

11.04 Considering brand equivalence/substitution for biosimilar medicines

1 Purpose of Item

1.1 The PBAC was requested to consider;

- a revised approach to considering brand equivalence/substitution for biosimilar medicines; and
- supporting the Department to improve the efficient use of health technology assessment (HTA) resources in deciding that biosimilar submissions not be lodged via the Therapeutic Goods Administration (TGA)-PBAC parallel process.

Table 1: Comparison of the existing and proposed approach to considering brand equivalence

Existing
<ul style="list-style-type: none"> • Absence of data to suggest significant differences in clinical effectiveness or safety compared with the originator product • Absence of identified populations where the risks of using the biosimilar product are disproportionately high • Availability of data to support switching between the originator product and the biosimilar product • Availability of data for treatment-naïve patients initiating on the biosimilar product • Whether the Therapeutic Goods Administration has deemed a product to be biosimilar with the originator product
Proposed
<ul style="list-style-type: none"> • The Therapeutic Goods Administration has determined that the product is a biosimilar of the reference medicine as evidenced by ARTG registration documentation • Availability of supportive data relating to the effects of switching between the reference product and the biosimilar product/s • Practical considerations relating to substitution by the pharmacist at the point of dispensing. This includes strength of formulation, number of units per pack and maximum quantities between the brands, which may make substitution at the pharmacy level difficult from a practical perspective

2 Background and Current Situation

2.1 At the March 2015 meeting, the PBAC:

“indicated it would consider the marking of equivalent (i.e. ‘a’ flagging) in the Schedule of Pharmaceutical Benefits (the Schedule) of biosimilar medicines with their reference medicine on a case by case basis, taking into account the evidence presented in each submission to list a biosimilar medicine.”

2.2 When brand equivalence of biosimilar brands and their reference brands was discussed by the PBAC at its special meeting on 17 April 2015, the PBAC advised that biosimilar products would be considered to be brand equivalent, “where the data are supportive of this conclusion.”

“The PBAC advised that the following would be relevant considerations in

establishing that a biosimilar product could be ‘a’ flagged with the originator product:

- Absence of data to suggest significant differences in clinical effectiveness or safety compared with the originator product;
- Absence of identified populations where the risks of using the biosimilar product are disproportionately high;
- Availability of data to support switching between the originator product and the biosimilar product;
- Availability of data for treatment-naïve patients initiating on the biosimilar product;
- Whether the Therapeutic Goods Administration has deemed a product to be biosimilar with the originator product.

The PBAC considered that where a biosimilar product could not be ‘a’ flagged at the time of PBS listing, data should be collected to support ‘a’ flagging at a later point.”

2.3 No new biosimilar brands were considered by the PBAC in 2017. From 2018 onwards, more submissions for biosimilars are anticipated.

2.4 It has been three years since the PBAC developed the above considerations, thus it is timely that a review is conducted for the following reasons:

- There is greater certainty and awareness of the regulatory pathway of biosimilars both nationally and internationally. This is supported by the materials produced via the Biosimilar Awareness Initiative and publication of an information guide for healthcare professionals by the European Medicines Association (EMA)². Biosimilar education has been made available through various providers, including the Pharmaceutical Society of Australia (PSA).
- Greater awareness of the need to consider the totality of the evidence supporting biosimilarity without an exclusive focus on phase 3 clinical trials. It has been proposed that with advancing technology, the development of biosimilar medicines may not require phase III clinical trials if analytical, pharmacokinetic and pharmacodynamic comparisons allow conclusion of similar efficacy and safety³.
- There is now greater certainty around the naming of biological medicines. The TGA decided to maintain the existing naming convention for biological and biosimilar medicines, that is continue using the Australian biological name (without a specific identifier suffix) and strengthen adverse event reporting. In 2015, there was a proposal by the WHO INN expert group to implement an international biological qualifier (BQ) to all biological medicines including biosimilars. In mid-2017, the WHO decided not to proceed with a BQ and has recommended an opt-in process whereby a BQ is only used if considered by an authority to be desirable. Availability of a single global

scheme will avoid proliferation of separate and distinct national qualifier systems.

- There is widespread agreement from Australian specialty groups that biosimilar use for treatment naïve patients is appropriate, as demonstrated by the responses to consultation of the biosimilar uptake drivers.
- Greater international acceptance of pharmacy level substitution of biosimilars. In the US, language around substitution previously required that the prescriber "must be notified" of any allowable substitution made at a pharmacy. Since 2015, the language has been adjusted to say "communicate with", which allows for a notation in an electronic medical record, or "pharmacy record that can be electronically accessible by the prescriber".
- There has been no safety signals recorded in the EU since the registration of the first biosimilar in 2006 via the EMA biosimilar pathway⁴. Published international post-market experience of biosimilar medicines has demonstrated no difference in the safety or health outcomes of patients who have switched from the reference to the biosimilar agent, compared with remaining on the reference biological medicine. There are publications of studies investigating multiple switching between biosimilars and the reference brand which show no loss of efficacy or increase in safety issues.

3 PBAC Outcome

3.1 The PBAC advised that the following revised considerations will be used to inform the formation of advice on brand equivalence ('a' flagged) of biosimilars with the reference brand;

- The Therapeutic Goods Administration (TGA) has determined that the product is a biosimilar of the reference medicine as evidenced by ARTG registration documentation;
- Availability of supportive data relating to the effects of switching between the reference product and the biosimilar product/s; and
- Practical considerations relating to substitution by the pharmacist at the point of dispensing. This includes strength of formulation, number of units per pack and maximum quantities between the brands, which may make substitution at the pharmacy level difficult from a practical perspective.

3.2 The PBAC considered that the information regarding biosimilars has evolved significantly over the last 3 years. The PBAC acknowledged that according to the biosimilar regulatory pathway guidelines, TGA cannot make a determination of biosimilarity if concerning evidence exists relating to differences in efficacy or safety between the biosimilar and the reference medicines.

- 3.3 The PBAC agreed to remove from the original considerations (see paragraph 2.2) the first, second and fourth dot point for advising on brand equivalence between the biosimilar and reference brands, as these considerations are addressed by the evaluation conducted by the TGA.
- 3.4 The PBAC reflected on the uniqueness of biosimilars in that both TGA and PBAC are focussed on the same comparative dataset. The PBAC noted that the TGA determination of biosimilarity relies on the totality of the evidence supporting the biosimilar which includes comprehensive comparability studies during the preclinical assessment phase of biosimilar development. The PBAC therefore concluded that the outcome of the TGA Delegate's consideration were essential to the consideration of any biosimilar submission from the time of making the application.
- 3.5 The PBAC was of the view that based on the revised considerations, TGA-PBAC parallel processing should not be made available for proposed biosimilar medicines (i.e. yet to be determined by the TGA).
- 3.6 The PBAC noted that the parallel process arrangement was originally established within an agreement with Medicines Australia, so this change to the process will require consultation.

References:

1. Regulation of biosimilar medicines. Version 2.0 December 2015 Therapeutic Goods Administration
2. Biosimilars in the EU: Information guide for healthcare professionals 2017. Prepared jointly by the European Medicines Agency and the European Commission
<http://www.medicinesforeurope.com/wp-content/uploads/2017/05/HCP-guide-on-Biosimilars.pdf>
3. Weise M. Evolving landscape on data requirements to demonstrate biosimilarity – the EU perspective. 14th Annual Biosimilar Medicines Group Conference. 28–29 April 2016; London, UK
4. Pasina L, et al (2016) Biological agents and biosimilars: Essential information for the internist. *European Journal of Internal Medicine* 33:28-35