Western Australia Drug Evaluation Panel

Statewide Medicines Formulary: Approach to Biosimilars

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Position Statement

In the next five years a number of high-cost biologic patents are due to expire. The WA Drug Evaluation Panel (WADEP) hopes to maximise the cost savings from biosimilars entering the market whilst ensuring patient care is not compromised.

Where the Therapeutic Goods Administration (TGA) have evaluated and considered a biologic medicine to be a biosimilar for a particular indication the WA Drug Evaluation Panel will:
- List on the SMF the lowest priced product, identified through the Pharmaceutical Tender process

Where a biologic is used for an indication not registered by the TGA (off-label) and there is a registered biosimilar, WADEP will:
- Determine whether it is appropriate to extrapolate the TGA’s evaluation of a biosimilar to the indication in question.
- On expert clinician advice and/or advocacy, consider listing a reference medicine where evidence of efficacy or safety shows a comparative difference or where evidence is lacking to justify the switch to a biosimilar.
- If extrapolation is deemed appropriate, list on the SMF the lowest priced product as identified through the Pharmaceutical Tender process.

WADEP will not consider a biological product to be a biosimilar if the TGA has not registered the product through the “Regulation of biosimilar medicines” process.

Patients may continue treatment with an alternative, non-formulary biologic, if treatment was started prior to a change in the listed biologic however patients beginning treatment must be started on the listed biologic.

For both the reference medicine and biosimilar, prescribers are required to write both generic name and the intended brand name on the prescription.
1 Introduction

The advent of biological medicine has changed the prescription medicine market as a step toward targeted, personalised therapy and has allowed significant gains in the treatment of many serious conditions including cancers, haematologic, auto-immune and neurological disorders.

Biologic medicines are large, complex molecules such as proteins or enzymes, produced from living cells. The creation of a biologic is highly sensitive and may produce different end results in the molecule from slight changes to the manufacturing process. Whilst a biosimilar may have the same encoding DNA sequence as the reference medicine, the complexity of the structure and its interaction with the patient means that it is not considered an identical version of the original product.

The use of biologic medicines in WA public hospitals cost over $60 million in the 2014-15 financial year, over 26% of the year's total expenditure on medicines\(^1\). With this cost in mind, an increasing health budget and cost containment becoming more challenging, the opportunity to use biologics in a competitive market should be taken advantage of within a framework that does not adversely affect the patient.

2 Definitions

**Biologics:** The TGA define biological medicines (biologics) as a therapeutic good derived from biological sources and are regulated as registered medicines. They include proteins and polysaccharides including:

- Vaccines,
- Products of the fermentation of recombinant cell-lines,
- Medicines derived from the fluids and tissue of humans and animals,
- Bacterially-derived proteins,
- Animal-derived polysaccharides like heparin.\(^2\)

**Biosimilar:** A biosimilar (also known as similar biological medicinal product, SBMP) is a version of a biological medicine that has demonstrable similarity in physicochemical, biological and immunological characteristics, efficacy and safety, based on comprehensive comparability studies.\(^3\) Biosimilars registered as such in Australia have been evaluated by the TGA according to the “Regulation of biosimilar medicines” guideline (see Section 10 Supporting Documents).

**Reference medicine:** The reference medicine, also known as the originator or innovator biologic, is the first of its type to be registered in any pharmaceutical market.

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1 Cost is based on gross expenditure from iPharmacy not including Commonwealth reimbursements, clinical trials or sponsor programs (i.e. compassionate access or medicine access programs).
3 Therapeutic Goods Administration (TGA), Evaluation of Biosimilars, Australian Government, Department of Health, TGA; 2013
3 Scope

This position statement applies to the evaluation and potential listing of biosimilar products on the Statewide Medicines Formulary (SMF) for use in WA hospitals and health services.

This position statement does not include the initial evaluation of a biologic for a new indication for inclusion on the SMF.

