

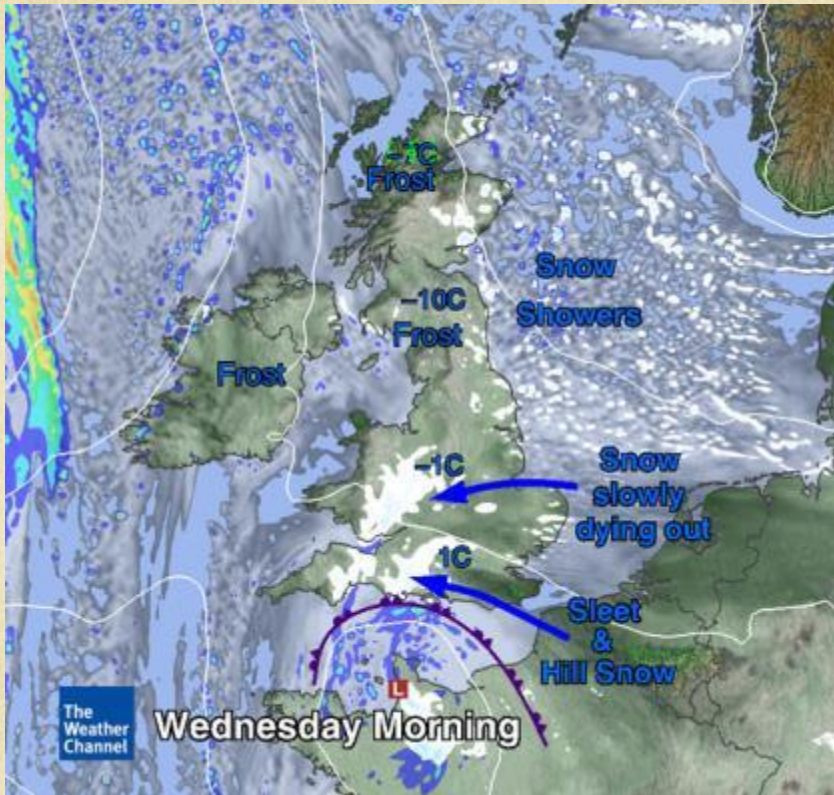
The GPs role with biologics for immune-mediated inflammatory diseases

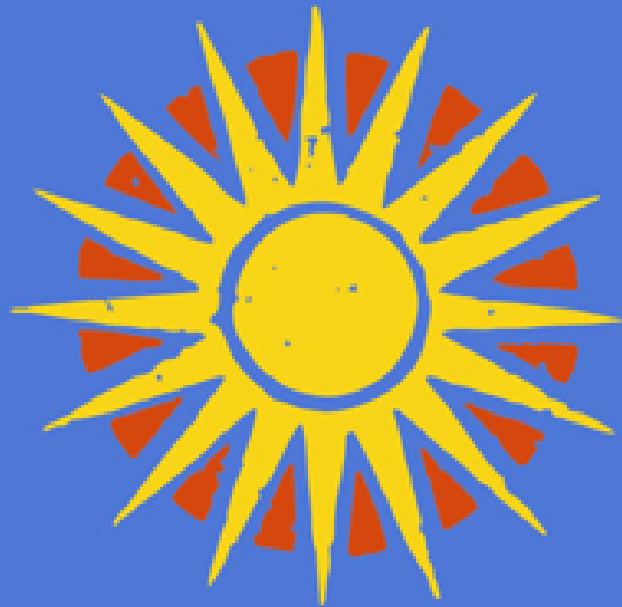
David Gardner
Rheumatologist
GPCME 2015

The views and opinions expressed in the following presentation are those of the presenter and do not necessarily reflect those of AbbVie Limited

