ONLINE PANEL DISCUSSION

Tuesday 30 November 2021

PLAQUE PSORIASIS: THE EVIDENCE TO GUIDE PRACTICE PATHWAYS

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.

TARGETED THERAPIES ALLIANCE

THE AUSTRALASIAN COLLEGE OF DERMATOLOGISTS

University of South Australia

NPS MEDICINEWISE

MEET THE PANEL

Prof Debra Rowett
Discipline Lead, Pharmacy
UniSA consortium lead

A/Prof Peter Foley
Dermatologist

A/Prof Stephen Shumack
Dermatologist

A/Prof Michael Ward
Discipline Lead, Pharmacy

Declarations of interest provided at end of slides

OUTLINE

The panel will discuss:

- The place of low-dose methotrexate in therapy
- Choice of biologic for first and second-line biological therapy
- The use of biologics in combination with other immunomodulators
- Fundamentals of biosimilars and their role in therapy
- Immunisation for patients with plaque psoriasis

BACKGROUND

- Evidence summaries developed on behalf of the Targeted Therapies Alliance.
- These underpin the design and delivery of services and resources for dermatologists and patients with plaque psoriasis.

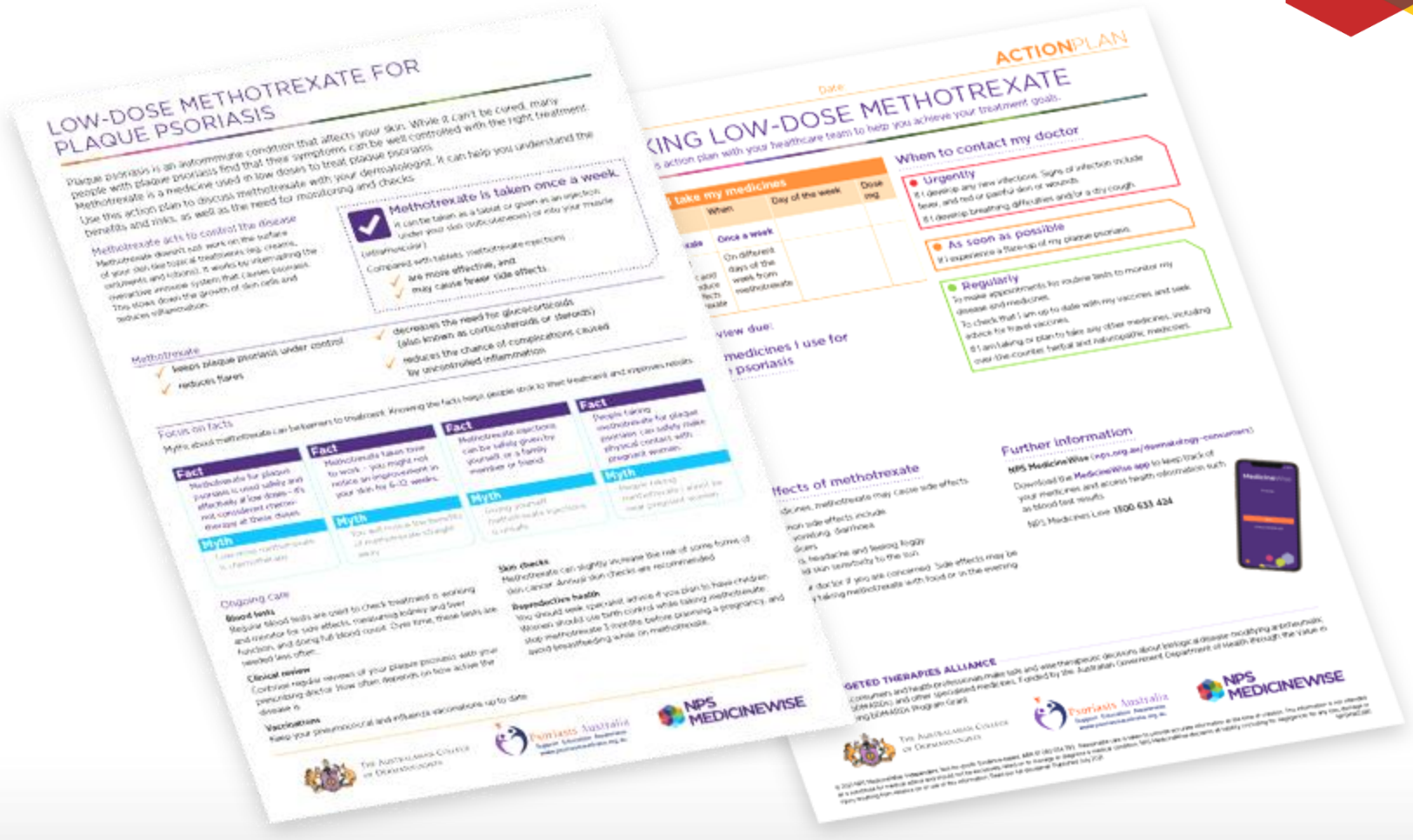
LOW-DOSE METHOTREXATE

ROLE OF SUBCUTANEOUS METHOTREXATE

- Benefits
  - Higher bioavailability
  - less GI adverse effects than oral MTX
  - acceptable for self-administration by patients

