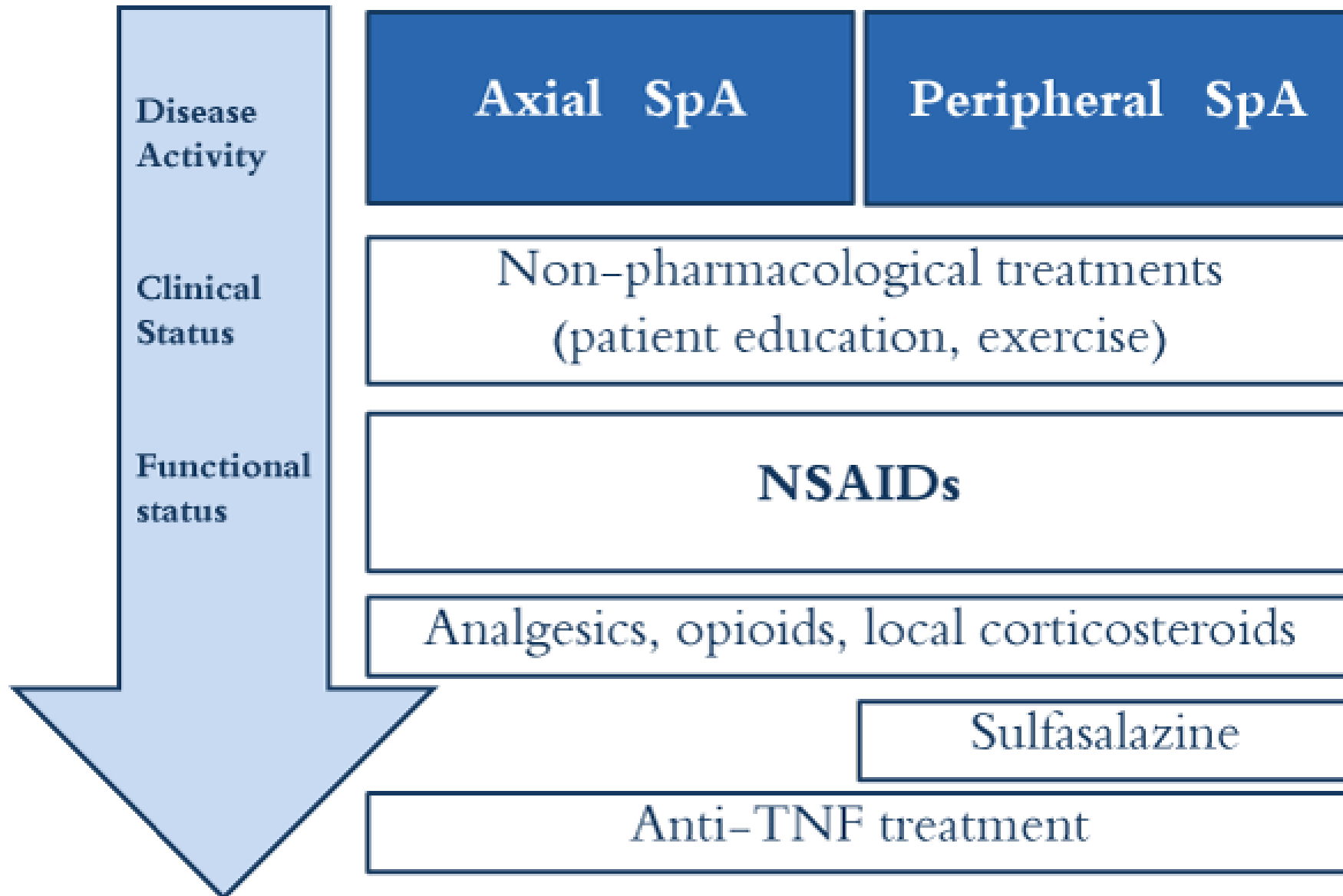
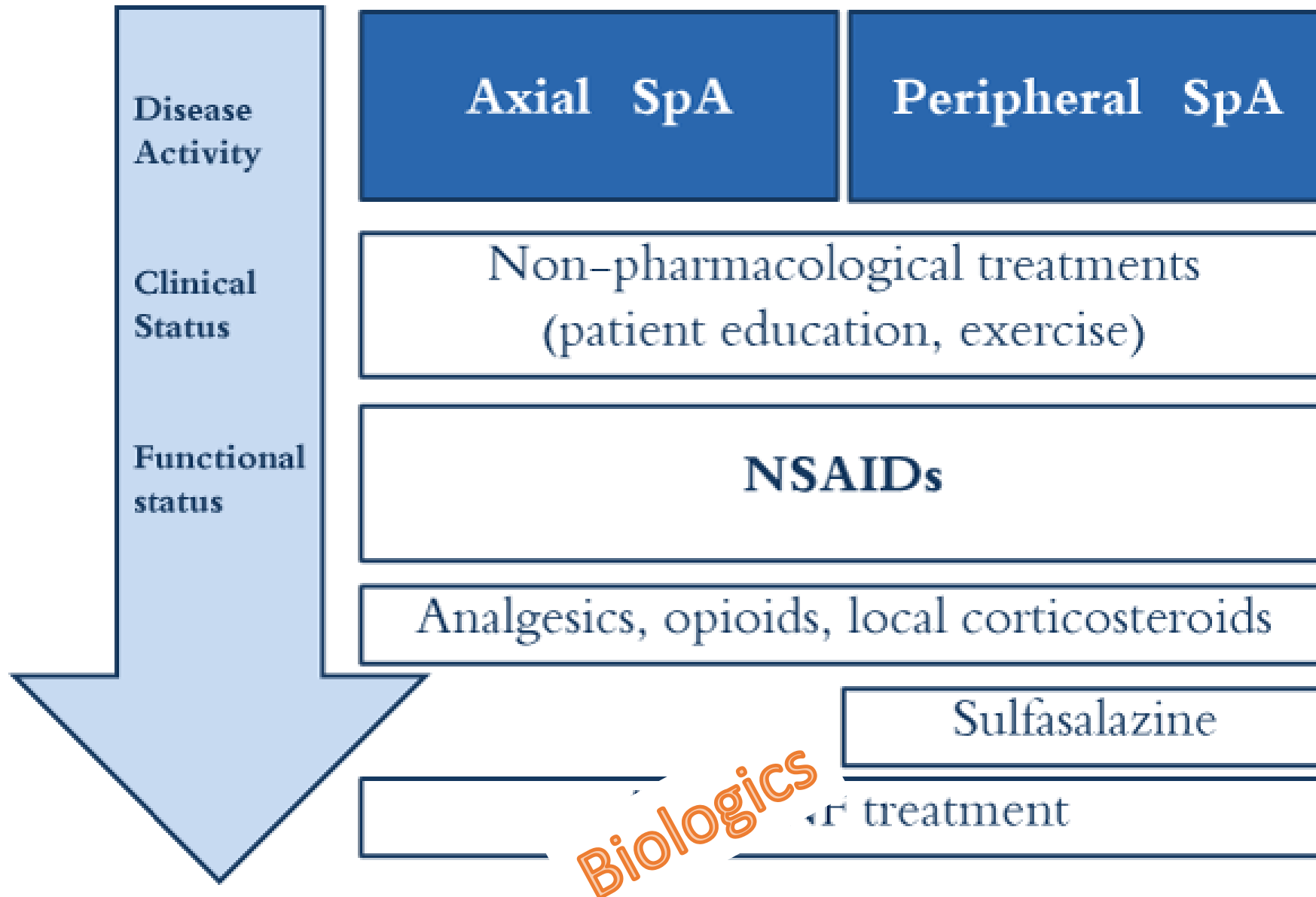