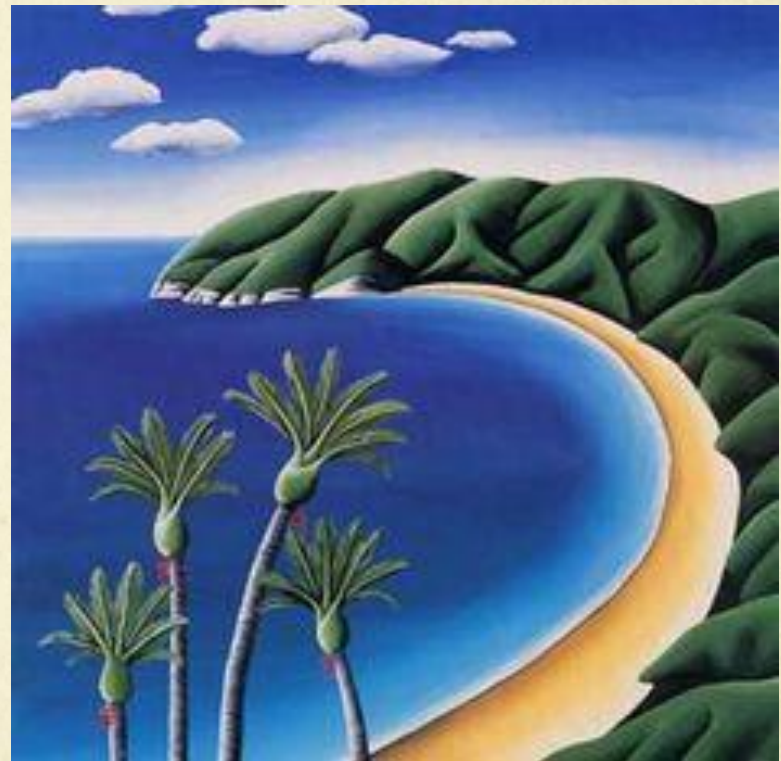
AbbVie Limited does not endorse the use of unregistered products or products outside of their registered indications

Please refer to the Full Datasheet for licensed instructions





HAWKE'S BAY
WINE COUNTRY
NEW ZEALAND



Overview

- What are biologics?
- When and why are they used?
- The care of patient starting and using biologics
- Questions you may be asked by patients

What are biologics?

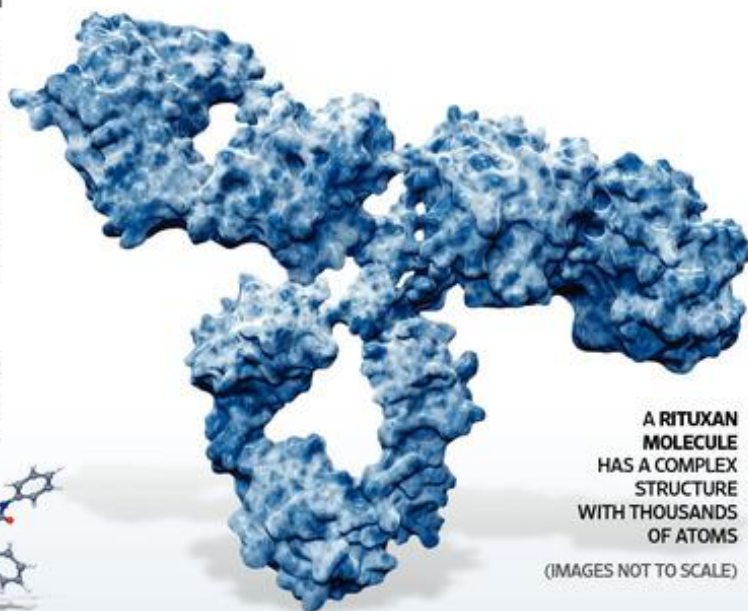
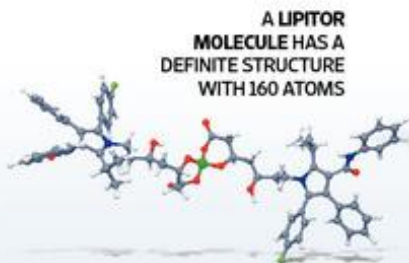
- Specific cell signalling pathways targeted
- Manufactured in a living system such as a microorganism, or plant or animal cells
- Very large, complex molecules or mixtures of molecules
- Produced using recombinant DNA technology

- Traditional drugs are small molecules and generally have well-defined chemical structures

No Ordinary Generic

The Challenge of Copying Biotech Drugs

Chemists can make exact generic copies of conventional pills. But, scientists making 'biosimilar' drugs are copying much more complex biotech drugs. A Rituxan molecule is about 120 times larger—in terms of molar mass—than the basic chemical unit of Lipitor, below.



