



ARA ADVICE REGARDING THE USE OF BIOSIMILAR DMARDs

Background

- The Australian Rheumatology Association (ARA) welcomes the introduction of biosimilars to the Australian market. We recognise the potential for competition to reduce prices and provide savings to the government. The ARA would like to see any savings reinvested in health, including broadening access for patients who need these therapies and currently do not meet the stringent requirements for subsidised treatment.
- Biosimilars are not generic forms of the originator and should not be considered as such. Biologics (including biosimilars) are large complex heterogeneous molecules.
- Both can potentially provoke an immune response (immunogenicity) in a patient, which may have implications for safety and efficacy.
- Biosimilars are manufactured in different systems and may undergo post-translational changes that can differ from the innovator product eg glycosylation.
- The ARA strongly recommends an enhanced program of surveillance and pharmacovigilance for these agents and urges the government to commit to this. Such a program should include a process whereby electronic prescribing permits accurate collection of data, linked to the individual patient. Prescribers also need information on what is actually dispensed to the patient in real time.
- Decisions regarding interchangeability and extrapolation of indications should be based on evidence, and where evidence is not available, this should be made clear in all communications relating to these products.
- There is a growing body of evidence that transition from the originator drug to a biosimilar is safe and efficacious. The duration of these clinical trials is relatively short (around 1 year), and typically involves a single indication for which the originator drug is approved.
- There are limited data around repeated switches, and until further evidence is available, this practice should be avoided.
- Determination of interchangeability should be within the role of the regulator, the Therapeutic Goods Administration (TGA), rather than the payer (PBAC).

Pricing

The true price paid by the PBS for medicines is subject to commercial confidentiality and is not known to the public.

- The introduction of biosimilars to Australian market has relied on the same approach used in small molecule generic drugs. This has been very successful in reducing prices paid by government for these drugs. Introduction of a second brand of a medicine moves both versions from the F1 to F2 formulary, and triggers an automatic cut in the rebate paid by government to the pharmacy (currently 25%) for all brands.
- Application of an '**a**' flag to an originator and its biosimilar by the Pharmaceutical Benefits Advisory Committee (PBAC) means that the drugs can be substituted for each other at the pharmacy counter without reference to the prescriber.
- Free movement between the brands is designed to encourage competition.

ARA ADVICE FOR THE PRESCRIPTION OF BIOSIMILARS

- **Currently available rheumatology biosimilars- infliximab, etanercept, rituximab**
- **Currently approved, not yet in market- adalimumab (more than one biosimilar brand)**
- Infliximab, etanercept and adalimumab biosimilars have been deemed by the PBAC as interchangeable with the originator, and approved across all adult indications for the originator.
- The PBAC has deemed that biosimilars of the above-named originators can be **substituted for the originator at the pharmacy without reference to the prescriber: 'a'-flagging.**
- It is possible to override unauthorised substitution by ticking the '**Brand Substitution not permitted**' box at the top of the prescription and specifying a brand. The pharmacist must then dispense the brand you have written- **your choice of either the originator or the biosimilar-** otherwise legally they **MUST** contact you.
If you do not specify a brand AND tick the box, the patient may receive the originator or any approved biosimilar for the initial prescription and each subsequent repeats (**multiple switching**).
- **The ARA recommends prescribing by brand name and ticking the 'brand substitution not permitted' box to provide certainty about what has actually been dispensed to the patient.**
- Please note that prescriptions using the international nonproprietary name or INN (eg etanercept) are being rejected by Medicare. You will be asked to specify a brand.
- Be aware that delivery devices will vary between manufacturers and may cause confusion to patients and carers.
- The lack of a unique naming convention for biologics and biosimilars in Australia makes tracking, tracing and reporting of adverse events more difficult. Prescribing by brand name will help to identify the agent responsible for any adverse event.
- Encourage your patients to keep packaging, or photograph the actual medicine dispensed and its barcode and bring this to every consultation.
- **Biosimilar uptake drivers.**
 - i. **Biosimilar preferential prescription for treatment-naïve patients.**

Government is working with software vendors to embed reminders in prescribing software. The following note appears in the schedule: '**Biosimilar prescribing policy** : Prescribing of the biosimilar brand(s) (Brand Name®) is encouraged for treatment naïve patients. Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments'. **It is not compulsory for a treatment-naïve patient to be prescribed a biosimilar**, but it is government policy.
 - ii. **Lower authority driver- Streamlined authority.**

For a patient prescribed biosimilar etanercept, continuing subsequent prescriptions do not require paper/electronic submission to the HSD unit for endorsement. These prescriptions can be endorsed by the prescriber with a code at the time of consultation. Initial prescription and the first continuing prescription must be in written form, as it is now. We expect this driver to also become available for biosimilar forms of adalimumab, when they come to market. The government seeks to drive biosimilar use by reducing the burden of paperwork on doctors.

Definitions.

'a'-flagging- in the pharmaceutical benefits schedule, a designation that indicates that brands have been deemed equivalent by the PBAC, and can be substituted at the pharmacy counter without reference to the prescriber. According to the PBS, 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 Therapeutic Goods Administration. It would thus be expected that these brands may be swapped without differences in clinical effect. This designation is applied by the PBAC.

Interchangeability- The capacity to be able to change one biological medicine for another similar biological medicine where that replacement has been shown to achieve similar clinical effectiveness and safety standards.

Substitution- situation in which a biologic originator drug may be replaced by a biosimilar or vice versa if the drugs have been deemed as interchangeable by the PBAC, without input from the prescriber. I.e at the pharmacy counter.

Switching- a single transition from the biologic to a biosimilar or vice versa.

Extrapolation- occurs when a biosimilar is permitted to be used across indications for the originator, even when clinical trial data is not available for all of those indications.

Further reading.

1. Australian Government Department of Health. Biosimilars on the PBS. www.pbs.gov.au/info/general/biosimilars
2. Council of Australian Therapeutic Advisory Groups. Overseeing biosimilar use. Guiding principles for the governance of biological and biosimilar medicines in Australian Hospitals. V2, September 2016, CATAG www.catag.org.au
3. American College of Rheumatology Position Statement on biosimilars. May 2018. <https://www.rheumatology.org/Portals/0/Files/Biosimilars-Position-Statement.pdf?ver=2018-05-21-134110-000>
4. European League Against Rheumatism (EULAR) Position Paper on Biosimilar. Jan 2018 https://www.eular.org/public_affairs_position_papers.cfm
5. Bridges SL, White DW, Worthing AB, et al, on behalf of the American College of Rheumatology. The science behind biosimilars: entering a new era of biologic therapy. Arthritis Rheumatol 2018;70 (3):334-44.
6. Dorner T, Strand V, Cornes P et al. The changing landscape of biosimilars in rheumatology. Ann Rheum Dis 2016;75(6):974-82.
7. Dorner T, Kay J. Biosimilars in rheumatology: current perspectives and lessons learnt. Nat Rev Rheumatol 2015;11(12); 713-24.
8. Kay, J. Overcoming barriers to biosimilars in inflammatory arthritis. Nat Rev Rheumatol 2020;16(2):65-66.

Biosimilars Working Group
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