# Biologics and Ankylosing Spondylitis

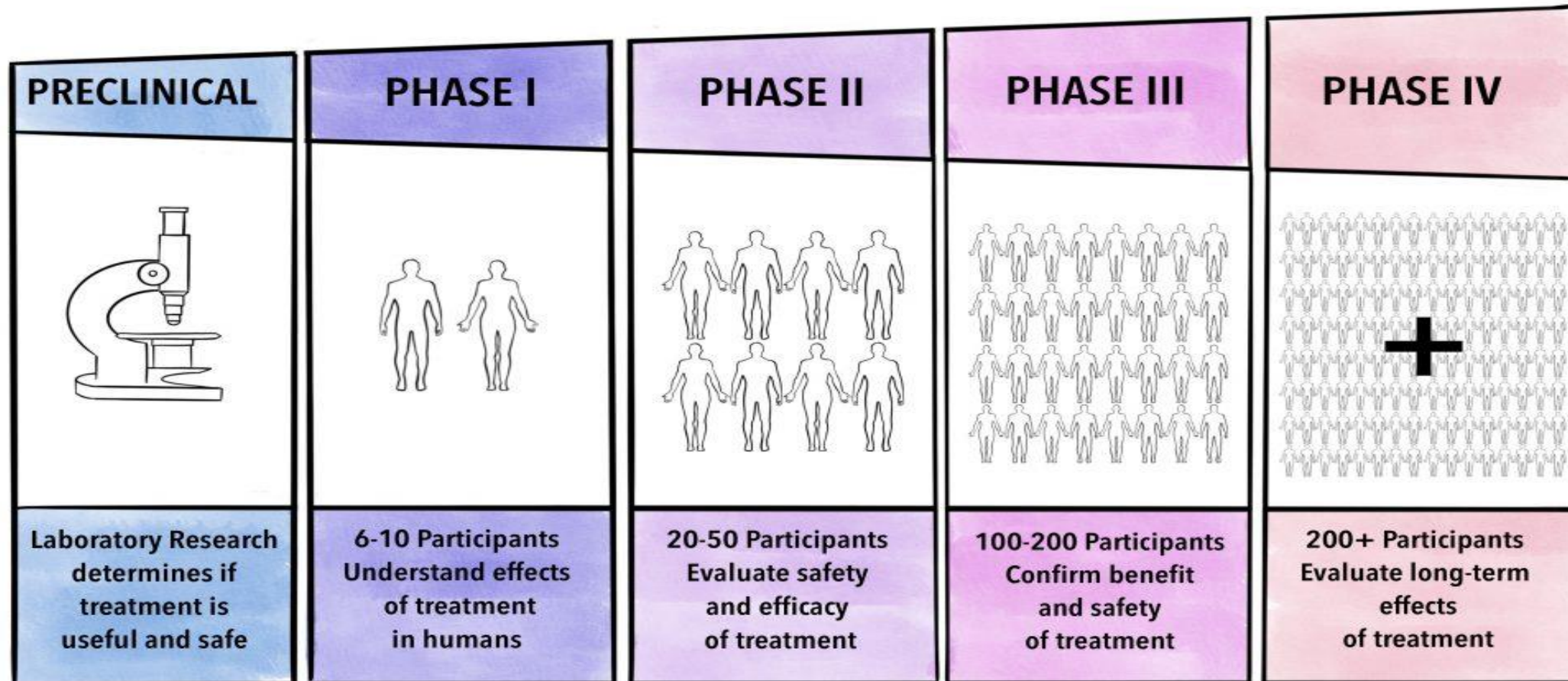


Colin Beevor  
Matron and Senior Clinical Nurse  
Specialist  
Service Manager

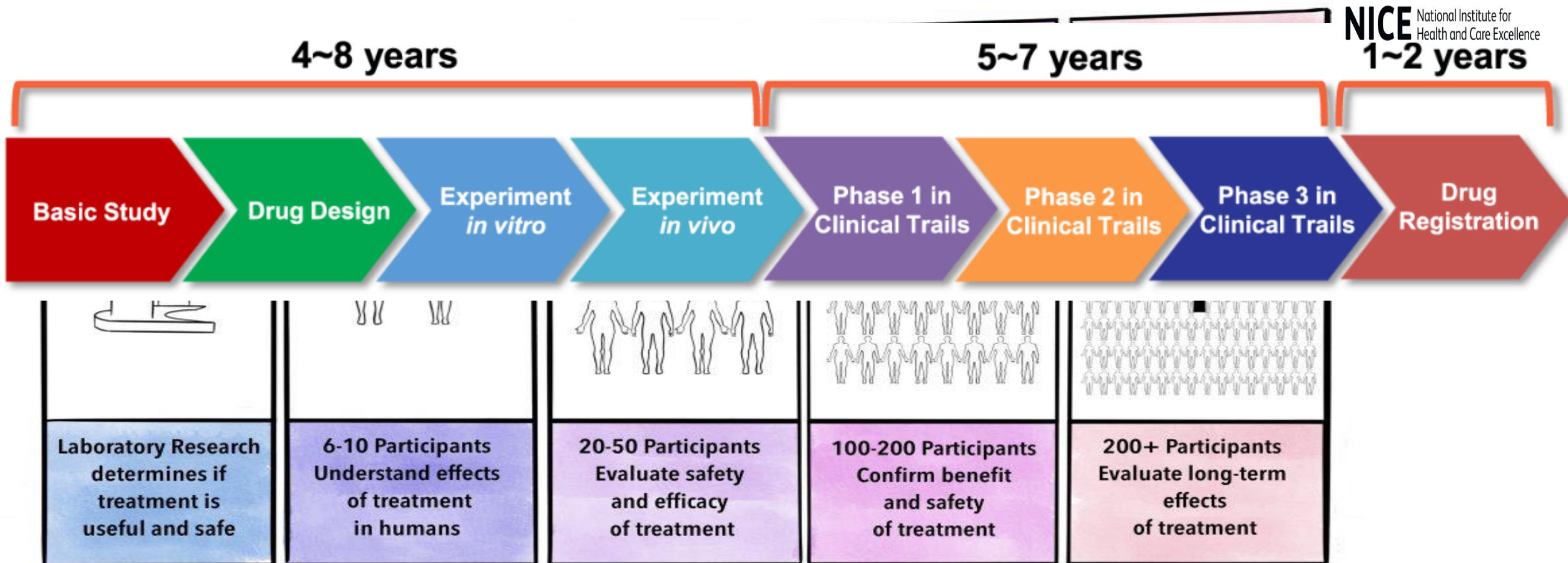




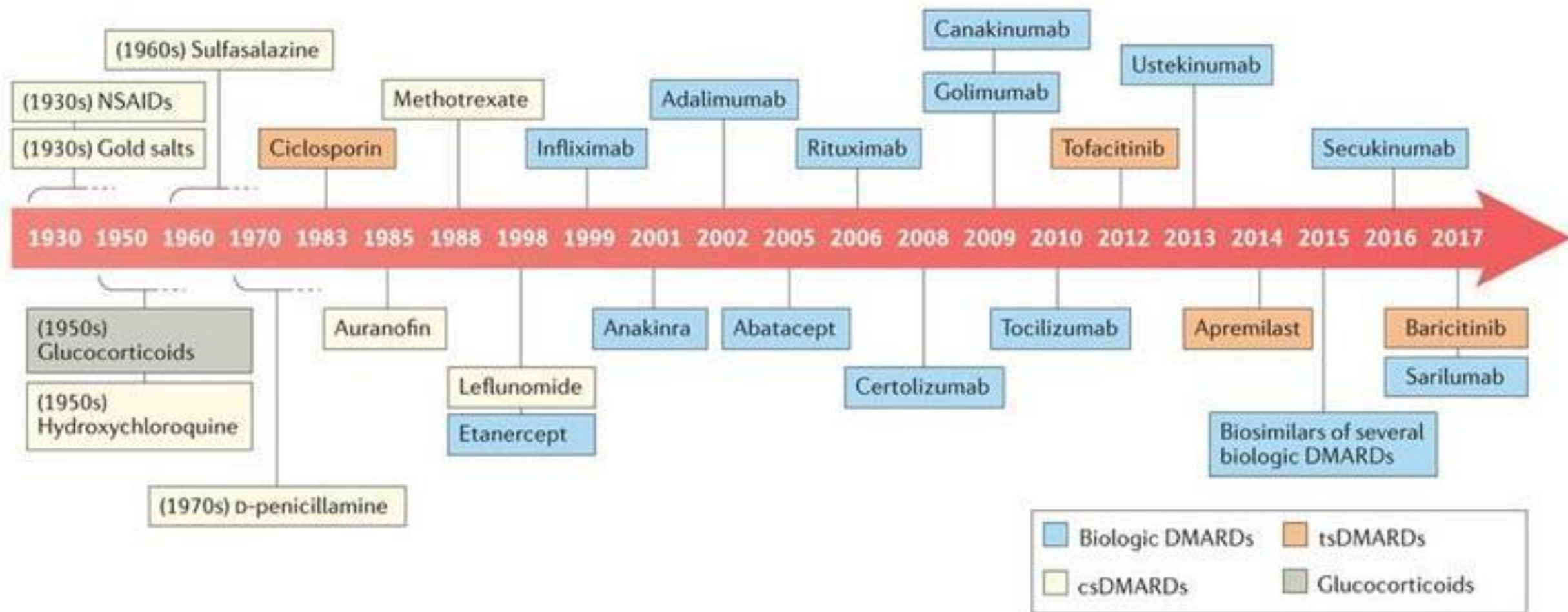
# Clinical Trials- Ankylosing Spondylitis

