



Biosimilar medicines: the basics

for health care professionals



What are biological and biosimilar medicines?



How are biosimilar medicines developed?



Who chooses whether the biosimilar medicine is used?



Is there a difference in health outcomes between the biosimilar medicine and the reference biological medicine?



How is the safety of biosimilar medicines monitored (pharmacovigilance)?



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What are biological and biosimilar medicines?

Biological medicines, including biosimilar medicines, contain one or more active substances that are derived from living cells or organisms.

These medicines are used to treat serious diseases such as cancers, diabetes, rheumatoid arthritis, severe psoriasis, kidney disease, multiple sclerosis, and inflammatory bowel diseases such as ulcerative colitis and Crohn's disease.

Biosimilar medicines are highly similar, but not identical, versions of an already registered biological medicine (the reference biological medicine). This is because the inherent variability of the biological systems used in the manufacturing process means that the resulting product is also variable. No two batches of a biological medicine, including biosimilar medicines, are ever exactly the same (even from the same manufacturer).

For a biosimilar medicine to be approved, its structural variability must not be greater than the acceptable limits of batch variation for the reference biological medicine. All critical quality attributes (i.e. those important for the function of the molecule) must be highly similar.

Biosimilar medicines that are approved for marketing have been assessed to have no clinically meaningful differences and to be therapeutically equivalent to the reference biological medicine.

Biosimilar medicines are expected to deliver significant savings, which can be reinvested into other areas of the Australian health system and **expand access to biological medicines as they become more affordable.**

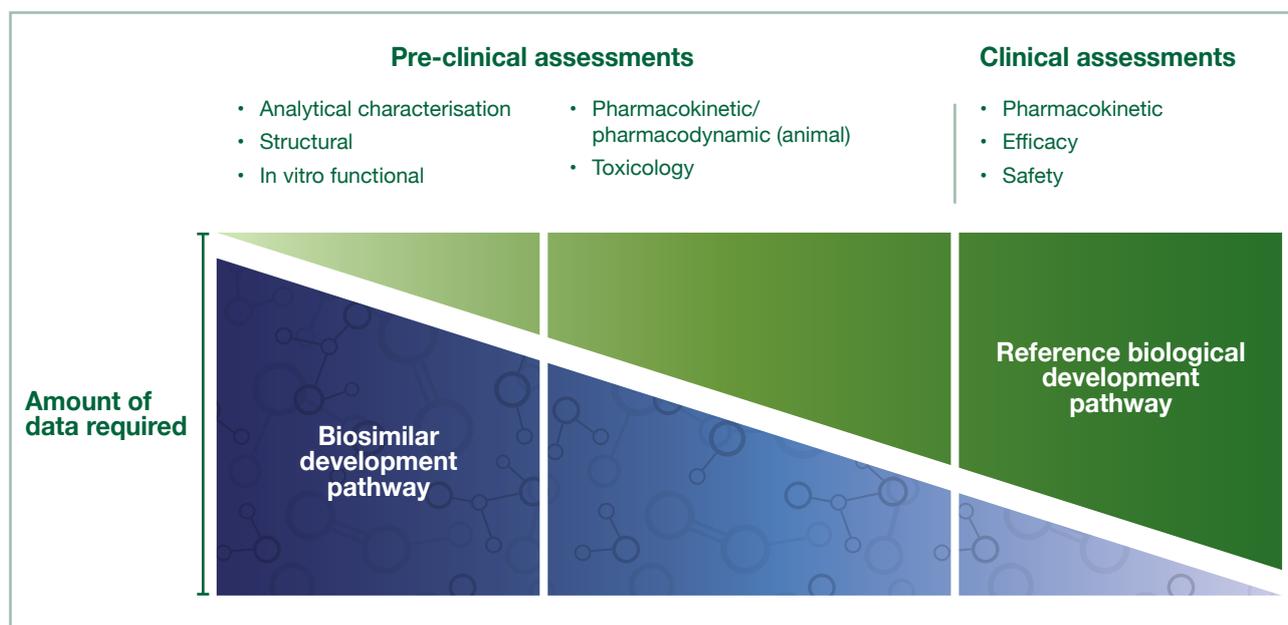
How are biosimilar medicines developed?

The development process varies between reference biological and biosimilar medicines:

- In reference biological medicine development, the majority of time and effort is spent in clinical studies that establish the clinical benefit of the medicine.
- In biosimilar medicine development, the majority of time and effort is spent in comprehensive analytical comparison studies that establish the similarity of the medicine to the reference biological medicine, because the clinical benefits have already been established.

As a result of these studies, it has been **determined that there are no significant differences in the critical quality attributes that affect safety, effectiveness or quality.**

Comparison of the development pathway of reference biological vs biosimilar medicines



Adapted from Bui et al (2015). Key considerations in the preclinical development of biosimilars. *Drug Discovery Today* 20(SI):3–15

Who chooses whether the biosimilar medicine is used?

The medicine used for treatment is a choice that is made by doctors in consultation with their patients. Health care professionals are encouraged to talk through these choices with their patients. The *Biosimilar medicines: the basics – information for consumers and carers* brochure is aimed at consumers and will help to answer common questions.

If one brand of medicine can be exchanged for another by the pharmacist, they are 'substitutable', which means pharmacists can substitute between brands in consultation with the patient but without needing to refer back to the doctor. Substitution between brands of biological medicines is considered by the Pharmaceutical Benefits Advisory Committee (PBAC) and recommended on a case-by-case basis.

Even if a medicine is substitutable, the doctor can tick the 'brand substitution not permitted' box when writing a prescription. If this box is ticked, by law the pharmacist cannot dispense a brand other than that prescribed.

