

**CONSUMER HEARING – BIOSIMILAR MEDICINES  
7 JULY 2015**

This consumer hearing on biosimilar medicines was convened by the Pharmaceutical Benefits Advisory Committee (PBAC), and was attended by representatives of the following groups;

Consumer organisations

Arthritis Australia  
Consumers' Health Forum  
Crohns and Colitis Australia  
Diabetes Australia  
Lymphoma Australia

Clinical groups

Australian Rheumatology Association  
Gastroenterological Society of Australia  
Haematology Society of Australia and New Zealand  
Medical Oncology Group of Australia  
Royal Australasian College of Physicians

Council of Australian Therapeutic Advisory Groups  
National Prescribing Service

Industry groups

AusBioTech  
Generic Medicines Industry Association  
Medicines Australia  
Pharmacy Guild of Australia

Department of Health

Pharmaceutical Benefits Division  
Therapeutic Goods Administration (TGA)

Introduction

This consumer hearing followed the Minister's 13 March 2015 announcement that the PBAC has begun holding consumer hearings prior to each PBAC meeting. The first of these hearings preceded the March 2015 PBAC meeting. Consumer hearings are an opportunity for consumer groups to be heard directly by the PBAC. The views presented contribute an important part of the information which the PBAC takes into consideration in its deliberations. Hearings are also an opportunity for attendees to gain an understanding of the factors and issues which the PBAC must consider when making a recommendation or providing advice.

This consumer hearing occurred in the context of the PBAC consideration of Basaglar<sup>®</sup> (insulin glargine), a biosimilar to Lantus<sup>®</sup> at its March 2015 meeting; the PBAC consideration of biosimilar subsidy in general at its April 2015 special meeting; and prior to PBAC considering, at its July 2015 meeting, Inflectra<sup>®</sup> (infliximab), a biosimilar to Remicade<sup>®</sup>.

Opening remarks

Professor Andrew Wilson, the PBAC Chair, welcomed attendees to the hearing. He highlighted that the purpose of consumer hearings is usually to allow the PBAC to hear from patient groups who have an interest in a drug that is being considered at the subsequent PBAC meeting. In this case, given the high level of interest regarding issues relating to the subsidy of biosimilar medicines, the hearing had been broadened to provide consumer organisations, clinical groups and industry representatives the opportunity to attend and

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allow the PBAC to hear directly some of the broader views which PBAC should consider in its deliberations.

The PBAC which was established under the *National Health Act 1953* (the Act) has two broad roles: firstly, to recommend to the Minister which drugs and medicinal preparations should be listed on the PBS, and secondly, to provide advice at the request of the Minister on other matters relating to the PBS. It is in this second context, that the PBAC is considering both the listing of specific biosimilar medicines and providing advice on some of the policy issues relating to the subsidy of biosimilars through the PBS.

Biosimilars are copies of biologic medicines. However, because of both the complex nature of biologics and the way they are made, even though biosimilar medicines act in the same way as the original patented biologic medicine, they may not be exactly the same.

There are over 65 biological medicines currently funded through the PBS:

- Expenditure on biologics has increased from approximately \$1 billion in 2009-10 to around \$2.3 billion in 2013-14 (an increase of 130 per cent).
- Of the ten most expensive PBS medicines in 2013-14, five were biologics with a combined cost to government of \$860 million in 2013-14.
- Currently only a modest portion of biosimilar medicines available overseas (in particular Europe) are on the market in Australia.
- All biosimilar medicines are assessed by the TGA for safety and efficacy in treating specific conditions.
- Before a biosimilar medicine can be listed on the PBS, it must have been deemed by the TGA to be as safe and effective as the reference biologic.

The budgetary implications of biologics will continue to grow into the future. The availability of biosimilar medicines may improve access to biologicals for more patients and will contribute to the financial sustainability of the Australian health care system.

Much of the recent public discussion about the PBS subsidy and use of biosimilar medicines has focussed on substitutability, that is, whether a pharmacist should be able to substitute biosimilar medicines for reference biologics at the point of dispensing, without reference to the prescriber. The process that permits this to happen on the PBS is called 'a' flagging, essentially a reference to the 'a' annotation against the PBS brand names indicating substitutability.

When making a recommendation for an 'a' flagged listing, the PBAC considers whether it is appropriate for a pharmacist to make such a substitution without reference to the prescriber. This consideration is additional to the PBAC's consideration of the efficacy and safety of the drug itself.