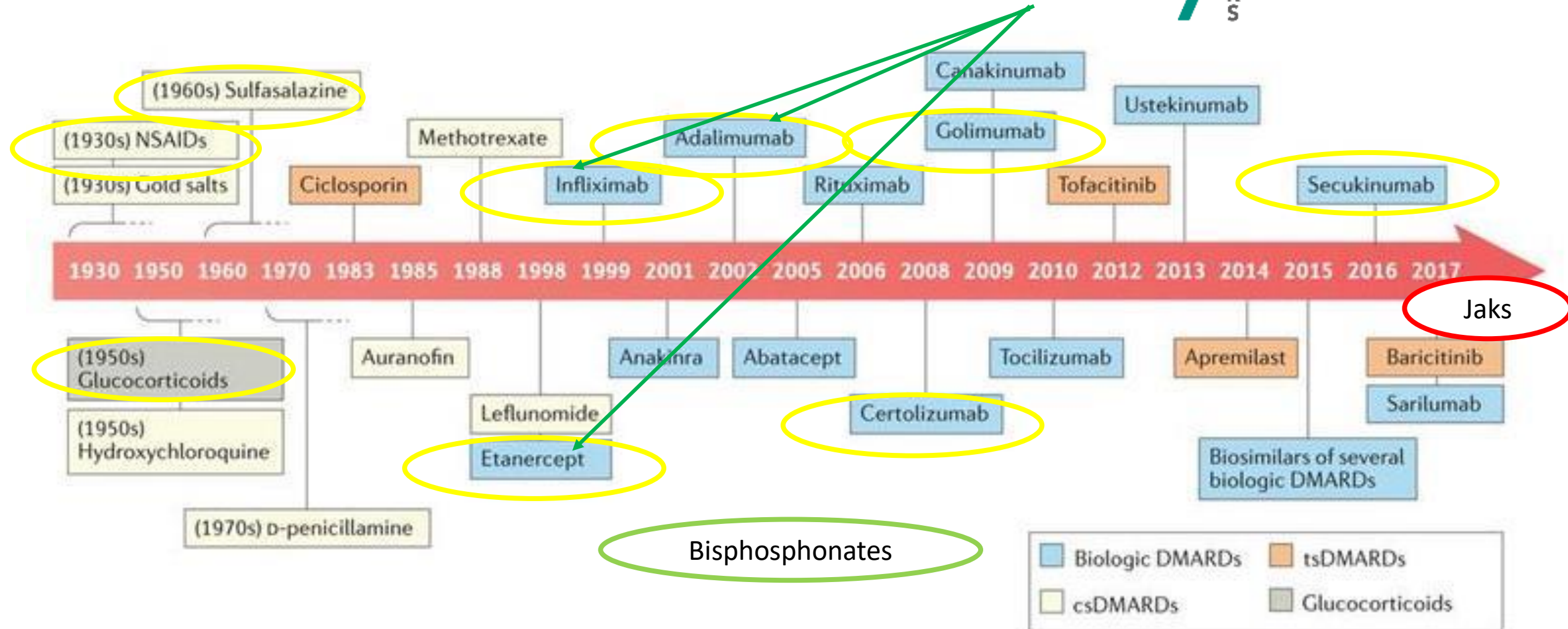


# Clinical Trials- Ankylosing Spondylitis









Infliximab  
Certolizumab  
Adalimumab  
Etanercept  
Golimumab

Skin



IL-17, IL-23p19  
IL-12/23p40, TNF

Joint



TNF, IL-17,  
IL-23p19, IL-12/23p40

Axial  
Skeleton



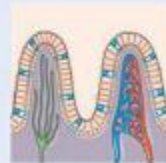