LIPITOR

(ATORVASTATIN)

High cholesterol

A handful of atoms, mostly carbon and hydrogen, combined in specific, replicable formula

LESS THAN **\$10 MILLION**

Chemicals are mixed at subzero temperatures

CHEMICAL VS. BIOTECH

INDICATIONS

INGREDIENTS

COST TO COPY

HOW IT'S MADE

RITUXAN

(RITUXIMAB)

Cancer, arthritis

Hundreds of amino acids bound together in a complex structure that scientists can't fully document

\$100M-\$300M

Living cells with altered DNA produce the injectable drug

A BIOSIMILAR RECIPE



1 Scientists copy key DNA sequences used to make branded drugs



2 The strands are inserted into living cells



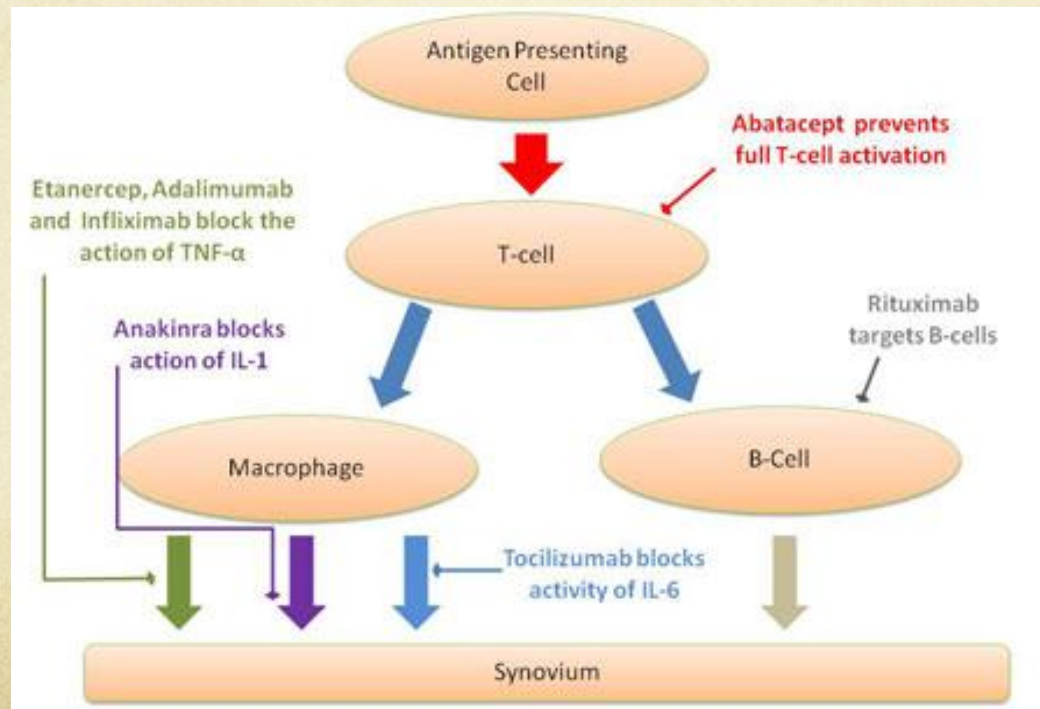
3 The cells replicate and secrete antibodies in a bioreactor



4 Antibodies to use in treatments are filtered out

Biologics in practice

- Most are monoclonal antibodies
- Directed against selected targets – TNF, IL-1, IL-6, IL-20, B and T cell surface markers



Infliximab

Adalimumab

Golimumab

Certolizumab

Etanercept

Abatacept

Tocilizumab



Chimera Human Human Humanized Pegylated Human protein Humanized

Human constant region

Mouse variable region

Humanized variable region

Recombinant human Variable region

Human variable region

Polyethylenglycol

Human fusion protein

Human constant region like protein

When are they used?

