Biologics and biosimilars best practice

Guiding principles for the governance of biologics and their biosimilars in Australian hospitals

Version 3 – October 2021

CATAG
Council of Australian Therapeutic Advisory Groups

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TARGETED THERAPIES ALLIANCE

Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health through the Value in Prescribing bDMARDs Program Grant.

The Alliance is led by NPS MedicineWise and includes Arthritis Australia, Australia and New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network, Australian Rheumatology Association, Cochrane Musculoskeletal, Council of Australian Therapeutic Advisory Groups, Pharmaceutical Society of Australia, Quality Use of Medicines and Pharmacy Research Centre (University of South Australia) and Society of Hospital Pharmacists of Australia.

Report production: James Armstrong

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Executive summary

Judicious, appropriate, safe, and cost-effective use of medicines in a health service organisation requires a commitment to the overall governance of the medicines management system within the organisation.

For Australian hospitals the Council of Australian Therapeutic Advisory Groups (CATAG) recommends the governance of medicines be achieved via a Drug and Therapeutics Committee (DTC) or equivalent, and has described the roles and responsibilities of such committees in the 2013 publication *Achieving effective medicines governance. Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*.

Biologics are important in the management of many conditions but often come at significant financial cost. Following the patent expiry of a medicine, additional pharmaceutical manufacturers are able to produce and market that medicine, which results in price competition between manufacturers. In the case of biologics, the medicine produced by another pharmaceutical manufacturer is referred to as a biosimilar. The term biosimilar is used to reflect the unique molecular characteristics of biologics and the resultant specific regulatory evaluation that is applied to ensure comparability between the medicine produced by the original manufacturer, referred to as the reference biologic, and any subsequent biosimilars. Within this document, the term biologic is used broadly to encompass both the reference product and their biosimilars.

This publication, *Biologics and biosimilars best practice: Guiding principles for the governance of biologics and their biosimilars in Australian hospitals* (Version 3 – October 2021) (Guiding Principles), builds upon the previously developed *Overseeing biosimilar use. Guiding principles for the governance of biological and biosimilar medicines in Australian hospitals* (Version 2 – September 2016) (2016's Guiding Principles). CATAG has prepared these Guiding Principles to assist those responsible for the prescription, preparation, dispensing, administration and monitoring of biologics in Australian hospitals to achieve good governance and decision making in relation to the use of these medicines. These Guiding Principles may be relevant to community and private practice settings, however further consultation is required to investigate their applicability in these settings.

The guiding principles for biologics/biosimilars are:

Guiding principle 1. Biologics, as for all medicines, should be subject to good governance processes that are timely and based on the evaluation of evidence of safety, efficacy and cost-effectiveness.

Guiding principle 2. Across all aspects of a patient's healthcare journey, ensure the appropriate and safe documentation and communication of biological medicines, including active ingredient and, where appropriate brand name, including adhering to the principles of active ingredient prescribing.

Guiding principle 3. Switching programs, between a reference biologic and its biosimilar(s), or between biosimilars should be agreed by the Drug and Therapeutics Committee in conjunction with clinical teams and other stakeholders.

Guiding principle 4. At dispensing, either the reference brand or its biosimilar can be supplied when they have been determined to be substitutable and the selected brand is appropriately documented and communicated.

Guiding principle 5. Patients should be actively engaged in shared decision making when considering and receiving treatment with biologics, at initiation or switching.

These Guiding Principles should be considered in conjunction with other resources for DTCs or equivalent and medicine decision-making tools, such as CATAG's:

- *Achieving effective medicines governance. Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*;
- *Rethinking medicines decision-making in Australian Hospitals. Guiding principles for the quality use of off-label medicines*; and
- *Managing Medicines Access Programs. Guiding principles for the governance of Medicines Access Programs in Australian hospitals*.