SAFETY

- MTX in the treatment of psoriasis does not pose an additional risk of developing cancer for people with psoriasis
- There may be a small additional increase in the risk of developing non-melanoma skin cancer



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SPECIAL CONSIDERATIONS

- Pregnancy
  - Post-conception methotrexate is contraindicated
  - Pre-conception - 2020 ‘American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases’
    - no evidence for mutagenesis or teratogenicity in men planning to father a pregnancy.

IMMUNISATIONS

- All vaccinations are administered and completed at least two weeks before starting treatment
- National Immunisation Handbook
  - Inactivated vaccines can be administered without treatment discontinuation of MTX.
  - Live attenuated zoster vaccine in patients taking <0.4mg/kg/week MTX and no other immunocompromising medication
  - Varicella vaccine
- COVID vaccine

LINE OF THERAPY – BIOLOGICS

- Where to start and move on to
  - Evidence for first-line choices of biologics in plaque psoriasis

LINE OF THERAPY – BIOLOGICS

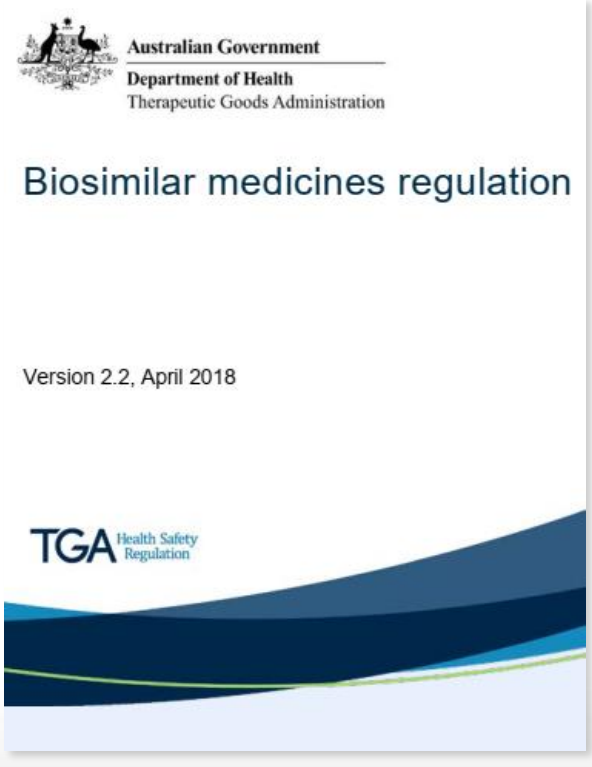
- Loss of response

CHOICE OF THERAPY WITH COMORBIDITIES

- First and second line biologic choices
- Comorbidity considerations

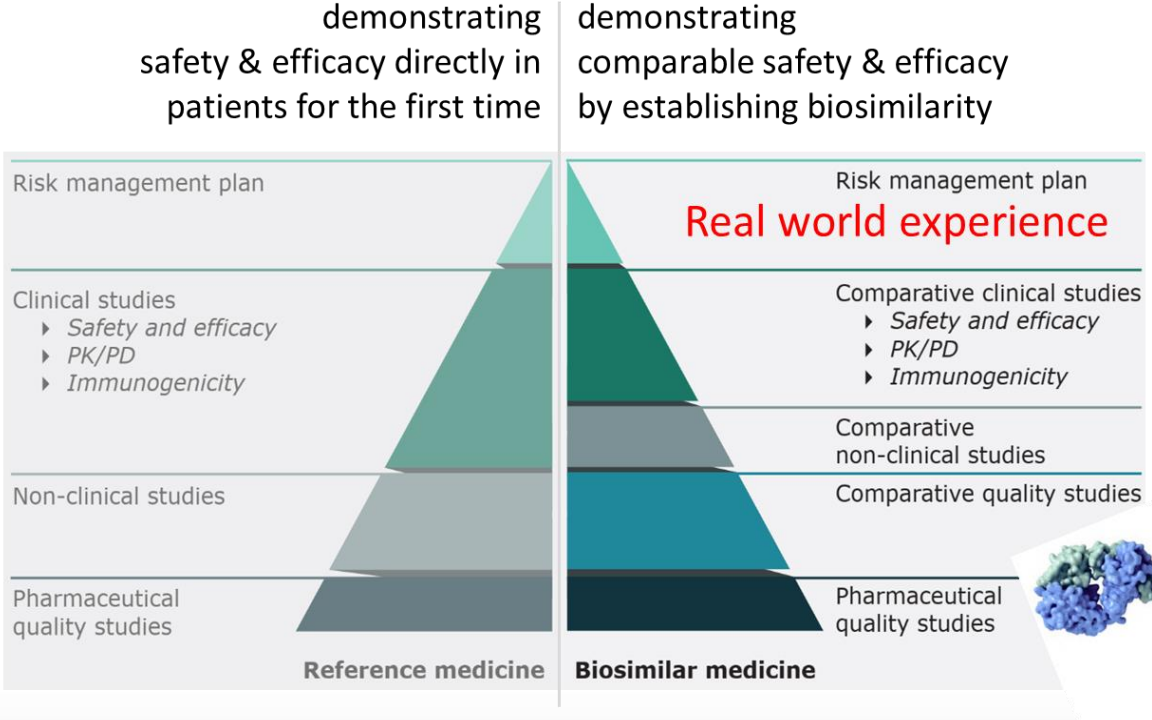
Comorbidity	Comments
Psoriatic arthritis	Depends on focus either PsO or PsA Possibly combine biologics with MTX in case of peripheral active joint involvement.
Crohn disease	Avoid IL-17 inhibitors
Ulcerative colitis	Avoid IL-17 inhibitors
Multiple sclerosis	Avoid TNF inhibitors
Heart failure	Avoid TNF inhibitors