IL-17, TNF

Enthesis



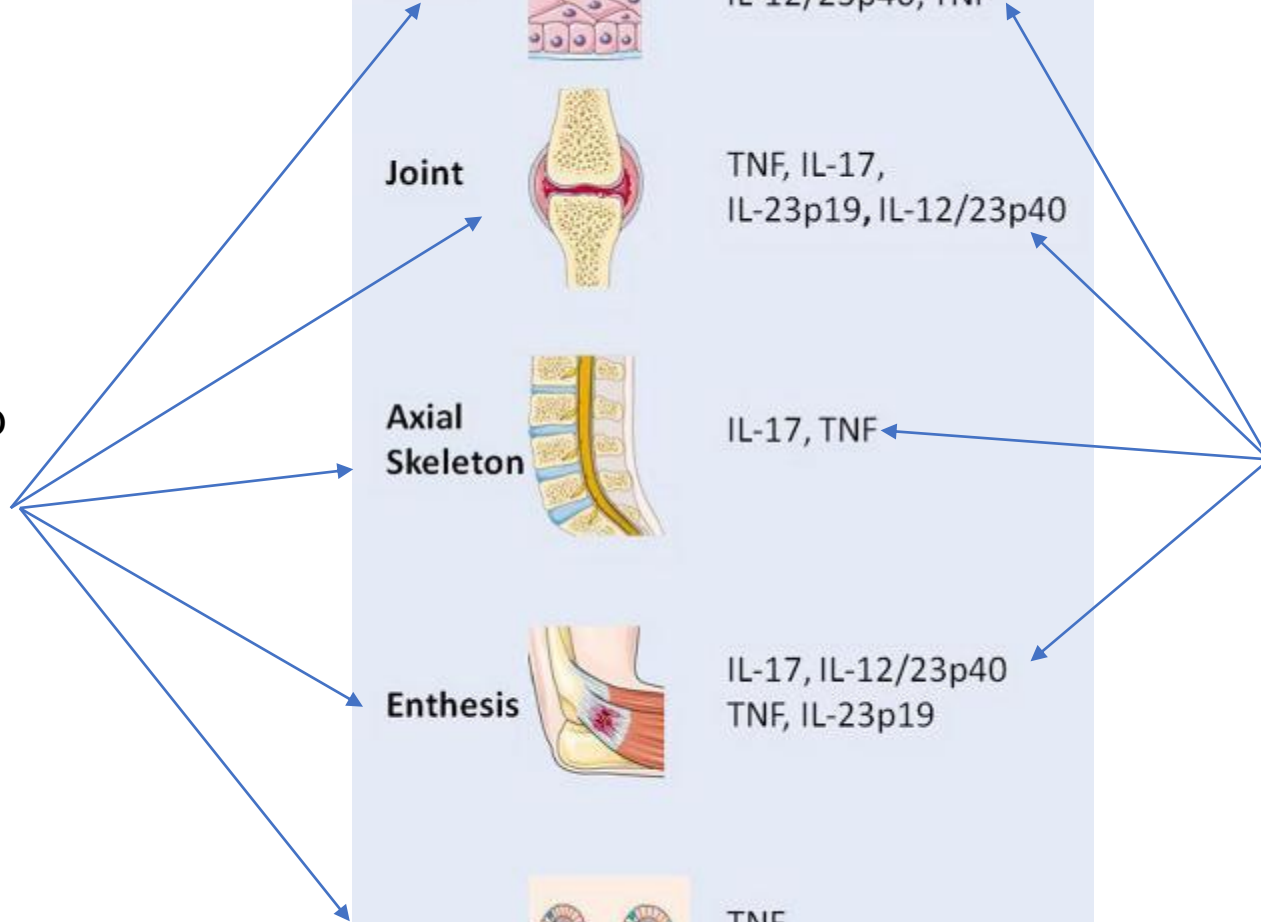
IL-17, IL-12/23p40  
TNF, IL-23p19

Gut

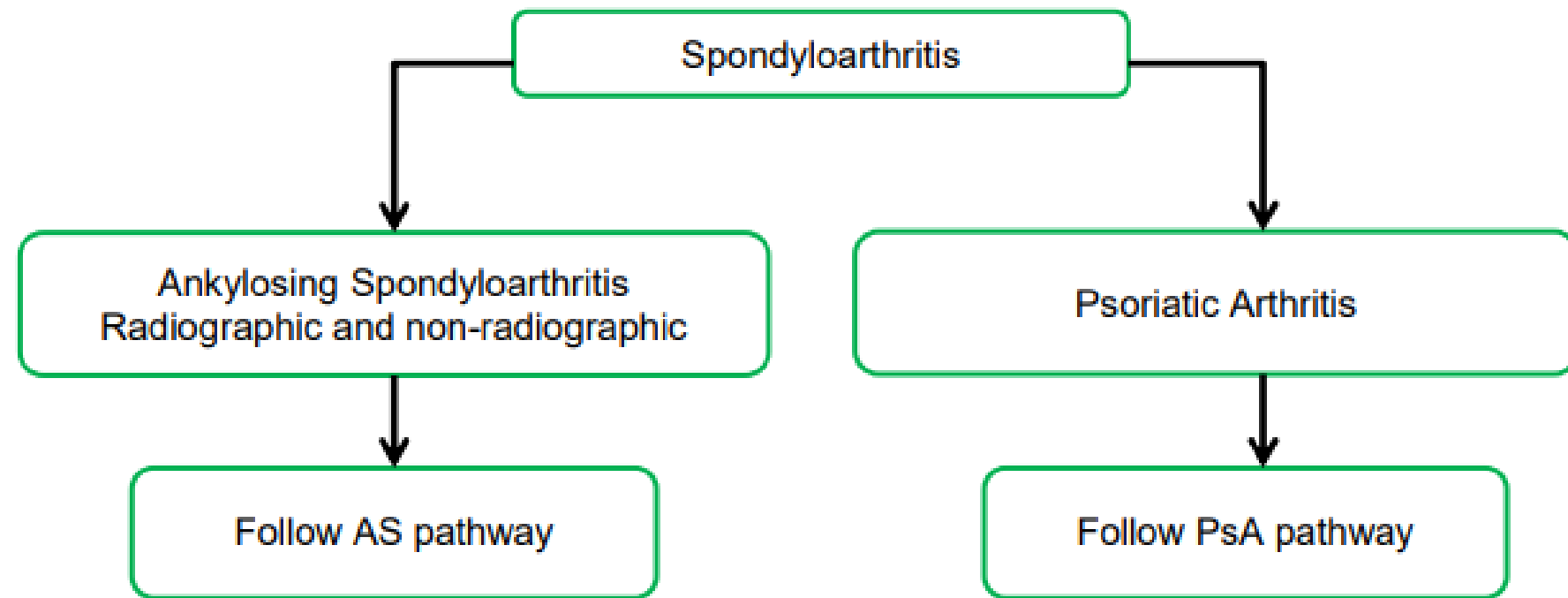


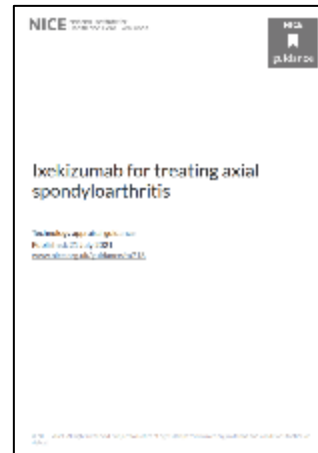
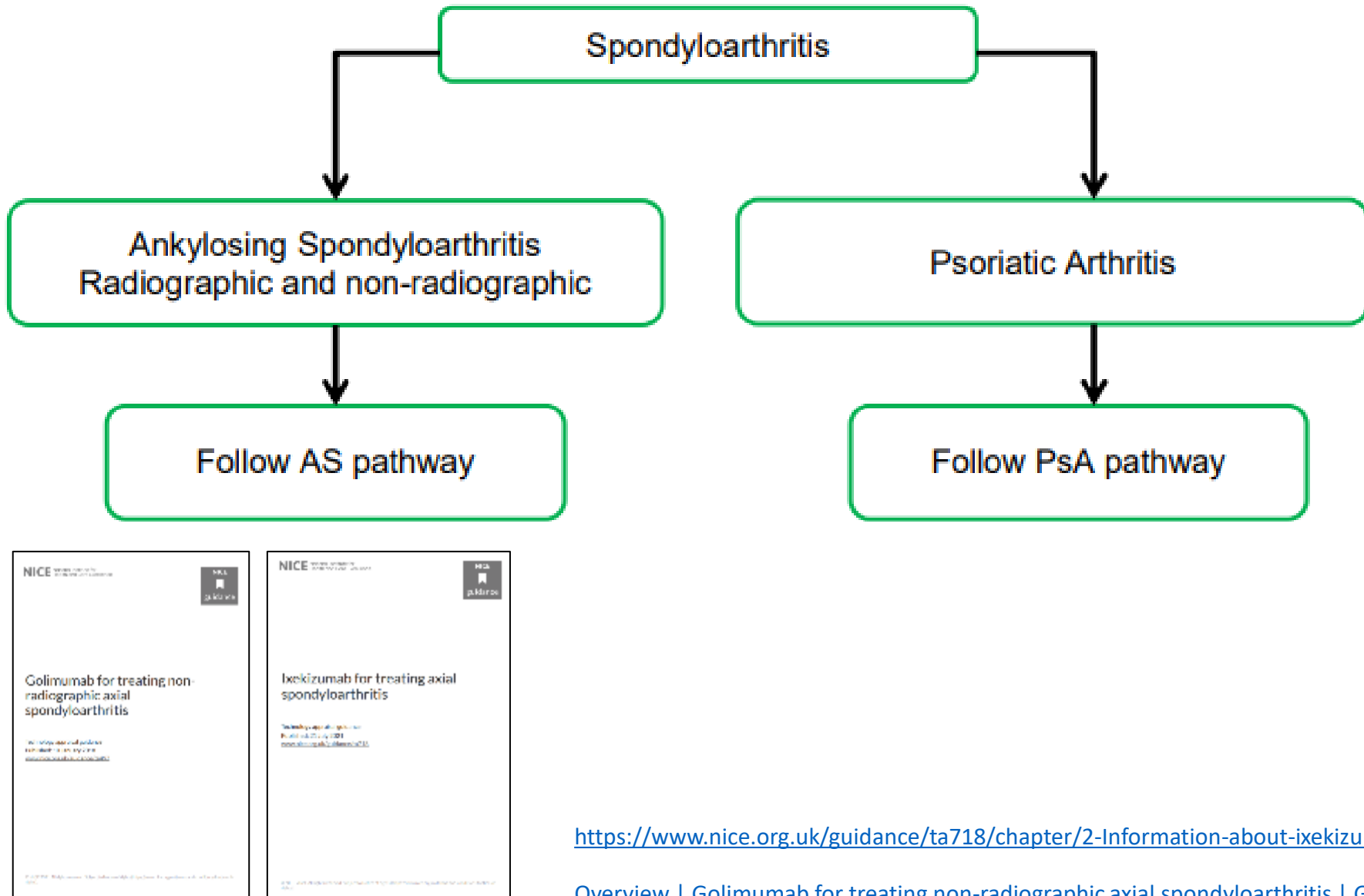
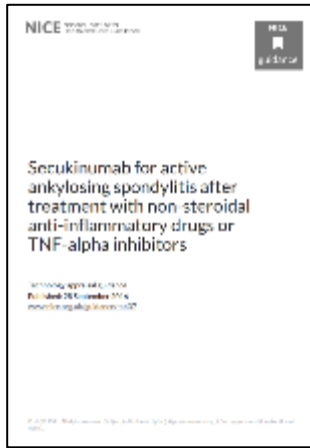
TNF  
IL-12/23p40, IL-23p19