Overview

Purpose

These Guiding Principles provide guidance for good governance and clinical decision making in relation to use of biologics in Australian hospitals. They contain guiding principles to:

- promote and support the safe, effective and consistent use of biologics;
- promote enhanced cost-effectiveness of biologics;
- provide guidance on implementing the use of biosimilars;
- promote prescriber confidence in using biosimilars;
- support a shared decision-making approach between the health professional and patient;
- encourage a nationally consistent approach;
- recognise the potential savings that can be achieved by the use of biosimilars.[1]

These Guiding Principles will assist those responsible for the prescription, preparation, dispensing, administration and monitoring of biologics in Australian hospitals. These Guiding Principles may be relevant to community and private practice settings, however further consultation is required to investigate their applicability in these settings.

Biologic

A biologic is a medicine whose active substance has a large, complex, molecular structure, which can only be made by or derived from a living organism (e.g. bacterium, yeast, human/animal cell line).[2] Biologics vary in complexity from small, highly purified proteins to more complex structures such as monoclonal antibodies.

Biologics include:

- peptide hormones and glycoproteins (e.g. insulin, human growth hormone, follitropin, filgrastim)
- immunological medicines (e.g. monoclonal antibodies and vaccines)
- other biological products, including polysaccharides (e.g. low molecular weight heparins).[3,4]

Biologics in this document encompasses both reference biologics and biosimilars.

Reference biologic

The term ‘reference biologic’ is used to refer to a biologic that is registered in Australia and where that registration was based upon a full regulatory evaluation of quality, safety and efficacy data.[3] This product is typically the first brand of that biologic available and as such may be referred to as the originator or innovator biologic.

Biosimilar

A biosimilar is a highly similar version of an already registered reference biologic that:

- has been demonstrated to be highly similar in physicochemical, biological and immunological characteristics, efficacy and safety, based on comprehensive comparability studies with the reference product; and
- has been evaluated by the Therapeutic Goods Administration (TGA) according to its guidelines and other relevant European Union (EU) guidelines adopted by the TGA.[3]

A biosimilar may also be termed:

- similar biological medicinal product (EU);
- similar biotherapeutic product (WHO); or
- subsequent entry products.[3,5]

Background

Introduction

Biologics provide highly specific and targeted therapy, in the management of many conditions, including rare or severe or chronic diseases but often come at significant financial cost. Following the patent expiry of a biologic, additional pharmaceutical manufacturers are able to produce and market that medicine, which with price competition between manufacturers, results in a reduction in the medicine price.

The availability of biosimilars in Australia has significantly decreased the cost of individual biologics and consequently could potentially:

- improve cost-effectiveness of biologics in various conditions;
- improve economic efficiencies;
- expand access to medicines via broader patient eligibility or broadening of approved and/or subsidised indications.

Medicines governance/oversight bodies and health professionals directly involved in the medicine management pathway need to carefully consider the clinical evidence, opportunities and risks associated with the introduction of biosimilars into clinical practice.

Biologics are inherently complex molecules, or mixtures of molecules. This complexity is a result of characteristics such as large molecular size, structure and post-translational modifications such as glycosylation.[2] These medicines are produced with the use of a living system (such as a microorganism or an animal cell line) with complex manufacturing processes and protocols, which are the proprietary information of the originator company. Although there is some within-product micro-heterogeneity, these variations are well-understood and controlled by the manufacturers.[6]

Biosimilars

The regulatory evaluation of biosimilars reflects the molecular complexity of biologics and the nature of their production process. A manufacturer of a biosimilar medicine must demonstrate the comparability of their product with the reference biologic. The TGA has adopted a totality of evidence approach to the regulatory evaluation of biosimilars in Australia. This totality of evidence approach takes into account detailed analytical comparison to the reference product in terms of:

- physicochemical characterisation – molecular structures and critical quality attributes (e.g. glycosylation);
- preclinical and clinical pharmacokinetic and pharmacodynamic data (e.g. in-vitro pharmacology, pharmacokinetics [phase I studies]); and
- clinical trials including clinical efficacy, safety and immunogenicity evidence (specifically designed phase III studies with pre-defined equivalence criteria based upon sensitive clinical endpoints).[6]

The process for evaluating biosimilars is described in the April 2018 TGA document, *Biosimilar medicines regulation*, version 2.2.[3]

The evaluation of biosimilars does not replicate the full range of studies that were conducted during the development of the reference product. Instead, the evaluation aims to demonstrate that there are no meaningful differences between the reference product and the biosimilar, such that the experience with the reference product can be reasonably applied to the biosimilar. On this basis, a biosimilar may be approved for indications, consistent with those of the reference product and which may be additional to those in which comparability studies were conducted; this is known as extrapolation of indications.

