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Biologics and biosimilars – a practical guide for pharmacists

This presentation has been developed in collaboration with the:

+TARGETED THERAPIES ALLIANCE

Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health through the Value in Prescribing bDMARDs Program Grant.

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Learning objectives

- Describe biologics and biosimilars
- Outline the role pharmacists play in the governance of biologics and biosimilars
- Recognise the importance of providing clear information throughout the patient journey
- Discuss the nocebo effect and what pharmacists can do to prevent this

Competency standards

Pharmacist competency standards* addressed include:

Standard 1.6.1 Collaborate to improve quality and safety across the continuum of care

Standard 3.1.3 Collaborate to develop a medication management strategy or plan

Standard 3.2.5 Provide counselling and information for safe and effective medication management

Standard 3.2.6 Facilitate continuity of care including during transitions of care

**National Competency Standards Framework for Pharmacists in Australia 2016*

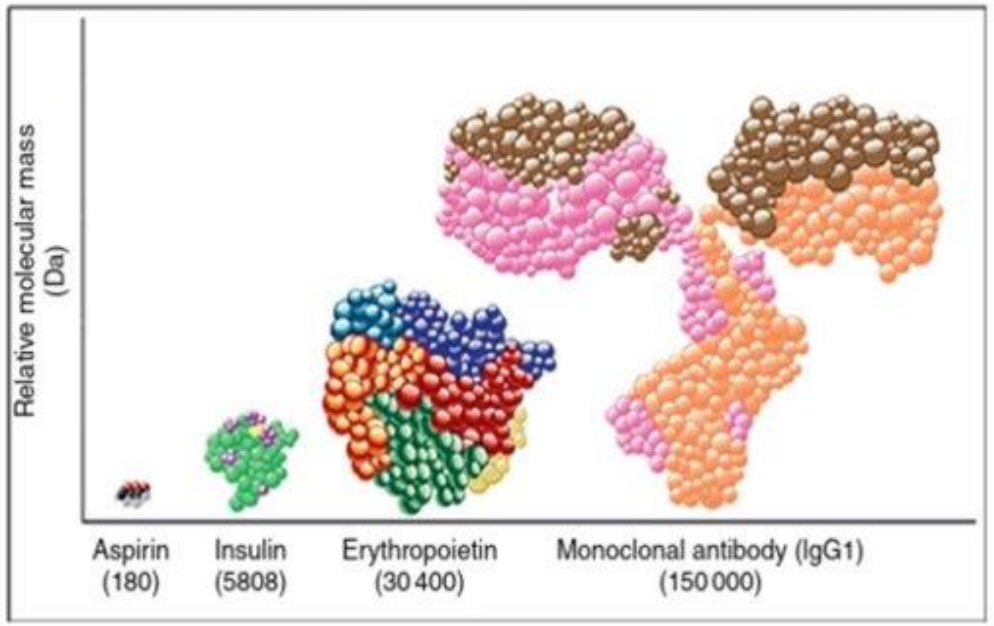
Accreditation

This activity has been accredited for 1 hour of Group-1 CPD (or 1 CPD credit suitable for inclusion in an individual pharmacist's CPD plan.

Accreditation number: S2021/49

Biologics

- Large complex molecules - usually proteins or protein containing fragments produced by or derived from a biological source such as living cells, rather being synthesized chemically



Relative molecular mass of small molecule and biologic drugs. *Source:* Mellstedt.

- Biologics include:
  - vaccines
  - recombinant hormones (insulin, somatostatin, erythropoietin)
  - enzymes, blood products, allergenic extracts
  - monoclonal antibodies (IgG) e.g. adalimumab
  - fusion proteins e.g. etanercept
  - antibody with drug conjugates e.g. trastuzumab with emtansine
  - human cells and tissues and gene therapies

- The first biologic (recombinant human insulin) was approved in 1982.

Reference biologic

- Refers to a biologic that is registered in Australia and where that registration was based upon a full regulatory evaluation of quality, safety and efficacy data

- Typically the first brand of that biologic available

Biosimilars

- Biological products that are found to be highly similar to the reference biologic product in the following characteristics:
  - Physiochemical
  - Biological
  - Immunological
  - Efficacy and safety based on comprehensive comparability studies
- A biosimilar is deemed to have no clinically meaningful differences to the reference product in terms of purity, potency and safety.
- While biologics have high rates of immunogenicity, immunogenicity profiles are similar across biosimilars

Why is this important?

Loss of exclusivity (LOE) and biosimilar entry timeline — LOE is approaching for many biologics, priming the market for more biosimilar entry.

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Organisational governance

- Decisions about which product will be available at a hospital or health service should be determined by the Drug and Therapeutics Committee (DTC) or equivalent in consultation with relevant medical specialists.