Secukinumab  
Ixekizumab









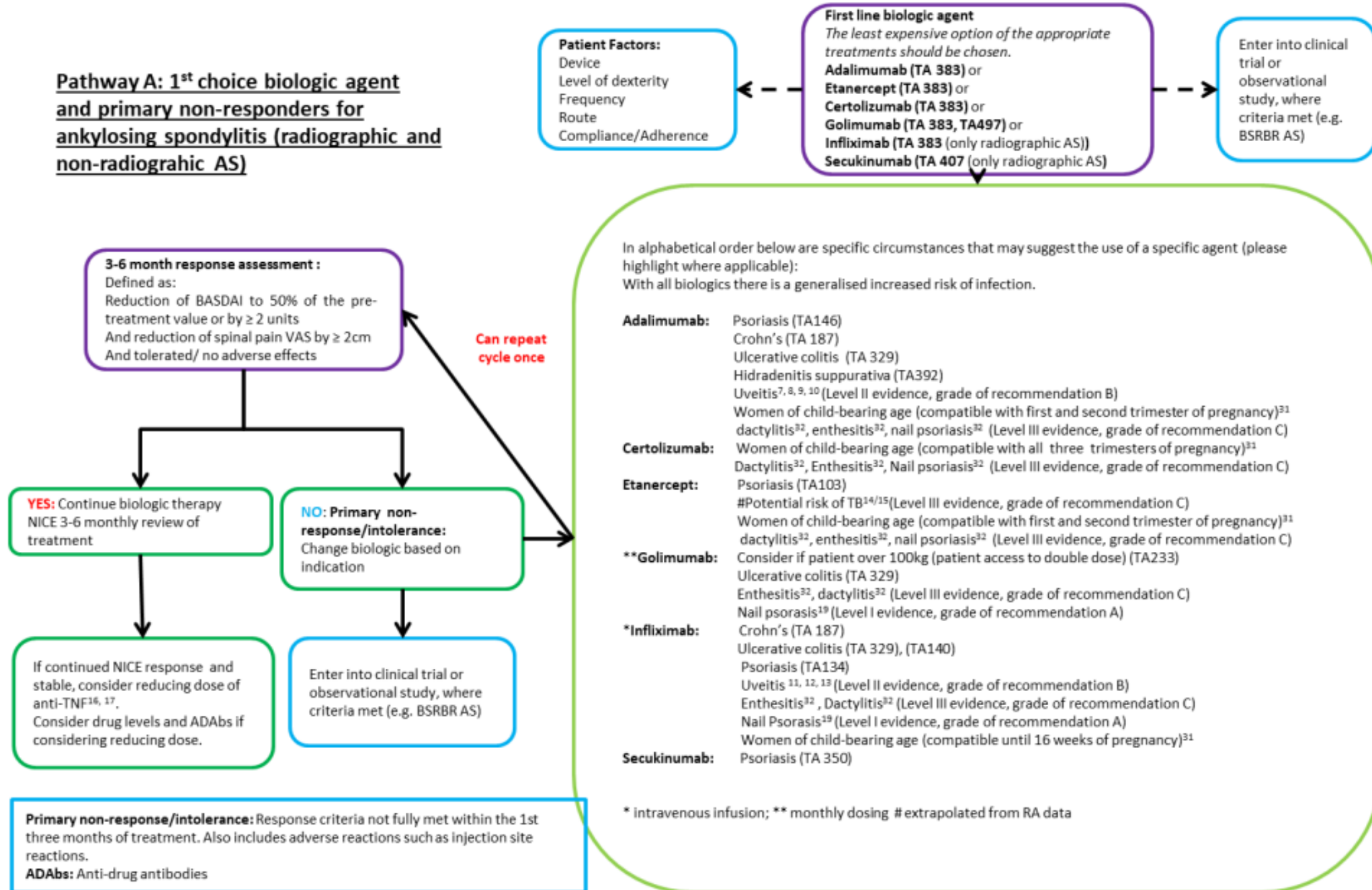
<https://www.nice.org.uk/guidance/ta718/chapter/2-Information-about-ixekizumab>

[Overview](#) | [Golimumab for treating non-radiographic axial spondyloarthritis](#) | [Guidance](#) | [NICE](#)

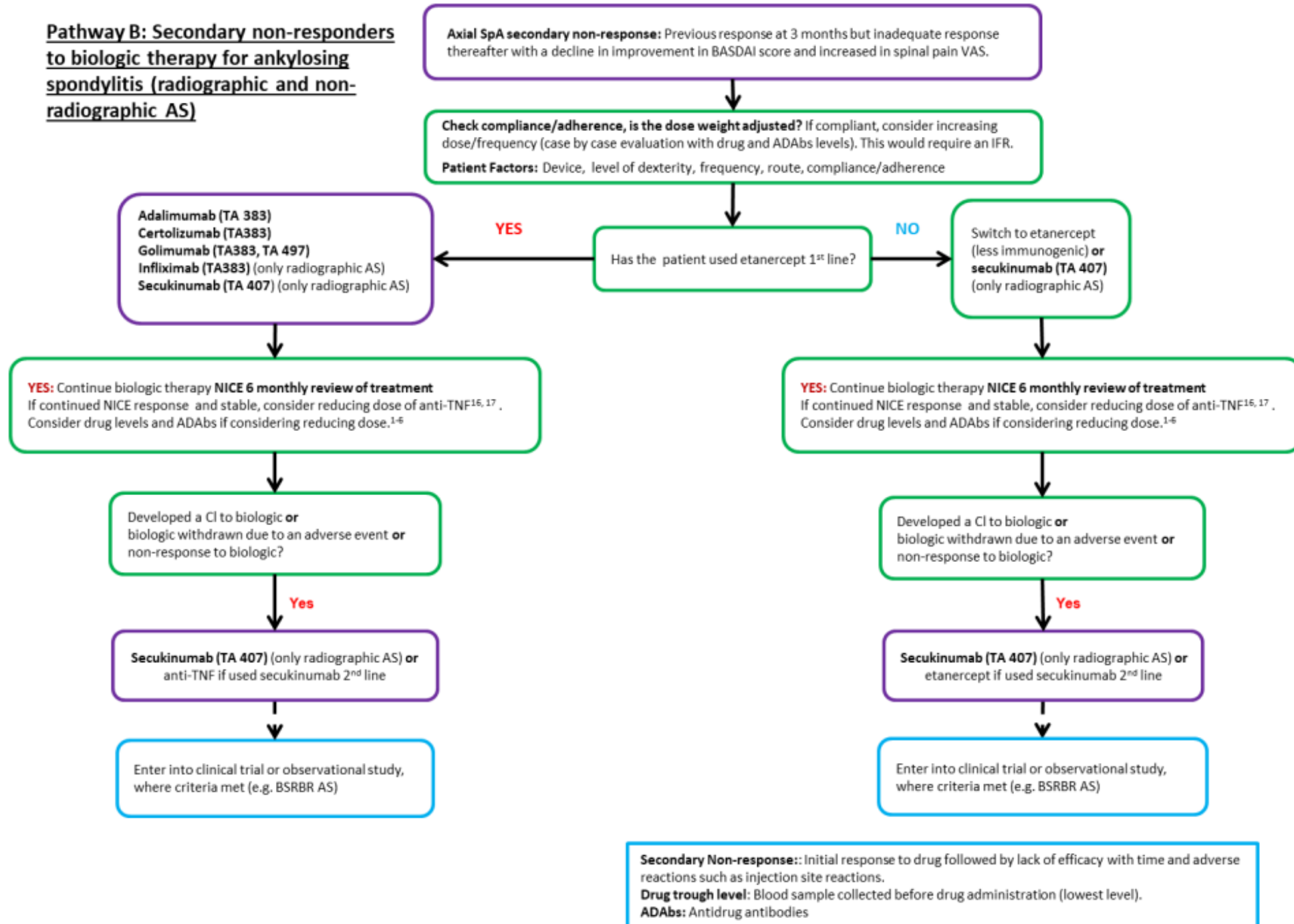
[Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors \(nice.org.uk\)](https://www.nice.org.uk/guidance/ta718)

[Update information](#) | [TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis](#) | [Guidance](#) | [NICE](#)

**Pathway A: 1<sup>st</sup> choice biologic agent  
and primary non-responders for  
ankylosing spondylitis (radiographic and  
non-radiographic AS)**



**Pathway B: Secondary non-responders to biologic therapy for ankylosing spondylitis (radiographic and non-radiographic AS)**



# TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis

Technology appraisal guidance [TA383] Published: 01 February 2016

[Guidance](#)[Tools and resources](#)[Information for the public](#)[Evidence](#)[History](#)

## History

A list of downloadable documents created during development.