The TGA approach to extrapolation of indications has been adopted from the European Medicines Agency (EMA) Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, which states:

> "The reference medicinal product may have more than one therapeutic indication. When biosimilar comparability has been demonstrated in one indication, extrapolation of clinical data to other indications of the reference product could be acceptable but needs to be scientifically justified. In case it is unclear whether the safety and efficacy confirmed in one indication would be relevant for another indication, additional data will be required. Extrapolation should be considered in the light of the totality of data, i.e., quality, non-clinical and clinical data. It is expected that the safety and efficacy can be extrapolated when biosimilar comparability has been demonstrated by thorough physicochemical and structural analyses as well as by in vitro functional tests complemented with clinical data (efficacy and safety and/or PK/PD data) in one therapeutic indication."[7]

To date, evidence in the literature, including clinical trials and real-world studies across multiple different biologics and their biosimilars, demonstrates that similar outcomes can be expected in terms of efficacy, safety, and immunogenicity in a patient who is switched from the reference product to a biosimilar or between biosimilar brands.[8–11]

Guiding principles

These guiding principles assist health professionals and medicines governance/oversight bodies, such as Drug and Therapeutics Committees (DTCs) or equivalents, to provide good governance and decision making in relation to their use of biologics.

Guiding principle 1

Biologics, as for all medicines should be subject to good governance processes that are timely and based on the evaluation of evidence of safety, efficacy and cost-effectiveness.

Hospital or health service DTCs have a central role within their jurisdictions in providing appropriate governance regarding the approval of a biologic, its use, monitoring for outcomes and adverse effects, including unexpected adverse effects. Decision making and medicines management processes should be transparent and accountable, based on robust evidence of safety and efficacy, and be cognisant of the societal responsibility to prescribe in a cost-effective manner. To maximise efficient resource utilisation and equity of access, biologics (reference and biosimilar) should be evaluated and purchased strategically within the local health system.

Formulary listings and approvals for individual patient use should incorporate considerations that maximise cost-effectiveness, subject to local considerations such as storage, administration devices and associated patient education requirements, as well as consultations with the relevant medical specialists. DTCs should strive to provide transparency regarding the decisions related to the introduction of biologics. As per the *Achieving effective medicines governance. Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals* standardised processes for ongoing formulary and individual patient usage management should be developed for appealing unsuccessful applications.

Decisions about which product, the reference biologic or biosimilar, will be available at a hospital or health service organisation, should be determined by the relevant DTC, in consultation with relevant medical specialists. Protocols for indications of use and the order of use (treatment pathways incorporating both biologics and non-biologics) should be approved by the DTC. Formulary decision making should take into consideration the presentation of the biologic, including its administration device and the impact a change may have on patients.

If a biologic, the reference biologic or biosimilar, has not yet been approved by the TGA for a specific indication or sub-population, and is being proposed for off-label use, its use should follow the same principles as for all off-label medicines. Local evaluation by the DTC is required to fully consider the product in terms of evidence of safety, efficacy and cost-effectiveness before approval can be given for clinical use in hospitals. (See *Rethinking medicines decision-making in Australian hospitals. Guiding principles for the quality use of off-label medicines*).

The transfer of patient care between health professionals and health service organisations requires the communication of current, accurate and comprehensive medicines information to ensure optimal patient outcomes.[12] The communication and documentation of critical information is particularly relevant when a patient is receiving a biologic. This information should include details of the medicine including both the active ingredient and brand name of the product, to avoid unintended switching and confusion.

Pharmacovigilance is particularly important with the use of any biologic. There should be a patient-centred pharmacovigilance framework within each hospital or health service to monitor and report outcomes and any adverse effects associated with biological therapy. The pharmacovigilance framework should demonstrate a shared responsibility between medical professionals, pharmacists, nurses, patients, and the pharmaceutical industry.[13] In all health care settings, prescribers, other health professionals and patients all have a responsibility to identify, monitor and report any adverse or unexpected adverse effects, through Adverse Event reporting and via local procedures.