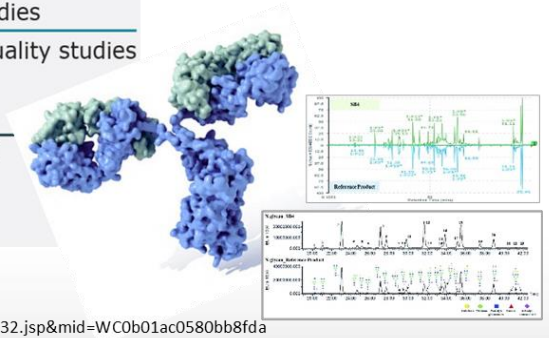
BIOSIMILARS



[Biosimilar product name] is a biosimilar medicine to [Reference medicine name]. The evidence for comparability supports the use of [Biosimilar product name] for the listed indication[s]

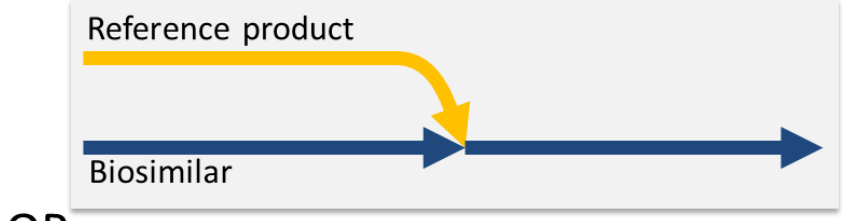
BIOSIMILAR DEVELOPMENT AND APPROVAL





http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/general/general_content_001832.jsp&mid=WC0b01ac0580bb8fda

SWITCHING AND SUBSTITUTION



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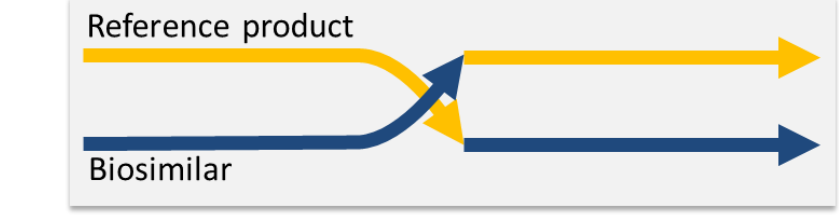