### Expected publication

[Download](#) [Equality Impact Assessment \(Guidance development\)](#)  
PDF 187 KB

01 February 2016

### Appraisal consultation

Appraisal consultation

[Download](#) [Appraisal consultation document](#)  
PDF 240 KB

29 May 2015

[Committee papers information](#)

[Download](#) [Committee papers](#) PDF 24.2 MB  
29 May 2015

### Appeal

[Appeal](#)

[Download](#) [NICE Final scrutiny letter : Final scrutiny letter](#) PDF 82 KB  
24 November 2015

[Download](#) [NICE Initial scrutiny letter : Scrutiny letter](#) PDF 40 KB  
24 November 2015

[Download](#) [MSD Response to initial scrutiny letter : Response to scrutiny letter](#) PDF 56 KB  
24 November 2015

[Download](#) [MSD Appeal letter : Appeal letter](#) PDF 154 KB  
24 November 2015

### Final appraisal determination

[Final appraisal determination information](#)

[Download](#) [Final appraisal determination document](#)  
PDF 742 KB

11 September 2015

[Committee papers information](#)

[Download](#) [Committee papers](#) PDF 3.46 MB  
11 September 2015

Ankylosing spondylitis and axial spondyloarthritis (non-radiographic) - adalimumab, etanercept infliximab and



## Tofacitinib for treating active ankylosing spondylitis [ID3865]

In development [GID-TA10771] Expected publication date: 17 August 2022

### Project information

Suggested title: To appraise the clinical and cost effectiveness of tofacitinib

Status	In progress
Process	STA 2018
ID number	3865

### Provisional Schedule

Committee meeting: 1	09 June 2022
Expected publication	17 August 2022

### Project Team

Project lead	Thomas Filer
--------------	--------------

### Email enquiries

If you have any queries please email: [taficer1@nhs.uk](mailto:taficer1@nhs.uk)

## Upadacitinib for treating active ankylosing spondylitis [ID3848]

In development [GID-TA10735] Expected publication date: 17 August 2022

### Project information

Suggested title: To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy

Status	In progress
Process	STA 2018
ID number	3848

### Provisional Schedule

Committee meeting: 1	09 June 2022
Committee meeting: 1	09 June 2022
Expected publication	17 August 2022

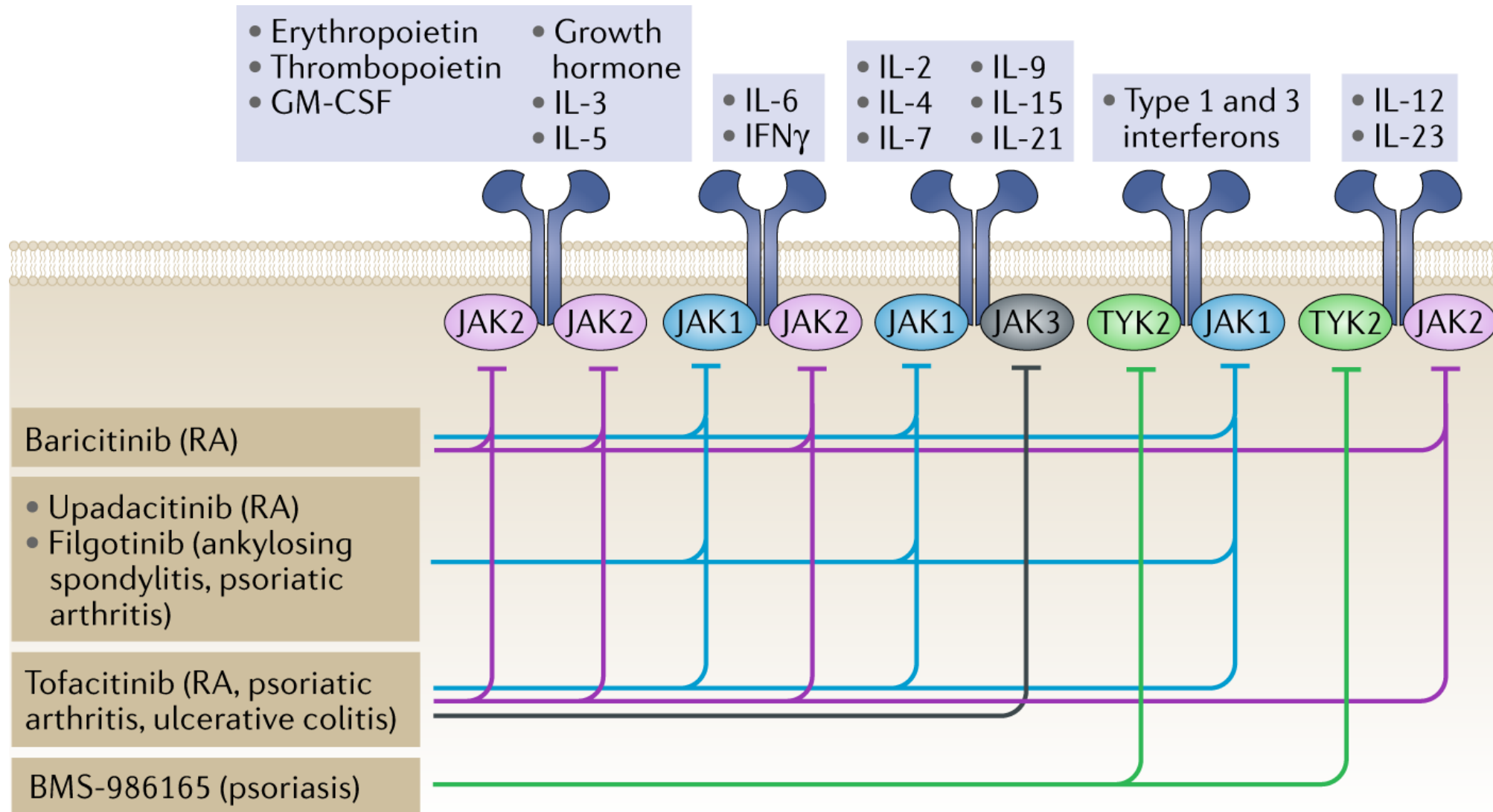
### Project Team

Project lead	Daniel Davies
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<https://www.nice.org.uk/guidance/indevelopment/gid-ta10771>

# Janus-associated tyrosine kinase JAK1.

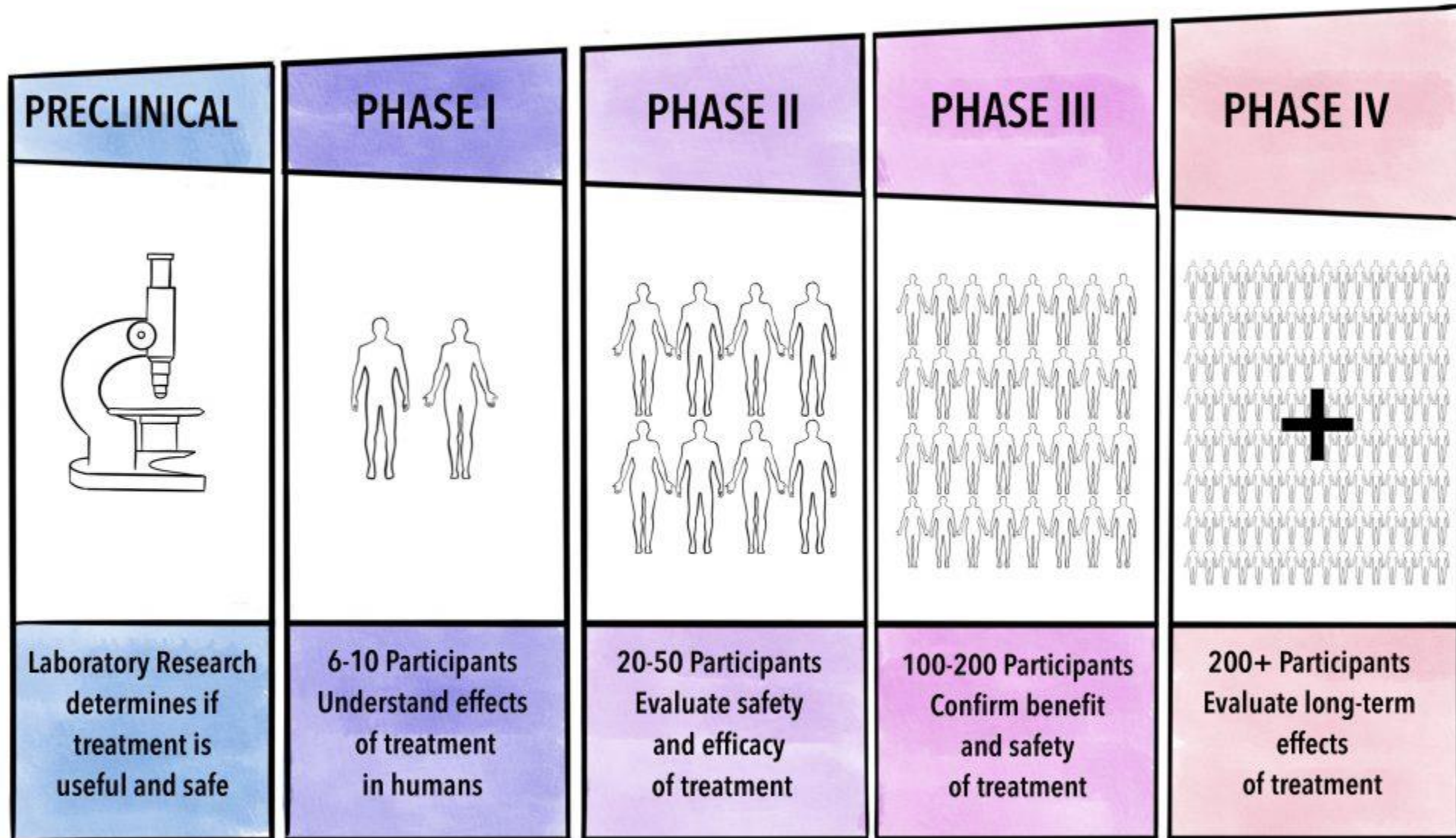


# Terminology

Treatment response to biologics and targeted synthetic disease-modifying antirheumatic drugs in rheumatoid arthritis (RA) patients can be classified as primary or secondary non-response, based on evidence of an initial response