Clinical registries which incorporate biologics, may assist in pharmacovigilance to build confidence and establish experience beyond what is already known from clinical trials or anecdotal experience.[1] The Australian Commission on Safety and Quality in Health Care's *Framework for Australian clinical quality registries* provides national guidance on the development and implementation of clinical quality registries in Australia.

For general guidance on good medicines governance, refer to the following publications on the CATAG website, as well as relevant local policies:

- *Achieving effective medicines governance. Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*;
- *Rethinking medicines decision-making in Australian Hospitals. Guiding principles for the quality use of off-label medicines*; and
- *Managing Medicines Access Programs. Guiding principles for the governance of Medicines Access Programs in Australian hospitals*.

Guiding principle 2

Across all aspects of a patient's healthcare journey, ensure the appropriate and safe documentation and communication of biological medicines, including active ingredient and, where appropriate brand name, including adhering to the principles of active ingredient prescribing.

a. For prescribers, active ingredient prescribing is a requirement for eligible PBS (Pharmaceutical Benefits Scheme) and RPBS (Repatriation Schedule of Pharmaceutical Benefits) prescriptions.

This requires each medicine on the prescription to be prescribed by the active ingredient(s). Reference biologics and their biosimilars should be prescribed in line with active ingredient prescribing.

A prescriber may include a brand name, in addition to the active ingredient name for clinical reasons and/or patient safety.[14] It may be preferable to include the brand in the following circumstances: to avoid miscommunication between clinicians, to prevent selection error, and to ensure accuracy interpreting and dispensing the prescription.[14] This should occur on a case by case basis. The addition of the brand name should also be considered where administration delivery devices have different instructions for use. Consumer familiarity with one product is an important contributor to consumer compliance, medicines continuity or safety.[14] 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.[14]

b. For dispensing, administration and medicine governance, the active ingredient and brand name of the biologic, whether it is the reference product or its biosimilar, should be documented across a patient's healthcare journey.

Identification and traceability of biologics to the product-level (including if compounded), should occur across the patient journey (including transitions of care) and medicines management pathway, including dispensing, administration, adverse drug reaction reporting, procurement and storage. This is particularly important as more biosimilars enter the market. To reduce the risk of inadvertent switching and support continuity and monitoring of care, CATAG recommends that for biologics, both the active ingredient and brand name are recorded in medicine's documentation and communication. This documentation includes in best possible medication histories, medication reconciliation documents, administration lists, medication lists for patients, discharge summaries, My Health Record or at any other transition of care.

In public and private hospital settings, prescribing choices are 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.[14] If a hospital or health service stocks multiple brands of a biologic, either on an on-going basis or in contract transition periods, a DTC approved governance process is required to ensure accuracy is maintained in prescribing, dispensing, and administration of the medicine, to avoid errors and ensure traceability regarding the brand(s) a patient has received.[6]

At each dispensing, the dispensing pharmacist and consumer should have a conversation regarding the choice of brand to ensure continuity of treatment. Any switching should be a deliberate decision made in the context of the available clinical evidence. Recording of the brand name and batch number should occur at dispensing and facilitates the traceability of the medicine in the event of an adverse event. It is recognised that this is not yet routine and requires a practical solution, for example with the use of scanning technology.

See Appendix 1 for resources on active ingredient prescribing.

Guiding principle 3

Switching programs, between a reference biologic and its biosimilar(s) or between biosimilars, should be agreed by the Drug and Therapeutics Committee in conjunction with clinical teams and other stakeholders.

An organisation-wide switch may be considered, where use of the biosimilar supports sustainable health care or results in a significant cost advantage, compared to the reference biologic. If an organisation-wide switch is to occur, DTCs or their equivalents, informed by high-quality evidence, should work with clinical teams, decision makers and other stakeholders to agree on any switching programs, and a management plan for the switch to occur.[1]

As with all medicines, when making procurement decisions, consideration should be given to the potential impact switching may have on medication safety or on those patients on long-term therapy or using brand-specific administration devices.