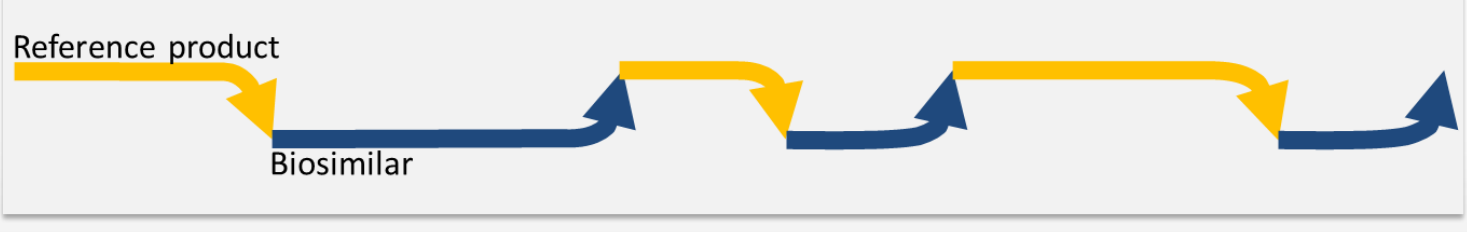

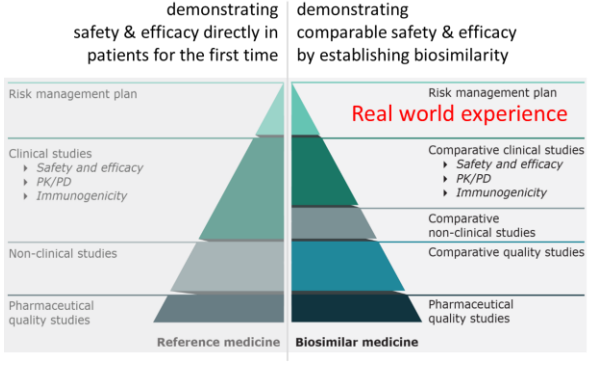

BIOSIMILAR INFLIXIMAB – REAL WORLD EXPERIENCE

Multi-centre reports with larger patient numbers

Conclusion

"In 802 arthritis patients treated with INX for median >6 years, a nationwide non-medical ***switch to CT-P13 had no negative impact on disease activity****. Adjusted 1-year CT-P13 retention rate was slightly lower than for INX in a historic cohort."*

Conclusion

"In summary, in our study with the largest cohort of patients with IBD treated with CT-P13 described so far, we have demonstrated in the evaluated time frame that ***the safety profile and efficacy of CT-P13 biosimilar is in line with the existing literature of infliximab. No alarming signals of immunization*** *have been detected in patients switched from the infliximab."*

Conclusion

"The principal finding of this study is that patients with chronic plaque psoriasis who respond to the infliximab originator can be ***switched to the biosimilar CT-P13 without experiencing a significant change in clinical response*** *or additional adverse events including infusion reactions. Moreover,* ***CT-P13 is effective also in naïve patients*** *with a PASI reduction being in line with that reported for the originator. In terms of* ***safety****, a limited number of adverse events including infusion reactions like those expected with the originator and* ***without any significant difference between the switch and naïve group*** *was observed."*

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BIOSIMILAR INFLIXIMAB

Studies that describe a challenging journey of implementation

Journal of Neurology
https://doi.org/10.1007/s00415-019-09234-y

ORIGINAL COMMUNICATION

Infliximab biosimilar for treating neurosarcoidosis: tolerance and efficacy in a retrospective study including switch from the originator and initiation of treatment

Quentin Riller[1] · Camille Cotteret[2] · Helga Junot[2] · Neila Benameur[2] · Julien Haroche[1] · Alexis Mathian[1] · Miguel Hie[1] · Makoto Miyara[3] · Patrick Tilleul[2] · Zahir Amoura[1] · Fleur Cohen Aubart[1]

Received: 8 December 2018 / Revised: 27 January 2019 / Accepted: 5 February 2019

Table 1 Clinical characteristics of patients who received the infliximab biosimilar

Patient	Sex, age	Clinical manifestations	Follow-up	S/I	Outcomes[a]	Relapses[b]	Side effects	Prior treatment	Concomitant treatment[c]
#1	F, 41	T, J (M, C, R)	27	I	CR	0	Pulmonary infection	MTX, GC	MTX, GC (5)
#2	F, 37	T, E, S (M, Med)	24	S	PR	0	0	MTX, CYC, AZA, GC	MTX, GC (10)
#3	M, 31	T, E, (C, Med, E)	28	S	–	1 (5)	Infection Urticaria	GC	MTX, GC (7)
#4	M, 32	T, E, (M, ICH)	26	I	PR	0	Urticaria	MTX, GC	MTX, GC (5)
#5	F, 52	T, E, (M, C, Med)	28	S	–	1 (5)	Larva migrans	CYC, GC	MTX, GC(10)
#6	M, 41	T (M, Med, C)	28	S	CR	0	0	CYC, GC	MTX, GC(5)
#7	F, 50	T, S, (M, Med, CN, R, C)	25	S	CR	0	0	MTX, CYC, MMF, GC	MTX, GC(5)
#8	F, 42	T, (M)	27	S	PR	1 (9)	0	MTX, CYC, GC	MTX, GC (5)
#9	M, 29	T, O, (Med)	24	I	PR	0	0	MTX, GC	GC (5)
#10	F, 47	T, (M, CN, ICH)	24	I	PR	0	0	AZA, GC	GC (5)
#11	M, 52	T, (ICH, M)	27	I	PR	0	0	MTX, GC	MTX, GC (5)
#12	F, 49	T, (Med, CN)	28	S	–	0 (2)	Headache	GC	MTX, GC (5)
#13	M, 42	T, S, (C, E, M)	23	I	PR	0	Pulmonary infection	GC, MTX	MTX, GC (5)
#14	M, 32	T, H, (C, M, Med)	24	I	PR	0	0	GC, MTX, CYC, AZA, MMF	AZA, GC (5)
#15	F, 50	T, (M)	22	I	PR	0	Whitlow	GC	GC (10)
#16	F, 47	Hep, (M, C, Med, ICH)	22	I	PR	1 (3)	0	GC	MTX, GC (10)
#17	M, 43	T, E, B (CN, M, C)	19	I	PR	0	0	GC, MTX	MTX (0)
#18	M, 43	B, (C, E)	27	S	PR	1 (7)	Urticaria	GC, CYC	AZA, GC (5)
#19	M, 42	T, B, J, O, (M)	19	I	PR	1 (15)	Diarrhea, urticaria	GC, MTX, HCQ	MTX, HC (0)
#20	M, 50	T, O, (CN)	25	I	CR	0	0	GC	GC (5)

