medicines Handbook. On-line, version last modified July 2022. Available from https://amhonline.amh.net.au/ [Accessed 2022 Nov 25].
28. WHO definition of generic. Generics and Biosimilars Initiative. Posted 24/02/2012. Available from http://gabionline.net/Generics/General/WHO-definitions-of-generics [Accessed 2022 Nov 25].
29. Therapeutic Goods Administration. Generic medicines. Prescription medicines: registration of new generic and biosimilar medicines. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/prescription-medicines-registration-new-generic-medicines-and-biosimilar-medicines [Accessed 2022 Nov 25].
30. Birkett DJ. Generics – equal or not? Aust Prescr (2003); 26(4):85–7.
31. Colgan S, Faasse K, Martin LR, Stephens MH, Grey A, Petrie KJ. Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review. BMJ Open (2015);5:e008915.
32. Yu Y, Maliepaard M. Interchangeability of generics – Experiences and outlook towards pharmacokinetics variability and generic-generic substitution. Clin Pharmacol & Ther (2019);105(2):292–4.

33. Davit BM, Nwakama PE, Buehler GJ, Conner DP, Haidar SH, Patel DT, Yang Y, Yu LX, Woodcock J. Comparing generic and innovator drugs: A review of 12 years of bioequivalence data from the United States Food and Drug Administration. Ann Pharmacother (2009);43(10):1583–97.
34. Australian Government Department of Health and Aged Care. Biosimilar medicines: the basics for health care professionals, March 2017.
35. Therapeutic Goods Administration. What is regulated as a biological. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/what-regulated-biological [Accessed 2022 Nov 25].
36. Therapeutic Goods Administration. What is regulated as a biological. Australian Regulatory Guidelines for Biologicals (ARBG), Version 3.0 January 2020. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/sites/default/files/what-regulated-biological.pdf [Accessed 2022 Nov 25].
37. Therapeutic Goods Administration. Prescription medicines: registration of new generic medicines and biosimilar medicines. Australian Government Department of Health and Aged Care. Available from www.tga.gov.au/prescription-medicines-registration-new-generic-medicines-and-biosimilar-medicines [Accessed 2022 Nov 25].
38. Council of Australian Therapeutic Advisory groups (CATAG). Overseeing biosimilar use. Guiding principles for governance of biological and biosimilar medicines in Australian hospitals. Version 3 – October 2021. Available from https://catag.org.au/wp-content/uploads/Guiding-principles-for-the-governance-of-biologics-and-their-biosimilars-in-Australian-hospitals-1.pdf [Accessed 2022 Nov 25].
39. Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook. 18th ed. Pp xii. Adelaide; 2017.
40. Services Australia. Efficient Funding of Chemotherapy (EFC) – section 100 arrangements. Australian Government, Available from www.humanservices.gov.au/organisations/health-professionals/topics/education-guide-efficient-funding-chemotherapy-efc-section-100-arrangements/31676 [Accessed 2022 Nov 25].
41. Pharmaceutical Benefits Scheme. Efficient funding of chemotherapy program, 2020. Australian Government Department of Health and Aged Care. Available from www.pbs.gov.au/info/browse/section-100/chemotherapy [Accessed 2022 Nov 25].
42. Nelson S, Slordal L, Spigset O. Generic prescribing of drugs: Long overdue. Journal of Norwegian Medical Association (2006) Feb 9; 126(4):441–3 (Article in Norwegian)
43. Policies and legislation. Generics and Biosimilars Initiative. Posted 16 April 2015. Available from http://gabionline.net/Country-Focus/United-Kingdom/Policies-and-Legislation [Accessed 2022 Nov 25].
44. Greater Manchester Health and Care Commissioning. Generic Prescribing Guidelines, Version 2.0 February 2019. NHS in Greater Manchester. [Accessed 2019 Sep 6].
45. Health Products Regulatory Authority. Guide to Interchangeable Medicines, June 2018. Available from www.hpra.ie/docs/default-source/publications-forms/guidance-documents/aut-g0115-guide-to-interchangeable-medicines-v5.pdf?sfvrsn=8 [Accessed 2022 Nov 25].
46. U.S. Food and Drug Administration. Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). Available from www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book [Accessed 2022 Nov 25].
47. U.S. Food and Drug Administration. Purple Book: Lists of Licensed Biological Products with Reference product Exclusivity and Biosimilarity or Interchangeability Evaluations. Available from www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or [Accessed 2022 Nov 25].

48. Ontario Ministry of Health. Ontario Drug Benefit Formulary/Comparative Drug Index. Ed. 43, 31 October 2022. Available from www.health.gov.on.ca/en/pro/programs/drugs/formulary43/edition_43.pdf [Accessed 2022 Nov 25].
49. Health Quality and Safety Commission New Zealand. Guidelines for the application of Specific Brand Advices within Electronic Systems. Reviewed 22 May 2019. Available from www.hqsc.govt.nz/assets/Medication-Safety/Other-PR/Specify-Brand-Advice-Guidance-May-2019.pdf [Accessed 2022 Nov 25].
50. Colgan S, Faasse K, Martin LR, Stephens MH, Grey A, Petrie KJ. Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review. BMJ open (2015);5:e008915.
51. Van Bever E, Elseviers M, Plovie M, Vandeputte L, Van Bortel L, Vander Stichele R. Attitudes of physicians and pharmacists towards International Non-proprietary Name prescribing in Belgium. Basic Clin Pharmacol Toxicol (2015);116(3):264–72.
52. Tamargo J, Le Heuzey J-Y, Mabo p. Narrow therapeutic index drugs: a clinical pharmacological consideration to flecainide. Eur J Clini Pharmacol (2015);71:549–67.