- Failure of standard DMARD therapy
- Side effects of traditional DMARDs

- Dermatology – psoriasis
- Gastroenterology – IBD
- Ophthalmology – uveitis/iritis
- Rheumatology – RA, psoriatic arthritis, ankylosing spondylitis, JIA

Who can start them?

- Initiated by specialist
- PHARMAC special authority criteria
- Review of special authority every 6 months
- Can be prescribed by any practitioner



Why are they used?

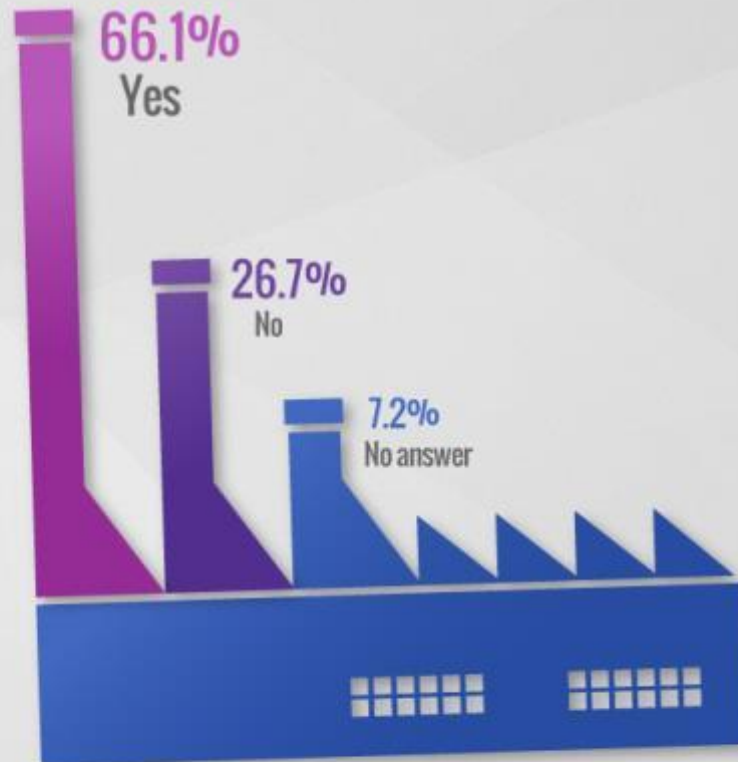
- Improve symptom burden
- Improve QOL
- Reduce long term effects of condition
- Reduce use of corticosteroids

Furst DE, Breedveld FC, Kalden JR, et al. Updated consensus statement on biological agents, specifically tumour necrosis factor (alpha) (TNFalpha) blocking agents and interleukin-1 receptor antagonist (IL-1ra), for the treatment of rheumatic diseases. *Ann Rheum Dis* 2005;64(Suppl 4):2-14.





Does having RA impact your ability to work?