"During the study period, a steering committee was convened consisting of rheumatologists, pharmacists, and internal medicine practitioners who decided to switch to the infliximab originator in individual cases if they had concerns about safety or efficacy."

"Among the six patients who relapsed, five subsequently received the infliximab originator. Four patients did not improve or relapsed with this switch to the originator, thus they were switched back to the biosimilar."

O → B → O → B

B → O → B

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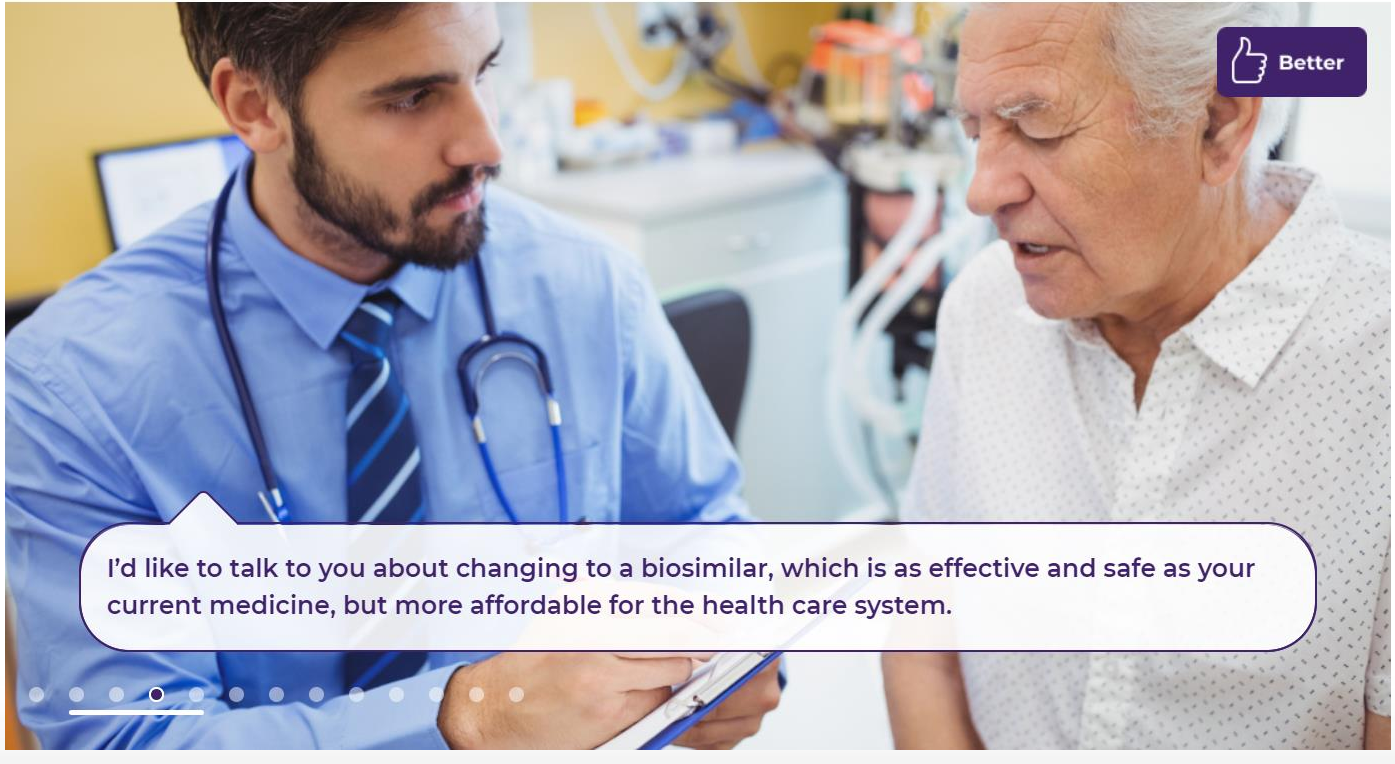
BARRIERS TO THE UPTAKE OF BIOSIMILARS

PERCEPTIONS ARE IMPORTANT



ADDRESSING NOCEBO THROUGH EDUCATION


Australian Government
Department of Health

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)?
- Where can I find more information?