- Pharmacovigilance – particularly important with biologics

How you can help…

- Be alert for patients using biologics and identify
  - Indication
  - Brand, route and device used
  - Who manages their treatment? (public clinic, private consultant)
  - When the next dose is due
  - Do they have their own supply?
- Be aware of your organisation’s policy for continuation of existing therapy

Organisation wide brand switching

- Led by DTC (or equivalent) with clear management plan
- Consideration of safety, efficacy, cost-effectiveness and the potential impact for patients on long-term therapy
- Close involvement with key stakeholders (prescribers and clinical teams)
- Careful monitoring of treatment response of individual patients

How you can help…

- Provide information to prescribers and clinical teams about the change
- Ensure compliance with the new brand
- Support patients who are affected by the change

Prescribing

- Shared decision making process
- Complex PBS criteria
- Multiple switching

Dispensing and pharmacist substitution

- Biologics that are ‘a’ flagged on the Pharmaceutical Benefits Scheme (PBS), can be substituted at the pharmacy level, with another ‘a’ flagged brand
  - unless the prescriber indicates ‘brand substitution not permitted’ on the prescription

- In hospitals, pharmacist substitution should only occur under the guidance of hospital DTC policy

How you can help…

- If considering substituting brand
  - Consult with the patient
  - Check brand patient is currently on (if appropriate)
  - Consider previous switches
  - Consider negative impact on adherence
    - Confusion
    - Ability to use device

- Consult with the prescriber

Nocebo effect

- A negative effect of a medical treatment that is induced by patients' expectations, and that is unrelated to the physiological action of the treatment

- How you can help:
  - Positive attitudes/positive framing (emphasis on the benefits)
  - Patient education tailored to the individual - investigate patient preconceptions and expectations
  - Provide balanced evidence-based information on equivalence in terms of quality, safety and efficacy

Avoiding the nocebo effect: talking to your patients about biosimilars

- Patient perception is an important factor in influencing outcomes associated with the use of biosimilars. A patient's mindset can influence their symptoms and sense of well-being. If they have a poor perception of biosimilars, they are at an increased risk of experiencing the nocebo effect.
- The nocebo effect is when negative expectations of a treatment lead to negative outcomes, unrelated to the physiological action of the treatment.[1,2]
- It can arise from language barriers, online media as an information source, interactions with healthcare professionals, the setting in which a patient receives information, and other factors outside the control of healthcare professionals.
- Positive attitudes shown by health professionals and patient education are important factors that mitigate the risk of the nocebo effect.

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Documentation along the patient journey

- Document active ingredient and brand name at all stages of the patient journey
  - Medication history and reconciliation documents
  - Patient notes in dispensing software
  - Medication charts or administration lists
  - Transitions of care (i.e. patient medication lists, discharge summary)
- Ideally also record batch number at point of dispensing

Patient counselling & education

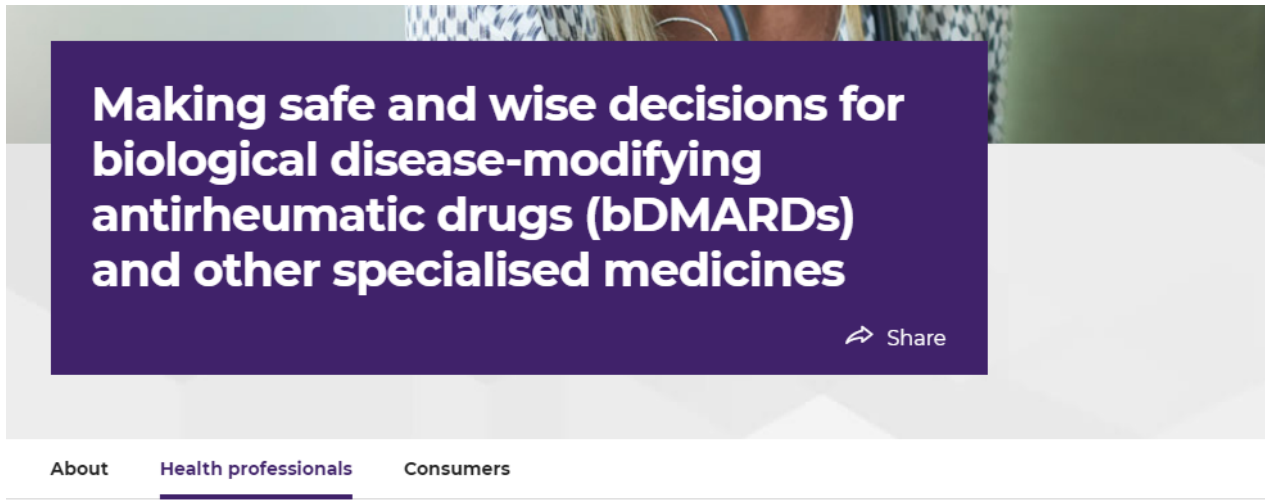
- Ensure patients are familiar with the brand they are taking
  - Photograph their packaging
- Provide clear information about a change in brand
- Storage requirements
  - Refrigerate
- Subcutaneous administration information
  - Bring device to room temperature
  - Rotate injection site
  - Sharps disposal

Patient counselling & education

- Adherence to therapy
  - Flares or loss of disease control
  - Don’t stop treatment without consulting doctor
  - Allow time for pharmacy to order in stock
- Devices are all slightly different
  - Make sure patient knows how to use their device

- Biologics are precious!