4 Evaluation and Listing Process

4.1 Evaluation by the Therapeutics Good Administration

To meet the requirements of a biosimilar for TGA registration in Australia the product must be evaluated through a more rigorous testing process than required for chemical generic products. This evaluation includes both clinical and laboratory-based comparability studies to determine the quality, safety and efficacy of each biosimilar individually.

The regulation of biosimilars by the TGA is outlined in the ‘Regulation of biosimilar medicines’ document and other overarching biosimilar guidelines. For the evaluation of biosimilars the TGA has adopted a number of European Union (EU) guidelines for data and assessment requirements including the European Medicines Agency (EMA) Guideline on Similar Biological Medicinal Products and the International Conference on Harmonisation (ICH) Comparability of Biotechnological/Biological Products (see Section 10 Supporting Documents).

4.2 Evaluation by the WA Drug Evaluation Panel

A biosimilar will be reviewed for listing on the SMF by WADEP when the product falls into one of the following two categories:

1. TGA registered biosimilars for approved indications
2. TGA registered biosimilars for non-approved (off-label) indications

Biologics that have not been approved by the TGA through the “Regulation of biosimilar medicines” process will not be considered a biosimilar by WADEP. In this case the biologic should be reviewed as a new medicine for efficacy, cost-effectiveness and safety according to the SMF Framework.

Throughout the evaluation process WADEP will invite and encourage prescribers to participate in the discussion and assessment of comparability. The Panel will take into consideration expert opinion backed by scientific justification for or against listing a biosimilar. If the biologic is used across a range of indications the Panel may conduct the review on an indication or medical specialty basis.
4.2.1 TGA registered biosimilars for approved indications

WADEP are confident that the TGA evaluation of biosimilars will be appropriate and rigorous. Where the TGA have approved a biosimilar, the product has been deemed to have comparable physicochemical characteristics, safety and effectiveness outcomes for that indication. Both the reference medicine and the biosimilar will be considered comparable by WADEP and the lowest priced product will be listed on the SMF.

4.2.2 TGA registered biosimilars for non-approved (off-label) indications

WADEP are aware that biologics are often used for off-label indications. Where a biologic is registered by the TGA for a different indication the Panel will assess the safety and effectiveness of the biosimilar for the indication in question. This assessment will follow the principles adopted by the TGA for the extrapolation of indications as outlined by the EMA “Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues” (see Section 10 Supporting Documents). Where biosimilar comparability has been demonstrated, extrapolation to other indications may be acceptable after an assessment of:

- Clinical experience
- Available literature
- Biological features of the disease
- The biologic’s mechanism(s) of action including target receptor specificity etc.
- Different populations
- Safety issues
- Immunogenicity and appropriateness of extrapolation

Where a biosimilar has been deemed comparable with the reference medicine the lowest priced product will be listed on the SMF. Where a biosimilar has been deemed not comparable, the reference medicine will be listed.

5 Purchasing Process

WADEP is not directly involved in the negotiation, purchasing or contract management of pharmaceuticals. This process is led by the Department of Finance and Office of the Chief Procurement Officer and when required, guided by a Client Reference Group (CRG). However, by listing a biosimilar on the SMF, WADEP will impact the choice of biologic at the purchasing level.

When a biosimilar is considered exchangeable with its reference medicine, the Contract Manager and CRG will be notified by WADEP. As shown in figure 1, biosimilars and the reference product will be moved from the non-competitive sole supply group (group A) to the competitive group (group B) and market competition is expected to impact the price of both products through the pharmaceutical tender process. The Tender Request document will include details of the interaction between WADEP, the SMF and the Pharmaceutical Contract.
The purchasing of biosimilars and reference medicines via the tender process does not exclude the purchasing of an alternative where required, such as for indications where only the reference medicine is appropriate.

6 Biologic Switching

One biologic product will be listed on the SMF and available for initiation in WA hospitals and health services for a particular indication.