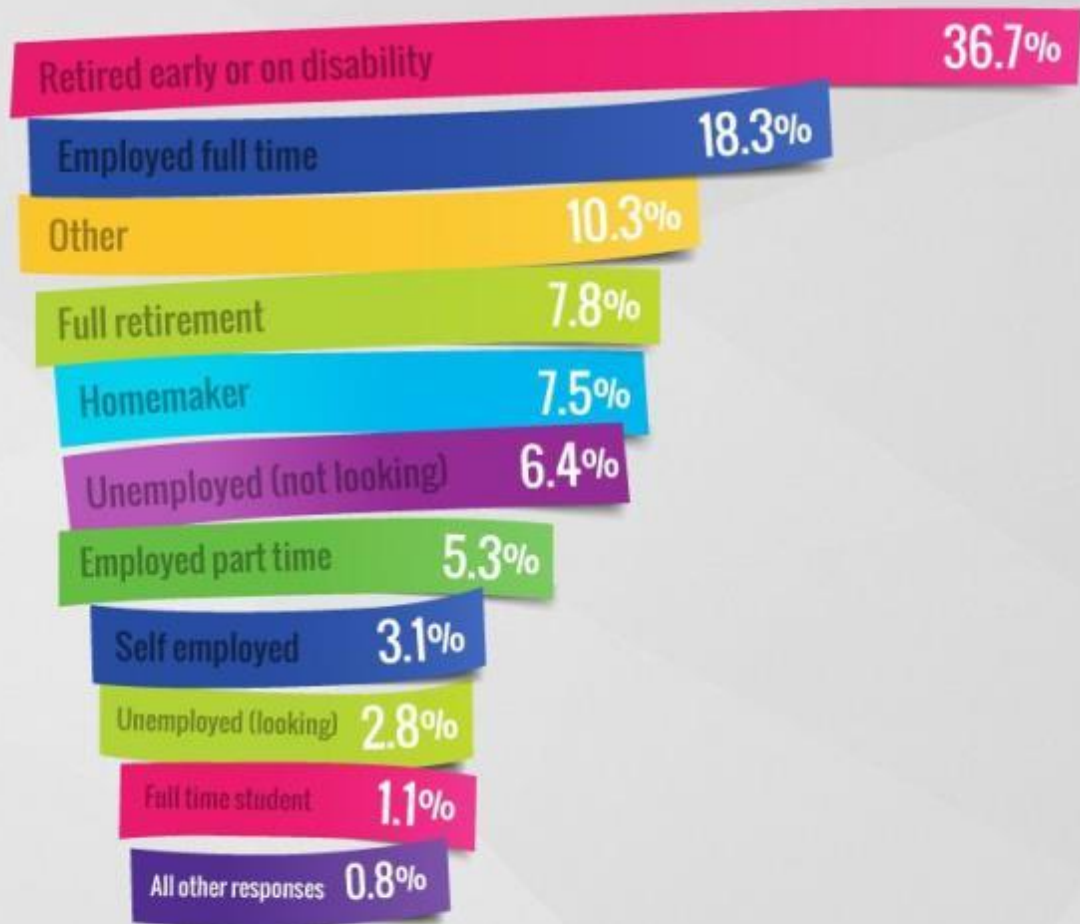


How has your **severe** RA impacted your ability to work?



What is your employment status?

(Participants with severe RA)



PREMIER study

	Baseline	Biologic	DMARD
Loss of job		13%	30%
Unable to work	45%	11%	17%
Difficulty at work	88%	15%	34%
Limitation climbing stairs	67%	12%	21%
Can not walk 1 block	45%	7%	13%

Patient story

- 38 year old fireman
- Psoriatic arthritis
- Back pain, plantar fasciitis, metatarsalgia
- Failed methotrexate, leflunomide, salazopyrin as well as NSAID and prednisone
- On verge of losing his job
- Started anti-TNF
- No symptoms, working and playing sport

GP's role

- Advocate for access to effective treatment
- Understand role of new agents
- Counsel patients on benefits and risks
- Facilitate safe initiation of treatment
- Reduce risk of complications once on new therapy

Contraindications

- Chronic or active infection
- Moderate to severe heart failure
- Malignancy in the past 5 years
- Personal or family history of demyelinating disease

Screening before starting biologics

- TB – QuantiFeron Gold +/- CXR
- HIV
- Hepatitis B and C



- Update immunisations – influenza, pneumovax, hep B
- Consider zoster vaccine
- **Live vaccines contraindicated once on immune suppression**

Injection site reactions

- Warm the pen
- Change the site regularly
- Ice pack to site after injection
- Topical steroid
- Antihistamine
- Avoid alcohol swab pre-injection
- Review injection technique
- Change to syringe rather than pen