As a general principle, balanced against other considerations, it is preferable that the frequency of switching of biological products is minimised. Frequent switching may confuse patients and their caregivers and increase the risk of medication errors. Patients should be involved in a shared decision-making process to switch, including as part of a managed program as per guiding principle 5.

When implementing a switch, treatment response in each individual patient should be monitored carefully, using established systems for monitoring disease activity.[1] A reported change in the patient's condition should be treated cautiously and not be immediately attributed to switching, particularly if the monitoring and reporting is based on subjective measures of disease control. Caution should be exercised when interpreting treatment response and other parameters, if switching occurs in the context of other concurrent therapy changes.

Real-world experience with switching has highlighted that patient perception is an important factor in influencing outcomes associated with switching, such that patients with a poor perception of biosimilars are at increased risk of experiencing the nocebo effect; that is a negative effect of a medical treatment that is induced by patients' expectations, and that is unrelated to the physiological action of the treatment.[15–17] Positive attitudes exhibited by health professionals and patient education providing evidence-based information on the equivalence between the reference and biosimilar brands in terms of quality, safety and efficacy are important factors that mitigate the risk of the nocebo effect.

See Appendix 2 for a template letter for medical staff or patients regarding switching.

Guiding principle 4

At dispensing, either the reference brand or its biosimilar can be supplied when they have been determined to be substitutable and the selected brand is appropriately documented and communicated.

Consideration of switching and substitution occurs after approval and registration of a biosimilar by the TGA. Biologics that are 'a' flagged on the Pharmaceutical Benefits Scheme (PBS), can be substituted at the pharmacy level, with another 'a' flagged brand, in consultation with and agreement of the patient, unless the prescriber indicates 'brand substitution not permitted' on the prescription.

Confusion arising from the availability of multiple brands of a biologic may occur at the point of prescribing, dispensing or administering the biologic. To avoid such confusion and avoid inadvertent or unintended changes in brand, along with ensuring pharmacovigilance and traceability, the DTCs in public hospitals should adopt a whole of health service approach to the management of individual biologics (as per guiding principle 3). DTCs should provide direction regarding the necessary documentation and communication of the biologic brand used to other prescribers (at all points in the medication management pathway), the patient and at transitions of care. The information given to the patient, along with who delivers the information, depends on several factors, relating to the patient, the chosen treatment and the health service organisation.[6]

In Australian public hospitals, substitution at the pharmacy level should only occur as part of a DTC policy that allows substitution at dispensing as part of the local management of biological medicines (see guiding principle 3). The development of any such policy should be in consultation with the relevant health professionals. The presentation of the substituted biologic including its administration device, compared to the previous biologic, should be taken into account when considering the choice of biologics to be listed on formulary or provided to an individual patient.

It is not mandated in Australia to contact the prescriber where equivalent brands are substituted and the prescriber has not indicated a need to dispense a particular brand. A proposed change of brand should be discussed with the prescriber in some circumstances, as part of good professional practice, for example when substitution of brands could result in confusion or have a negative impact on adherence.[18] In Australian public hospitals, the policy for appropriate documentation and communication of brand changes when substitution is made at the pharmacy level should be approved by the DTC.

Pharmacists should provide unbiased information and patients should be actively engaged in decisions regarding any proposed substitution[18] as per guiding principle 5.

Guiding principle 5

Patients should be actively engaged in shared decision making when considering and receiving treatment with biologics, at initiation or switching.

As with any medicine, it is important that patients are actively engaged in the treatment decision and any changes to their treatment are discussed (including any differences between therapies or substitutions).[1] As with all medicines, patients should be informed of the therapeutic options available (including the consequences of no treatment) and the potential benefits and harms of the various therapies. Prescribers and patients should be cognisant of the societal responsibility for medicines to be prescribed in a cost-effective manner which may include organisation-wide managed switching programs. Prescribers should consider brand availability and substitution at pharmacy/dispensing level, at the time of prescribing. Patients must be informed of the brand of the medicine dispensed and have the right to make an informed decision regarding the brand of medicine the patient will receive at a pharmacy level.