- **Primary Non Responders-** primary non-response is generally considered if the drug was ineffective, with no clinical response within the initial treatment period
- **Secondary Non Responders-** secondary non-response would be considered if, after an initial response, the effectiveness is lost over time

# Clinical Trials





Overview of the development, pricing, licensing and appraisal processes for new drugs

PRECLINICAL	PHASE I	PHASE II	PHASE III	PHASE IV
				
Laboratory research determines if treatment is useful and safe	6-30 Participants: Understand effects of treatment in human	20-50 Participants: Evaluate safety and efficacy of treatment	100-300 Participants: Confirm benefit and safety of treatment	200+ Participants: Determine long-term effects of treatment



Drug discovery	<ul style="list-style-type: none"><li>Pharmaceutical companies (and others, including research institutes) screen molecules or develop and test new complex molecules to find those that might have a positive effect for a disease.</li></ul>
Animal testing and clinical trials	<ul style="list-style-type: none"><li>Pharmaceutical companies test drugs in labs, first in animals and then in humans to ensure safety and assess their therapeutic effects. In England, the Medicines and Healthcare products Regulatory Agency (MHRA) oversees this.</li></ul>
Marketing authorisation	<ul style="list-style-type: none"><li>For England, two licensing authorities, the MHRA and European Medicines Agency (EMA) assess safety, manufacturing quality and efficacy before deciding if a drug can be sold in the country.</li></ul>
Initial pricing decisions	<ul style="list-style-type: none"><li>At this stage, the pharmaceutical company typically decides what price they will set for a new drug on release in a new country.</li></ul>
Health technology appraisal	<ul style="list-style-type: none"><li>In England, the National Institute for Health and Care Excellence (NICE) assesses the drug's clinical and cost effectiveness given the price set by the manufacturer and evidence of its impact. At this stage, there may be negotiations on the price of the drug for the NHS.</li></ul>
Funding decision	<ul style="list-style-type: none"><li>NICE decides whether the NHS should pay for the drug and in what circumstances, eg, severity of illness. For drugs with a high budget impact, there is scope for further price negotiations on the price.</li></ul>
Drug available for NHS patients	<ul style="list-style-type: none"><li>Once a drug has received marketing authorisation, has been recommended by NICE, and there is an agreed price, it is then available to prescribe to patients.</li><li>In general, the NHS should make the drug available within three months after NICE's funding decision.</li></ul>





Drug information  
**Certolizumab pegol**

**CERTOLIZUMAB PEGOL**  
is used to treat rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis

**VERSUS**  
ARTHRITIS

Drug information  
**Etanercept**

**ETANERCEPT**  
is used to treat rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis

**VERSUS**  
ARTHRITIS

Drug information  
**Infliximab**

**INFLIXIMAB**  
is used to treat rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

**VERSUS**  
ARTHRITIS

Drug information  
**Adalimumab**

**ADALIMUMAB**  
is used to treat rheumatoid arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and psoriatic arthritis

**VERSUS**  
ARTHRITIS

Drug information  
**Golimumab**

**GOLIMUMAB**  
is used to treat rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis and juvenile idiopathic arthritis

**VERSUS**  
ARTHRITIS

## Biologic therapy for axial SpA (AS)



For anyone living with axial spondyloarthritis (AS)  
including ankylosing spondylitis (AS)



# Biologic Screening Referral

week month

month year

REFERRALS

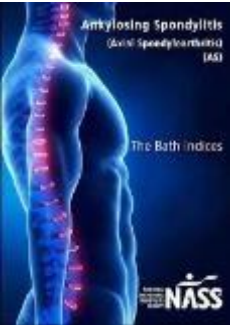
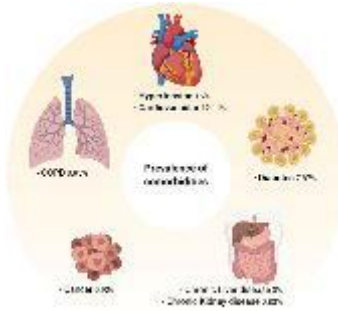
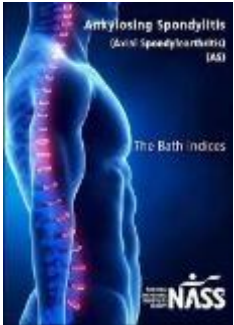


☒ **Pass**

☐ **Fail**

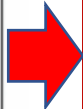


CRITERIA



CRITERIA

**FAIL**



**KEEP CALM AND REASSESS THE SITUATION**



# Top Tips and Questions to ask your Health Care Professional Team or pharmacist about side effects of your medications:

- What are common side effects?
- What are uncommon side effects?
- Can I consume alcohol while taking this? What might happen if I do?
- Should I report side effects if they persist?
- Are there alternative medications?
- Tell your Health Care Team about the medicines you are taking before starting a new one
- Tell your Health Care Team about any allergies you have
- Do not take expired medication
- Take your medication on time
- Store your medication safely
- Mention any unexpected side effects to your doctor
- Unexpected side effects, while not common, can occur. In the case of an emergency, call 111





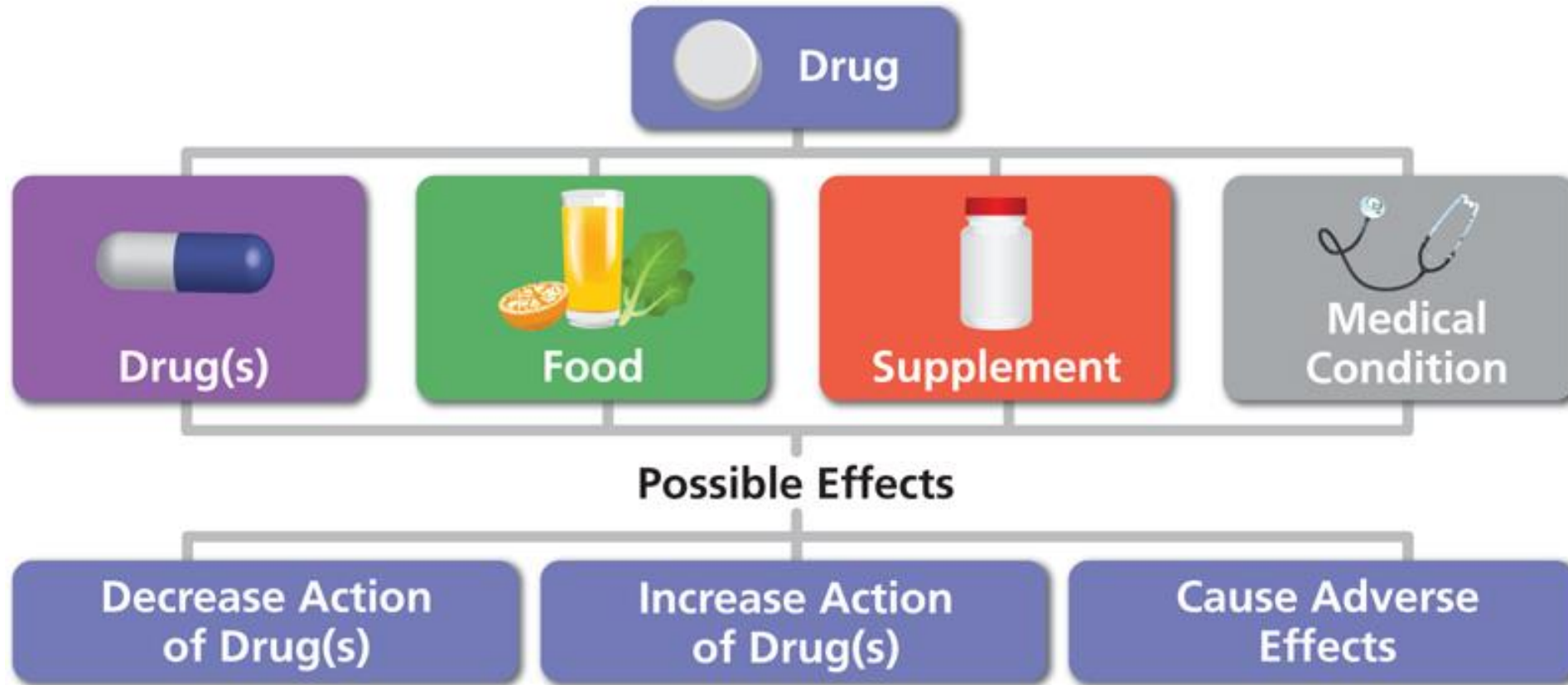
# Opinion of others- here say!