In the public hospital setting, brand decisions are made by clinician-led committees and are based on the safety, efficacy and cost-effectiveness of the medicine. For more information, refer to the guiding principles from the Council of Australian Therapeutic Advisory Groups on the governance of biological and biosimilar medicines in Australian hospitals (www.catag.org.au/resources/#guidance).

Is there a difference in health outcomes between the biosimilar medicine and the reference biological medicine?

Biosimilar medicines that are approved for marketing have been assessed to have no clinically meaningful differences and to be therapeutically equivalent to the reference biological medicine. As such, they have similar health outcomes.

The table below outlines some of the questions that have been raised about biosimilar medicines.

Questions commonly asked about biosimilar medicines

Question	Response
Are there more adverse effects with the biosimilar medicine?	No. The incidence of adverse effects is not higher for biosimilar medicines than for the reference biological medicines. For a biosimilar medicine to be approved for use in Australia, it must have demonstrated to the Therapeutic Goods Administration (TGA) that it has the same safety profile, including the same incidence and severity of adverse effects.
Are there more immunogenic reactions with the biosimilar medicine?	No. The incidence of immunogenicity for biosimilar medicines is not higher than for the reference biological medicines. Immunogenicity data are assessed during the development and registration of all biological medicines, including biosimilar medicines.
Is indication extrapolation appropriate?	Yes. Internationally, indication extrapolation is allowed in all regions that have adopted biosimilar regulations. Indication extrapolation refers to the extension of the efficacy and safety data from a condition for which the biosimilar has been clinically tested to other conditions for which the health outcomes for the reference biological medicine have been established. Extrapolation of data is not a new concept and is based on sound scientific principles. Decisions about indication extrapolation are made by the TGA.
Will switching adversely affect patient outcomes?	No. Since biosimilar medicines have been assessed to be as safe and effective as the reference biological medicine, they also provide the same health outcomes. Published international post-market research has found no difference in the safety or health outcomes of patients who switched to biosimilar medicines and those who remained on the reference biological medicine.

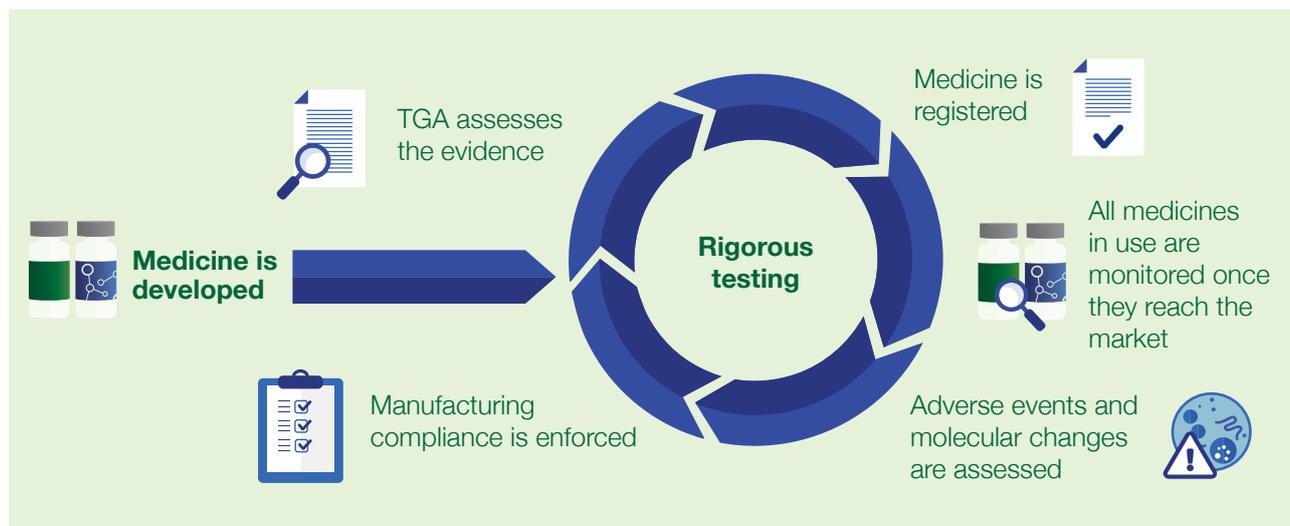
How is the safety of biosimilar medicines monitored (pharmacovigilance)?

Before any biological medicine is released to market, the manufacturer must develop a risk-management plan, which is assessed by the Therapeutic Goods Administration (TGA) as part of its approval assessment.

Once the medicine is on the market, the TGA continues to monitor its performance for safety, effectiveness and quality, with a particular focus on adverse effects. Pharmaceutical companies are required to report any adverse effects that they are aware of. Reports can also be made by health care professionals, consumers or carers.

The adverse reaction reports are placed in a database (the Australian Adverse Drug Reaction Reporting System), and the database is analysed regularly by the TGA for safety signals.

The TGA monitors the benefit–risk profile of medicines throughout the product lifecycle



Where can I find more information?

Detailed information for health care professionals is available on the Biosimilar Awareness Initiative webpage at www.health.gov.au/biosimilars.

Information available from the Therapeutic Goods Administration

- Product Information: www.tga.gov.au/product-information-pi
- How to report an adverse event of a medicine: www.tga.gov.au/reporting-problems

References

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4. Weise M, Bielsky M, De Smet K, et al (2012). Biosimilars: what clinicians should know. *Blood* 120:5111–5117.
5. Weise M, Kurki P, Wolff-Holz E, et al (2014). Biosimilars: the science of extrapolation. *Blood* 124:3191–3196.
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