When discussing the choice of biologic (reference product or biosimilar) with a patient, health professionals need to be aware of the nocebo effect. The nocebo effect should not be underestimated and may occur when switching from the reference product to a biosimilar or when initiating treatment with a biosimilar. A patient's preconceptions and expectations should be thoroughly investigated and health professionals adopt strategies to minimise the nocebo effect. Strategies to minimise the nocebo effect include tailoring patient education to the individual, adequately explaining and educating the patient about the medicine, providing balanced, evidence-based information, explicitly discussing the possibility of the nocebo effect, and positive framing, which places emphasis on the benefits from therapy instead of instilling negative preconceptions.[19–21] See Appendix 3 for link to nocebo resource.

The administration device (e.g. pre-filled syringes, pens or pumps) can play a significant role in patient acceptability of a medicine and thus affects patient adherence and potentially patient outcomes. When considering the appropriate brand, the usability and acceptance of the administration device must be taken into account.[5] Appropriate information and education with regard to administration devices should accompany consideration and supply of the biologic.

Written information, such as the Consumer Medicine Information (CMI) leaflet, should be available to promote patient understanding.

In addition, patients should be familiar with their preferred brand of medicine, to avoid inadvertent multiple switching and treatment continuity.

See Appendix 3 for information for patients.

Appendices

APPENDIX 1: Active ingredient prescribing resources

Resources

- PBS/RPBS information on active ingredient prescribing
- NPS MedicineWise 'hub' for active ingredient prescribing
- Australian Commission on Safety and Quality in Health Care resource page for active ingredient prescribing:
  - *Active ingredient prescribing – User guide for Australian prescribers*
  - List of Medicines for Brand Consideration (LMBC).

APPENDIX 2: Biosimilar medicines switch communication templates

Resources for Australian hospitals

- GBMA patient letter template
- Healthcare Improvement Scotland. *Biosimilar Medicines: A National Prescribing Framework template*.

Example of a letter to medical staff

Dear [**doctor's name**],

Managed introduction of biosimilar [active ingredient]

We are planning to introduce biosimilar [**active ingredient, brand name**] across the organisation and anticipate a wholesale switch from [**reference biologic brand**] to [**biosimilar brand**] within the [**Hospital or Health Service**] in [**date**].

Increasing the use of biosimilar medicines within the [**Hospital or Health Service**] is expected to deliver significant cost-savings to the organisation,

The Therapeutic Goods Administration (TGA) considered [**biosimilar brand**] to be a biosimilar of [**reference biologic brand**]; and the Pharmaceutical Benefits Advisory Committee (PBAC) considered that all PBS-listed brands of [**active ingredient**] are substitutable.

Please see attached information on biosimilar [**active ingredient**] from the Australian Department of Health.

Patient education will begin in as soon as it is practical, and we anticipate dosing with the biosimilar in [**date**].

An electronic template is available for download at: www.catag.org.au.

Example of a memorandum to medical staff

To: Medical Staff: Specialty Medicine, [**relevant stakeholders**]

cc: Pharmacy Department

From: [**Director of Pharmacy**], [**Chair of DTC**]

Subject: Introduction of biosimilar [**active ingredient**]

What is happening?

There are currently [**x**] brands of [**active ingredient**] registered in Australia: the reference product ([**reference biologic brand**]) and the biosimilar ([**biosimilar brand**]).

The [**Hospital or Health Service**] is transitioning all patients to the biosimilar [**active ingredient**] product ([**biosimilar brand**]). The decision to introduce or switch to a [**biosimilar brand**] has been considered and supported by the medicines governance group, DTC or equivalent.

The registered indications, dosing, administration and PBS item codes are identical for the two products.

The Therapeutic Goods Administration (TGA) and Pharmaceutical Benefits Scheme (PBS) both consider that [**reference biologic brand**] and [**biosimilar brand**] are therapeutically equivalent.

How will it impact me?