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.

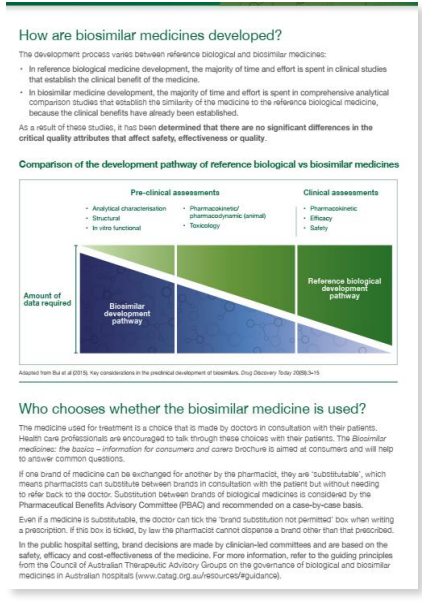
These medicines are used to treat serious diseases such as cancers, diabetes, rheumatoid arthritis, severe psoriasis, kidney disease, multiple sclerosis, and inflammatory bowel diseases such as ulcerative colitis and Crohn's disease.

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(8):3–15

Who chooses whether the biosimilar medicine is used?

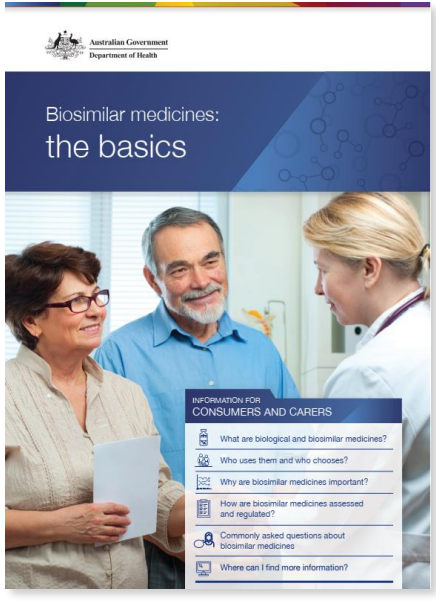
The medicine used for treatment is a choice that is made by doctors in consultation with their patients. Health care professionals are encouraged to talk through these choices with their patients. *The Biosimilar medicines: the basics – information for consumers and carers* brochure is aimed at consumers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

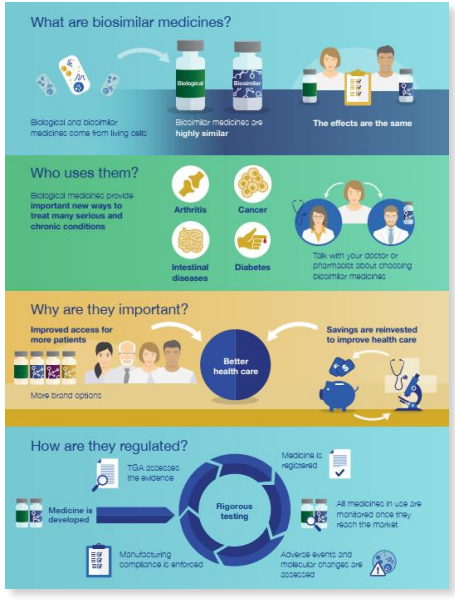
http://www.health.gov.au/internet/main/publishing.nsf/content/biosimilar-awareness-initiative/$File/Biosimilar-medicines-the-basics-for-healthcare-professionals-Brochure.pdf


Australian Government
Department of Health

Biosimilar medicines:
the basics

INFORMATION FOR
CONSUMERS AND CARERS

- What are biological and biosimilar medicines?
- Who uses them and who chooses?
- Why are biosimilar medicines important?
- How are biosimilar medicines assessed and regulated?
- Commonly asked questions about biosimilar medicines
- Where can I find more information?



http://www.health.gov.au/internet/main/publishing.nsf/content/biosimilar-awareness-initiative/$File/Biosimilar-medicines-the-basics-for-consumers-and-carers-Bochure.pdf

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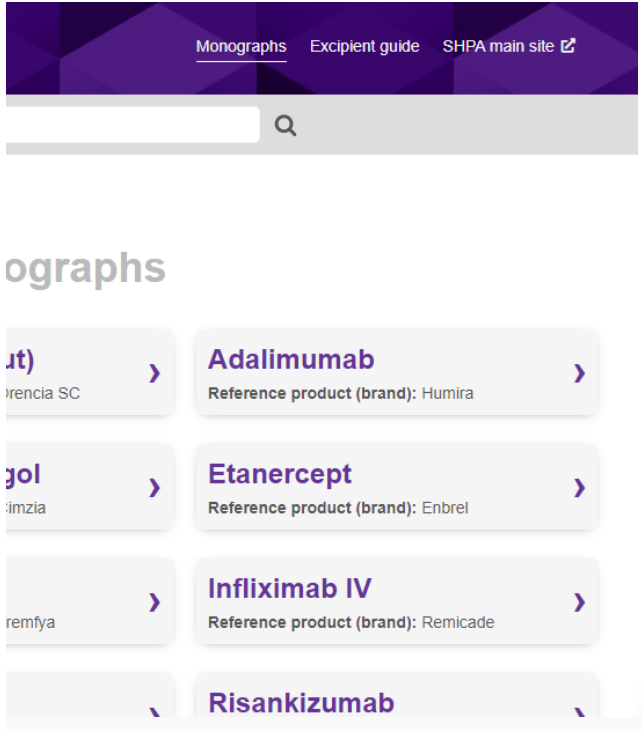
Biologics and biosimilars best practice