Where a condition is being successfully treated with a biologic, the patient and their treating team may be reluctant to change products due to the small risk that treatment response may differ. However, treatment response and adverse effects of a biosimilar are likely to be comparable to the reference medicine and is assessed by the TGA through comparative testing in the “Regulation of biosimilar medicines” process. **WADEP encourage switching to the lowest priced, listed biologic where possible.**

6.1 Biosimilars on the PBS

Biologics listed on the SMF will be consistent with the product subsidised by the PBS when listed for the same indication.

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**Figure 1. WA Health pharmaceutical contract design**

**Figure 4: Segmentation of the Pharmaceuticals Product Market, page 23, Procurement Plan: Supply of Pharmaceuticals to Western Australian Public Health Care Unit, 2015**
The Pharmaceutical Benefits Advisory Committee (PBAC) made a recommendation to allow biologics to be substituted by clinicians and pharmacist if the biosimilar is found to be safe and effective equivalent treatment. The PBAC will make an assessment, case by case, on whether the biosimilar should be listed as substitutable (i.e. a-flagged).

Prescribers should note that ‘a-flagged’ biologics may be substituted by the pharmacist, in privately owned pharmacies following discussion with the patient unless the “Brand substitution not permitted” box is ticked. Currently there are no requirements for the prescriber to be contacted under the PBS framework.

6.2 Pharmacy substitution

Where a prescription is presented to pharmacy for the initiation of a biologic that is not listed on the SMF and an IPA has not been granted by the DTC, the pharmacist will notify the prescriber of the product change. The Pharmacy Department will only be required to contact the prescriber when the biologic is dispensed for the first time.

7 Prescribing a biologic/biosimilar

When prescribing a biologic the prescriber has the following responsibilities:

- Ensure the generic and trade name of the intended biologic is written clearly on the prescription,
- Be aware of which biologic product is listed on the SMF for initiation of treatment
- Know which product the patient is being treated with and have record of an IPA for an alternative, non-formulary biologic if applicable
- Play an active role in the pharmacovigilance of biologics/biosimilars by identifying, monitoring and reporting adverse events.

Indicating the generic and trade name on all prescriptions is of particular importance whilst the TGA review their policy on naming convention for biosimilars.

7.1 Second-line biosimilar therapy

Second-line biosimilar therapy applies to the use of a biosimilar following failure of treatment with the reference medicine or vice versa.

Due to the potential variability in patients, biologics and diseases there may be patients who do not respond or are intolerant to the listed product. In certain circumstances a trial of the alternative product, reference medicine or biosimilar, may be appropriate. However due to the low chance that the biosimilar may have a different effect, multiple trials of biologic products are unlikely to be cost-effective. In this case the prescriber must first apply for an IPA via their local DTC.

7.2 Prescribing of non-formulary products

Prescribers wanting to initiate a patient on a biologic which is not listed on the formulary must apply for an IPA via their local DTC.
8 Communication of changes

Changes in the listing of biologic on the SMF will be communicated in advance to prescribers and pharmacy departments. This information will be communicated via email to relevant Heads of Department (HODs) as soon as the listed product has been confirmed through the procurement process. Information will also be available on the Drug Formulary System (DFS), through iPharmacy and on the WADEP website (www.watag.org.au/wadep).

9 Approach to Biosimilars: Review

Over the coming years the understanding of biosimilars will continue to mature as jurisdictions around the world adopt its use. As such this document and the WADEP approach to listing a biosimilar on the SMF may need to be reviewed in order to best reflect local, national and international experience.

The TGA will continue to review the guideline on the Regulation of biosimilar medicines. Major changes likely to impact the WADEP listing and review process will be considered by the Panel as required.

Regular reviews will occur at a minimum every two years and evidence supporting either the comparability or non-comparability of biosimilars to reference biologics, in terms of both efficacy and safety will be considered. WADEP welcome clinician participation in the review process.

Safety and outcome monitoring will be important to inform the review and listing process for biosimilars. WADEP encourage clinicians to participate in research, audits and outcome reporting and believe that cost-savings from the adoption of biosimilars should be used for these purposes.

10 Supporting Documents


## 11 Document History

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