- The change will commence on [**date**].
- All patients will be given biosimilar [**active ingredient**] ([**biosimilar brand**]) at their next dose, unless the order clearly specifies that the patient must remain on [**reference biologic brand**].
- Existing PBS prescriptions can be used to supply [**biosimilar brand**].
- The Pharmacy Department keeps a record of the brand of [**active ingredient**] that each patient has received.

Additional queries or questions?

Please contact your site Pharmacy Department.

Printable information for prescribers, patients and carers is available from the Australian Generic and Biosimilar Medicines Association: www.biosimilarhub.com.au

An electronic template is available for download at: www.catag.org.au.

Example of a letter to a patient

Dear [**patient name**],

[**Hospital or Health Service**] is changing the brand of [**active ingredient**] we provide.

What does this change in brand involve?

Your medicine's active ingredient is [**active ingredient**]. The active ingredient is what makes the medicine work. This is not changing.

In the past you were given the brand [**reference biologic brand**].

From [**date**] you will be given a biosimilar [**active ingredient**] called [**biosimilar brand**].

Is the biosimilar the same as the medicine you were taking?

The [**biosimilar brand or active ingredient**] works in the same way as the original biologic medicine you were taking. The word biosimilar is used as manufacturers cannot create identical copies of the originator biological medicine.

The Therapeutic Goods Administration (TGA) has found it is as safe and effective as [**reference biologic brand**].

You can read more about biosimilar medicines in the attached information from the Australian Government Department of Health.

How will this change affect you?

Your treatment will not be interrupted by the change to the biosimilar brand of medicine we provide. Your medicine contains the same active ingredient and is equally effective and safe as the brand you were previously using.

Sometimes the device you use to deliver your medicine, such as a pen or syringe, may be different from the original biologic medicine you were using. Ask the pharmacist, nurse or doctor if you need any help learning to use the new device.

Why are we making this change?

The biosimilar [**biosimilar brand or active ingredient**] has been available for [**x**] years in Australia, since the patent for [**reference biologic brand**] expired.

Changing to a biosimilar can result in significant cost savings for hospitals. The costs saved through this change will mean more money can be invested into the health care for people in our community.

Please contact [**name, role, phone, email**] if you have any questions about this change.

An electronic template is available for download at: www.catag.org.au.

APPENDIX 3: Patient information

Information on biosimilars for patients may be found at:

- NPS MedicineWise. Understanding biological medicines, their biosimilars and the PBS:
  - Understanding biosimilars: For your patients
  - Avoiding the nocebo effect: talking to your patients about biosimilars
- Biosimilar medicines the basics for consumers and carers: Biosimilar medicines: the basics
- Biosimilar Hub:
  - Information on biosimilars for consumers and carers
  - Consumer/carer brochure: Information on biosimilar medicines (available in multiple languages)
  - Consumer/carer essentials factsheet: Essential information on biosimilar medicines
  - FAQs: Answers to the most frequently asked questions on biosimilar medicines.

APPENDIX 4: Glossary

TERM	DEFINITION
Adverse drug reaction	A drug response that is noxious and unintended and that occurs at doses normally used or tested in humans for the diagnosis, prophylaxis or treatment of disease, or for the modification of physiological function.[22]
Adverse event	An incident in which harm resulted to a person receiving healthcare.[22]
'a' flagging	The Pharmaceutical Benefits Advisory Committee (PBAC) determines if a biosimilar is substitutable with its reference biologic on the PBS, as indicated by '■a' immediately before the brand names of a particular strength of an item. This follows acceptance by the Therapeutic Goods Administration of evidence submitted by the sponsor of the biosimilar demonstrates the two products are either bioequivalent or therapeutically equivalent, or that justification for bioequivalence or therapeutic equivalence data is not required. In these circumstances it is expected that these brands may be substituted without the recipient experiencing differences in clinical effect.[23]
Biologic	A medicine whose active substance has a large, complex, molecular structure, which can only be made by or derived from a living organism (e.g. bacterium, yeast, human/animal cell line).[2]
Biologicals	Classified by the Therapeutic Goods Administration as human cell and tissue-based therapeutic goods, and live animal cells, tissues and organs.[24]
Drug and Therapeutics Committee (DTC)	The group assigned responsibility for governance of the medication management system, and for ensuring the safe and effective use of medicines in the health service organisation.[22] These may also be known as a medicines advisory committee, pharmacy and therapeutics committee, drug committee, drug and therapeutics advisory committee, formulary committee or quality use of medicines committee.
Formulary	A continually updated list of medications and related information, reflecting the clinical judgment of health professionals and other experts in the diagnosis, prophylaxis or treatment of disease and promotion of health. A formulary includes, but is not limited to, a list of medicines and medicine-associated products or devices, medication-use policies, important ancillary drug information, decision-support tools, and organisational guidelines.[25]
Health professional	For the purpose of these Guiding Principles, health professional includes nurses, midwives, medical practitioners, pharmacists and other registered individuals who deliver health care.
Health service organisation	A separately constituted health service that is responsible for implementing clinical governance, administration and financial management of a service unit or service units providing health care at the direction of the governing body. A service unit involves a grouping of clinicians and others working in a systematic way to deliver health care to patients. It can be in any location or setting, including pharmacies, clinics, outpatient facilities, hospitals, patients' homes, community settings, practices and clinicians' rooms.[22]