Guiding principles for the governance of biologics and their biosimilars in Australian hospitals

Version 3 – October 2021



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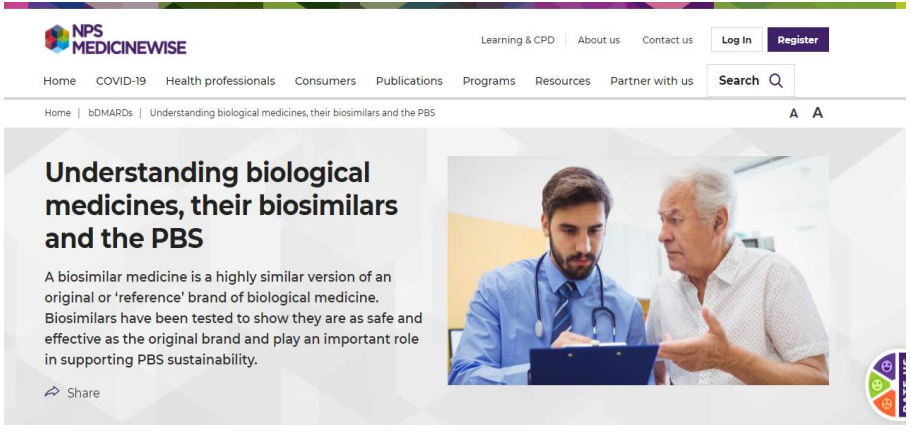
RESOURCES



Understanding biosimilars: For your patients

Find answers to consumers' common questions about biosimilars

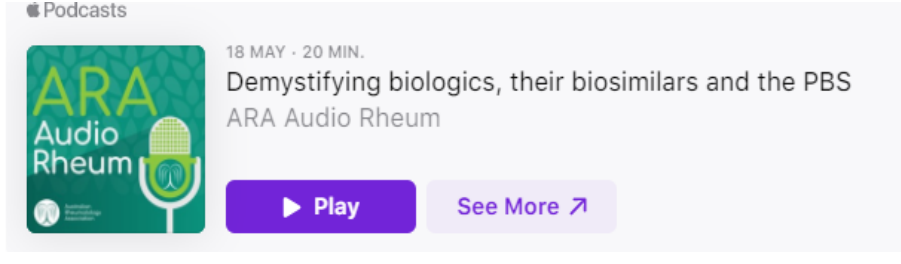
Understanding biosimilars →

Biologics, biosimilars and PBS sustainability

Biologics have a significant and positive impact on the treatment of many severe acute and chronic diseases. After the patents on the original (reference) biologics expire, competing manufacturers are able to develop biosimilars, which are highly similar versions of a specific reference biologic (sometimes called the 'originator' biologic). Once this happens, market competition usually drives prices down