The prescriber can always prevent pharmacy level brand substitution by ticking the box on the prescription which indicates no substitution is permitted. If the box is ticked, it is an offence under the PBS legislation for a pharmacist to dispense a brand other than that specified on the prescription. If the box is not ticked, good pharmacy practice requires the pharmacist to consult with the patient before substituting. These features mean that there is no automatic or uncontrolled substitution in clinical practice in Australia.

At the April 2015 PBAC special meeting consideration of the PBS subsidy of biosimilar medicines, the PBAC considered the following principles to be relevant:

- Biosimilar medicines must be equivalent in efficacy and toxicity to the reference brand;
- The cost to the patient and to the Commonwealth is a factor in prioritising the use of a biosimilar medicine on the PBS;

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- In any prioritisation, patients should not have to pay more for a biosimilar brand than for a reference brand;
- PBS policies must not discourage competition; and,
- Education for prescribers and patients is critical to ensure that decisions are supported by the most reliable information.

The PBAC noted that when a reference medicine and its biosimilar medicine are PBS subsidised for a condition, there are three potential ways that a patient may receive initial treatment with a biological medicine:

- When receiving their first treatment with a biological medicine for this condition (i.e. treatment naïve);
- When transitioning from one biological medicine to a different biological medicine following failure of the first medicine. For example, moving to a different biological disease modifying anti-rheumatic drug (bDMARD) following failure of an earlier bDMARD for rheumatoid arthritis; and,
- When receiving a second or subsequent course of a biological medicine for relapse of an episodic condition.

In the first two situations, assuming that the TGA has assessed the biosimilar to be safe and effective, and the PBAC has assessed the biosimilar to be of equal effectiveness and safety as the reference biologic, it seemed reasonable to the PBAC that the patient could be commenced on either the biosimilar or reference biologic.

The PBAC also considered it to be reasonable that the patient could be commenced on either the biosimilar or reference biologic in the third, more complex situation where a patient is receiving a second or subsequent course of a biological agent for relapse of an episodic condition, and a biosimilar medicine is available.

At the April 2015 special meeting, the PBAC considered the circumstances under which 'a' flagging might be considered appropriate for biosimilar and their reference medicines. The PBAC clearly noted that any such recommendations would be made on a case-by-case basis, by which PBAC meant that being a biosimilar in itself, did not mean it could automatically be 'a' flagged.

The PBAC considered that, on a case-by-case basis, the following factors would be relevant considerations in establishing that a biosimilar medicine could be 'a' flagged with the reference (originator) medicine:

- There should be evidence that the biosimilar was safe and effective in treatment-naïve patients initiating on the biosimilar product;
- There should be no evidence (data) that there was significant differences in clinical effectiveness or safety compared with the reference (originator) medicine;
- There was no evidence that identified populations where the risks of using the biosimilar medicine was disproportionately high;
- The evidence should support equal safety and effectiveness when switching between the reference (originator) medicine and the biosimilar medicine; and,
- Whether the TGA has deemed a medicine to be biosimilar with the reference (originator) medicine.

The PBAC advised that biosimilar products would be 'a' flagged, and therefore suitable for substitution at the pharmacy level, where the data are supportive of this conclusion. The PBAC considered that when data supported biosimilarity but there was insufficient data to support 'a' flagging, it may be appropriate for data pertaining to 'a' flagging to be collected to facilitate future reconsideration.

The introduction of biosimilar medicines and substitutability should be supported by an education campaign designed to support and promote the use of these medicines, improving awareness and confidence for both health professionals and consumers to choose these products.

### Discussion

The following is a summary of issues which were discussed, broadly grouped into four areas:

#### Availability of biosimilar medicines on the PBS

- There is widespread acceptance from all sectors represented at the hearing that biosimilars are as safe and efficacious as their reference biological.
- There is widespread support for the availability and PBS subsidy of biosimilar medicines. It was generally acknowledged that price competition is an important mechanism for supporting a sustainable PBS.
- There is widespread support for treatment naïve patients who are commencing treatment with a biological medicine to be treated with the biosimilar, and for patients transitioning from one biological medicine to a different biological medicine to be treated with the biosimilar.
- There are mechanisms other than pharmacy level substitution which could drive the uptake of the use of biosimilar medicines. For example, tendering or physician driven substitution programs.