Infection risk in immune diseases

- Relative risk approximately 2x general population
- Inherent risk from immune disease
- Affected by comorbidities
- Corticosteroids worst
- Infection rates increased in first 6 months of biologic therapy – especially respiratory



J D Greenberg. Association of methotrexate and tumour necrosis factor antagonists with risk of infectious outcomes including opportunistic infections in the CORRONA registry. *Ann Rheum Dis.* 2010;69(2):380-386

C J Grijalva. Initiation of rheumatoid arthritis treatments and the risk of serious infections. *Rheumatology* 2010;49:82-90

What to do when an infection occurs



- **Withhold biologic**
- Lower threshold for investigation and treatment with antibiotics
- Lack of signs and symptoms common
- Increased rate of zoster and atypical infections
- Contact specialist team

Other complications

- Psoriasis
- Drug induced lupus
- Non-melanoma skin cancers

- Treatment failure

BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies

<http://rheumatology.oxfordjournals.org/content/suppl/2010/09/14/keq249a.DC1/keq249b.pdf>

Blood tests

- Most patients still on traditional DMARDs e.g. methotrexate
- Monitor FBC, LFTs and CRP every 3 months
- Creatinine in patients with CKD or >60 years old



Perioperative care

- No consensus
- Withhold treatment 1-2 dose intervals before surgery
- Restart once wounds healed and no sign of infection



Pregnancy

- Plan pregnancy!
- Increasing evidence of safety
- No increased risk of birth defects
- Underlying condition and steroids can lead to premature labour



Anti-TNF- α therapies are safe during pregnancy in patients with inflammatory bowel disease: a meta-analysis

[https://www.ecco-ibd.eu/index.php/publications/congress-abstract-s/abstracts-2014/item/dop040-anti-tnf- \$\alpha\$ -therapies-are-safe-during-pregnancy-in-patients-with-inflammatory-bowel-disease-a-meta-analysis.html](https://www.ecco-ibd.eu/index.php/publications/congress-abstract-s/abstracts-2014/item/dop040-anti-tnf-α-therapies-are-safe-during-pregnancy-in-patients-with-inflammatory-bowel-disease-a-meta-analysis.html)

Manufacturer Medsafe Product Information for Anti-TNF agents: Pregnancy

(See respective Data Sheets for more information)

HUMIRA (Category C)

There are no data from clinical trials for pregnant women being treated with Humira. Because animal studies are not always predictive of human responses, the use of Humira during pregnancy is not recommended. Women of child bearing potential should be advised to use adequate contraception during Humira therapy. The long half-life of Humira should also be considered when discontinuing therapy.

ENBREL (Category B2)

The safe use of etanercept during pregnancy has not been established. Therefore, ENBREL should be used during pregnancy only if clearly needed...There are, however, no studies in pregnant women.

REMICADE (Category C)

It is not known whether REMICADE can affect reproductive capacity or can cause foetal harm when administered to a pregnant woman. REMICADE should be given to a pregnant woman only if clearly needed...It is recommended that adequate contraceptive measures should be taken for at least 6 months after the last REMICADE treatment.

Storage/Travel

- Ideally keep at 2-8 °C
- Can be stored at room temperature for 14 days
- Do not recool



Summary

- Biologics are very effective treatments for immune mediated inflammatory conditions
- Injection site reactions and infection are most common side effects
- Plan immunisations prior to starting new treatment
- Withhold if serious infection present or surgery planned
- Increasing safety data in pregnancy and on travelling with medication

Resources

- **Biologic medicines for the treatment of inflammatory conditions: What does primary care need to know?**

<http://www.bpac.org.nz/BPJ/2013/December/biologic.aspx>

- **Disease and Medication Information**

<http://rheumatology.org.au/community/PatientMedicineInformation.asp>

- **Arthritis New Zealand**

<http://www.arthritis.org.nz>



Questions