Resources



- NPS MedicineWise bDMARDs site
  - Biologics, biosimilars and PBS sustainability (article and podcast)
  - Understanding biosimilars: for your patients
  - Avoiding the nocebo effect: talking to your patients about biosimilars

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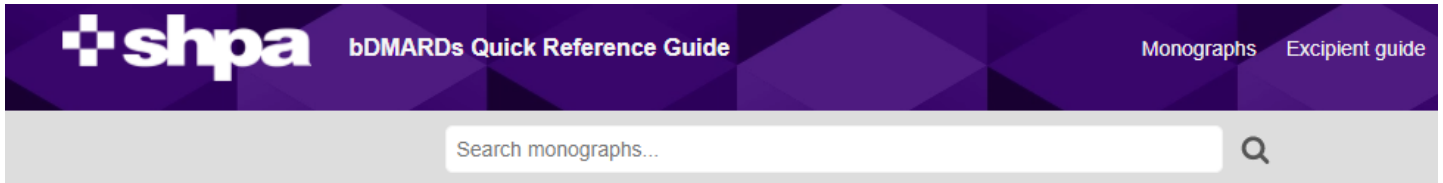

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Infliximab

Home › Monographs › Infliximab

Active ingredient	Infliximab
Mechanism of action	Tumour necrosis factor (TNF) – alpha inhibitor
Molecule type	IgG monoclonal antibody (chimeric)

PBS listed indications

Rheumatology	Ankylosing spondylitis Severe psoriatic arthritis Severe active rheumatoid arthritis
Dermatology	Severe chronic plaque psoriasis
Gastroenterology	Acute severe ulcerative colitis* Moderate to severe ulcerative colitis* Moderate to severe Crohn disease* Severe Crohn disease Complex refractory fistulising Crohn disease

**Paediatric dosing information is outside the scope of this guide. Please refer to paediatric specific references if required*

Reference product (brand)	Remicade
Biosimilar brands	Inflectra, Renflexis

Indication	PBS item code	Brands funded
Ankylosing spondylitis	11482H 11489Q	Inflectra Remicade

Infliximab

‹ Monographs

Administration information

Mode of administration	IV infusion
Administration devices and strengths	Vial containing powder for injection 100mg
Frequency of administration	Every 8 weeks (maintenance dosing)
Storage	Store at 2-8°C (refrigerate do not freeze) The product information for Remicade indicates that it may be stored at temperatures of up to a maximum of 30°C for a single period of up to 12 months; but not exceeding the original expiry date (new expiration date should be written on the carton). Upon removal from refrigeration, Remicade cannot be returned to refrigerated storage. The product information for Renflexis and Inflectra do not contain this additional storage information. Prepared infliximab infusions are stable for 24 hours when stored between 2-30°C. As no preservative is present, it is recommended the infusion begin within 3 hours after preparation.
Standard dosing	**Rheumatoid arthritis:** 3mg/kg, repeat at 2 and 6 weeks after initial infusion, then every 8 weeks. **Ankylosing spondylitis and psoriatic arthritis:** 5mg/kg, repeat at 2 and 6 weeks after initial infusion, then every 8 weeks. **Plaque psoriasis:** 5mg/kg, repeat at 2 and 6 weeks after initial infusion, then every 8 weeks. **Crohn disease and ulcerative colitis:** 5mg/kg, repeat at 2 and 6 weeks after initial infusion, then every 8 weeks. *Treatment with csDMARDs (e.g., methotrexate) may continue during treatment with infliximab.*
Dose variations	**Rheumatoid arthritis:** Consider increasing dose in 1.5mg/kg increments to a maximum of 7.5mg/kg if response is inadequate after 12 weeks or response is lost during maintenance. *This dosing may be outside PBS funding. Specialist prescribers may arrange supply through alternate pathways.* Patients with rheumatoid arthritis who are in remission or have low disease activity may have their dose of infliximab down-titrated by their rheumatologist. • Dose reduction - 50% of standard dose. • Dose interval increase - stepwise increase in dose interval every year (up to 3 years with complete stop at third step). **Crohn disease and ulcerative colitis:** higher doses may be used, commonly 5mg/kg 6 weekly or 7.5mg/kg or 10mg/kg 8 weekly if response is inadequate or lost during treatment. *This dosing may be outside PBS funding. Specialist prescribers may arrange supply through alternate pathways.*
Special notes	Initial infliximab infusions must be given over a period of not less than 2 hours. Infusion reactions are common and are most likely to occur within a few hours and with the first and second infusion. Monitor the patient during and for at least 2 hours after the infusion for dyspnoea, urticaria, hypotension, flushing and headache. Slow or stop the infusion if necessary. Patients who tolerate three 2-hour infusions may cautiously receive future infusions over at least 1 hour. Check your local guidelines. If an

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