TERM	DEFINITION
Medicines management pathway	Describes nine (cognitive and physical) steps and three background processes, that should be involved in the best practice organisation of pharmaceutical products with the patient as a central component and involved in all steps. The nine steps include: decision on appropriate treatment and decision to prescribe medicine, record of medicine order/prescription, review of medicine order/prescription, issue of medicine, provision of medicine information, distribution and storage, administration of medicine, monitor for response, transfer of verified information.[26,27]
Nocebo effect	A negative effect of a medical treatment that is induced by patients' expectations, and that is unrelated to the physiological action of the treatment.[15,16]
Pharmacovigilance	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.[28]
Substitution	The practice of dispensing one brand of a biologic instead of the prescribed brand of the biologic when those brands have been endorsed as equivalent and substitutable by an appropriate body e.g. Pharmaceutical Benefits Advisory Committee. Substitutable medicines are marked in the Schedule of Pharmaceutical Benefits with an 'a' (a-flagged). Brand substitution by pharmacists is permitted without reference to the prescriber when the patient agrees to substitution and the prescriber has not indicated on the prescription form that 'brand substitution not permitted'.[23,29]
Switching	Changing between two brands of the same medicines. This could be changing from the reference biologic to biosimilar, or vice-versa or between biosimilars.

APPENDIX 5: How these Guiding Principles were developed

These Guiding Principles are a revised and updated version of 2016's Guiding Principles and reflect available evidence and contemporised according to current practice. The initial *Overseeing biosimilar use. Guiding principles for the governance of biological and biosimilar medicines in Australian hospitals* (Version 1 – February 2015) built on key concepts from previous work by the South Australian Medicines Advisory Committee and published in *Biosimilars – Guiding principles for the governance of biological and biosimilar medicines* (Version 1.0 – September 2014).

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A draft of these Guiding Principles was prepared by the CATAG Project Team for discussion and review by an Expert Advisory Group (EAG). The EAG was comprised of individuals with recognised expertise in a range of areas, such as therapeutics/quality use of medicines, evidence-based medicine use, medicines governance and patient issues. All comments provided by the EAG were discussed and agreed upon for incorporation into these Guiding Principles. During the development the document, CATAG member organisations undertook consultation, at various stages, with their wider constituents, including hospital DTCs, hospital pharmacy departments and clinicians. External consultation with key national organisations was also undertaken. A final version was approved by the EAG and CATAG.

These Guiding Principles were developed in consultation with and endorsed by representatives from the CATAG member organisations listed below:

- ACT Health
- NSW Therapeutic Advisory Group (NSW TAG)
- Northern Territory Drug and Therapeutics Committee
- Queensland Health Medicines Advisory Committee (QHMAC)
- South Australian Medicines Advisory Committee (SAMAC)
- The Tasmanian Medication Access and Advisory Committee (TMAAC)
- Victorian Therapeutics Advisory Group (VicTAG)
- Western Australian Therapeutics Advisory Group (WATAG).

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