#### 'A'-flagging of biosimilar medicines and their reference biological medicine

- A robust process and policy with regard to 'a' flagging of biosimilar medicines and their reference biological medicine is required to build public confidence. The current system for handling generic drugs provides a frame of reference, but biosimilar medicines may require an adapted process.
- There is support for the PBAC's position to make case-by-case recommendations with regard to 'a' flagging of biosimilar medicines and their reference biological medicine. There is broad agreement that biosimilarity is not in itself sufficient to establish the safety of switching.
- The importance of evidence-based consideration was emphasised, as was the need to ensure the PBAC's rationale for 'a' flagging recommendations is clearly communicated in each case.
- Substitution of biologic medicines already occurs in Australian public hospitals.
- Some representatives considered that decisions about substitution should occur in the therapeutic relationship between the prescriber and the patient with the patient giving informed consent.
- Many, although not all, representatives were concerned that pharmacy level substitution would be automatic and may entail risks for patients. These risks were considered primarily related to the safety of switching between biosimilar medicines and their reference biological medicine, and not to the safety of biosimilar medicines in general. It was explained that the prescriber can prevent pharmacy level brand substitution by ticking the box on the prescription which indicates no substitution is permitted. If the "no substitution" box is ticked, it is an offence under the PBS legislation for a pharmacist to dispense a brand other than that specified on the prescription. There is Australian evidence that shows that pharmacists do not substitute when the "no-substitution" box is ticked.
- A number of representatives considered there is a lack of evidence and data on safety and efficacy related to multiple switches between a biosimilar medicine and the reference biologic medicine and that 'a' flagging should only occur when there was robust evidence available on multiple switches. Apart from data specific to switching between the biosimilar medicine and reference biologic, some representatives also showed a

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preference for data to be provided for each indication for which the biosimilar was proposed for subsidy rather than being extrapolated from one indication to another. However this position in relation to biosimilars is not consistent with providing expedited access to new drugs on the basis of early evidence, for example, in the context of a managed entry scheme.

- Some representatives expressed concern that substitution of particular drugs may entail use of a different drug delivery system, which could lead to confusion for self-administered drugs (e.g. insulin). The PBAC noted that this issue was not limited to biosimilar substitution, and considered that differences in drug delivery devices may be able to be managed in the course of the regular patient education and counselling on the use of the devices that is provided to patients by prescribers, pharmacists and other health care professionals. The PBAC noted it would consider these issues on a case by case basis.
- Prescribers are currently able to switch patients between the intravenous and subcutaneous routes of administration of some of the same brands of a biological drug, and the data provided in support of such switches may be less than that routinely provided for biosimilar versions of a biological drug, and less than would be sufficient to meet the expectations of some representatives in relation to biosimilars, even though the efficacy and safety issues are similar.
- There are different perceptions as to what constitutes a 'safety issue' or 'safety concern' in relation to substitutability. For some, this phrase is used to describe a concern about adverse events due to immunogenicity or toxicity, for others, a concern about a loss of efficacy of the drug, or a concern about not being able to track whether the biosimilar medicine or the reference medicine has been administered to a patient.

#### Education

- There is considerable negativity and misinformation about biosimilar medicines in the media.
- Public confidence in biosimilar medicines is paramount to the success of biosimilar uptake.
- Biologics and biosimilars are not part of patient speech, so there is a need to build patient understanding.
- Patient consent and consultation when substituting is critical.
- There is a need for a structured education plan to inform prescribers, pharmacists and patients about the use of biosimilar medicines.
- Professional societies could play a role in the development of policy and education in this area.

#### Tracking and monitoring

- Concerns were raised regarding the ability of prescribers to track use of a biosimilar and the reference biologic in a patient in order to assess if any emergent safety or efficacy issues were brand related.
- There is a potential role for the personally controlled electronic health record (PCEHR) system in this space.
- There is a desire for a clear naming convention of biosimilar medicines and their reference biologicals which would also help with tracking and data analysis.
- Establishing a registry was suggested as a means to enhance pharmacovigilance and post-market surveillance and monitor the broader clinical impact of biosimilars, particularly as there is limited experience with the use of these medicines. More collection of data would provide more timely understanding of utilisation patterns and patient outcomes.

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The PBAC Chair thanked representatives for their attendance and contributions to the consumer hearing, and committed to continuing to consult and engage with the community on the matters discussed.