Read the full article →

Podcast: Demystifying biologics, their biosimilars and the PBS



nps.org.au/bdmards/biologics-and-biosimilars

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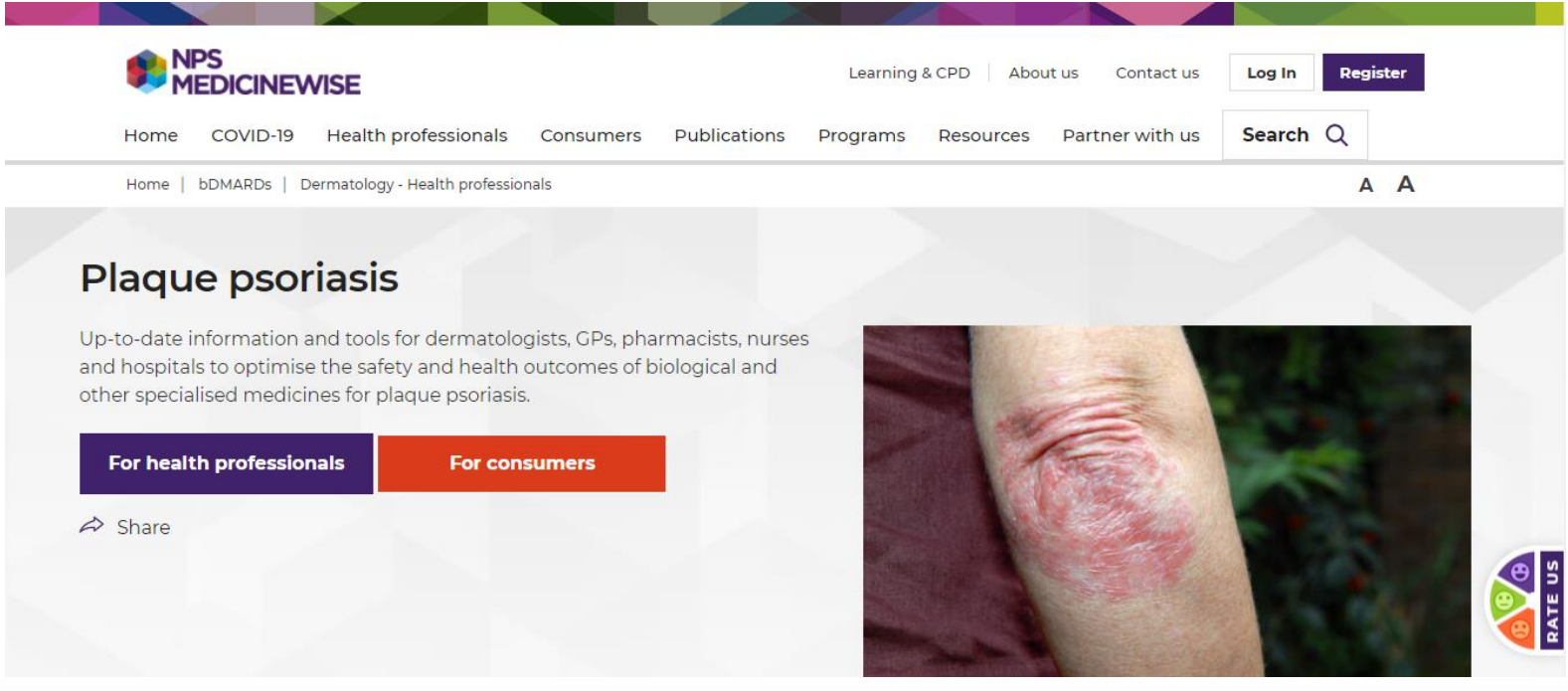
RESOURCES



nps.org.au/bdmards/dermatology

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RESOURCES

- **NPS MedicineWise nps.org.au/bdmards**
  - Factsheet: Treating your plaque psoriasis with creams and ointments
  - Decision aid: Plaque psoriasis: My options when topical treatments aren't enough
  - Action plan: Low-dose methotrexate for plaque psoriasis
  - Online content: Understanding biosimilars

- **CATAG**
  - Guiding Principles for the governance of biologics and their biosimilars in Australian hospitals
  - CATAG Position Statement on the use of low-dose methotrexate

- **SHPA**
  - bDMARDs Quick reference guide

QUESTIONS

DISCLOSURES

Debra Rowett

No disclosures to declare

Stephen Shumack

Investigator for the following companies:

Abbvie, Pfizer, Janssen, Leo Pharma, Lilly,

Advisory Board positions for the following companies:

Lilly, AbbVie, Janssen, Novartis

DISCLOSURES

Peter Foley

Abbvie;[A,I,R,SP,T] Amgen;[A,I,R] BMS;[A,C,I] Boehringer Ingelheim;[A,I] Janssen;[A,C,I,R,SP,T] Leo Pharma;[A,C,I,SP,T] Lilly;[A,C,I,R,SP,T] Merck;[A,I,R,SP,T] Novartis;[A,C,I,R,SP,T] Pfizer;[A,C,I,R,SP,T] Sun Pharma;[A,I,R,T] UCB Pharma;[A,C,I,SP] Valeant;[A,I,SP] Aslan;[C,I] Astra Zeneca;[I] Arcutis;[I] Argenx;[I] Aslan;[I] Botanix;[I] Celgene;[A,I,R,SP] Celtaxsys;[I] CSL;[I] Cutanea;[I] Dermira;[I] Galderma;[A,C,I,R,SP,T] Genentech;[I] GeneSeq;[I] GSK;[A,I,SP] Hexima;[C,I] Mayne Pharma;[A,C] MedImmune;[I,C] Regeneron Pharmaceuticals Inc;[I] Reistone;[I] Roche;[C,I,SP,T] Sanofi;[A,I,R,SP,T]

[A] = advisory board; [C] = consultant; [I] = investigator (clinical trials); [R] = research grants; [SP] = speaker's bureaux/honoraria; [T] = travel grants

DISCLOSURES

Michael Ward

Has been engaged by GBMA Education to conduct literature reviews on biosimilar medicines as a component of the Department of Health Biosimilar Awareness initiative.

THANK YOU