Translates to



John

# Drug Interaction



## Paracetamol

<p>The interactions content in BNF publication has changed. Find out more.</p>	
<p>Paracetamol</p>	<p><b>Adverse effects</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Contraindications</p>	<p><b>Contraindications</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Interactions</p>	<p><b>Interactions</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Pharmacokinetics</p>	<p><b>Pharmacokinetics</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Pharmacodynamics</p>	<p><b>Pharmacodynamics</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Precautions</p>	<p><b>Precautions</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Concomitant use</p>	<p><b>Concomitant use</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Concomitant use</p>	<p><b>Concomitant use</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Concomitant use</p>	<p><b>Concomitant use</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>
<p>Concomitant use</p>	<p><b>Concomitant use</b></p> <p>The interactions content in BNF publication has changed. Find out more.</p>

<https://www.webmd.com/interaction-checker/default.htm>

<https://bnf.nice.org.uk/interaction/>

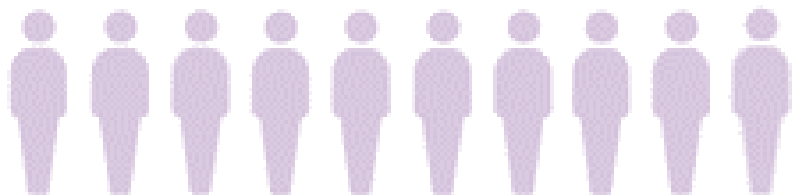


# Frequency of adverse drug reactions

- Very common 1 in 10
- Common (frequent) 1 in 100 + < 1 in 10
- Uncommon (infrequent) 1 in 1000 + < 1 in 100
- Rare 1 in 10,000 and < 1 in 1000
- Very rare < 1 in 10,000



1 in 10



1 in 100



1 in 10



1 in 100

1 in 1000



1 in 1000



**Seeing a  
shooting star**  
**1,000-1**



# Risk of Infection

All biologics suppress the immune system and increase the risk of infections.

- Common infections.** People who take biologics are more likely to get infections such as upper respiratory infections, pneumonia, urinary tract infections, and skin infections.

- Opportunistic infections.** These types of infections are less common in healthy people and more common in people whose immune systems do not work correctly.

Examples of opportunistic infections include Hepatitis B, Tuberculosis (TB), and fungal infections

Research suggests the risk of infection is greatest during the first 6 months after starting TNF inhibitors, which are the most commonly used type of biologic. People taking any biologic are encouraged to report any suspected infection to their doctors.

If a person who is taking biologics and gets an infection, a doctor will typically recommend that the person stop taking the biologic until the infection is cleared. Medical treatment may be required to clear the infection.

# Reducing infection risk



Eat a heart-healthy diet.



Limit your alcohol intake.



Be physically active.



Don't smoke – or use any form of tobacco.



Make your home smoke-free.



## Help Prevent Food Poisoning



Wash hands before and after preparing food.

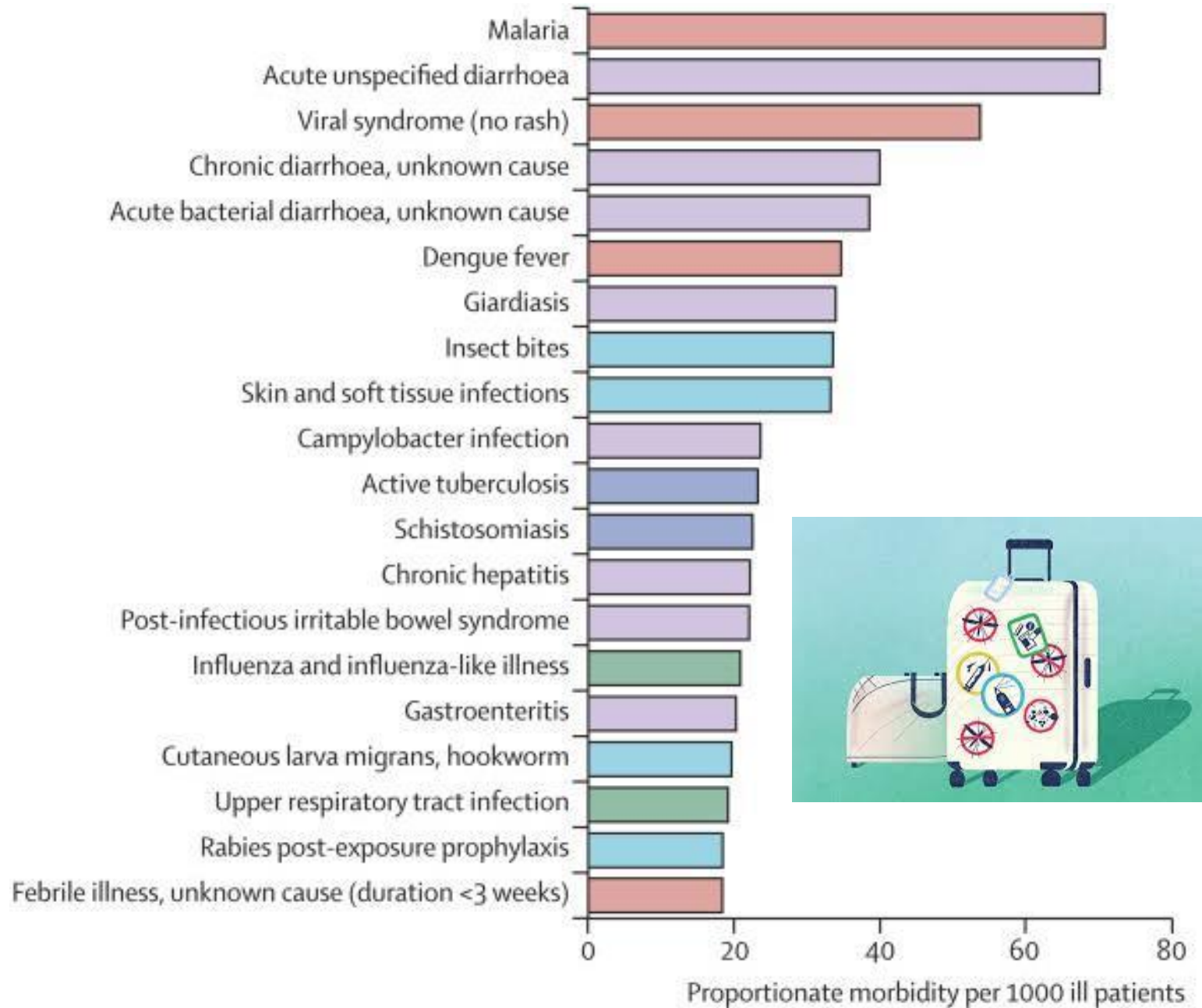


Cook meat, poultry, fish, and eggs thoroughly.



Wash fruits and vegetables well before eating.

# Infectious diseases



# Allergic Reactions

After taking a biologic it is possible to experience allergic reactions and even anaphylactic shock.

- A severe allergic reaction to an infusion is most likely to result in trouble breathing, chills, redness, and/or itchiness—including itchy eyes and lips.
- A mild allergic reaction to a biologic injection is most likely to cause redness, itchiness, and/or warm and tender skin around the injection site. Some people also experience a full-body rash.

***Any signs of an allergic reaction should be reported to a doctor right away.***

# Other Side Effects

**In addition to allergic reactions, patients may experience:**

- Feeling of weakness
- Diarrhoea and/or constipation
- Nausea
- Vomiting
- Coughing

**Other, less common, side effects include:**

- Vision problems
- Numbness or tingling
- Swelling of the ankles and/or hands
- Mood/ depression
- Joint pain
- A rash across the face and/or chest that gets worse in the sun

***Doctors are unable to predict who will experience which side effects from biologics. People starting on any new drug are encouraged to report all side effects to their doctors***



# Cancer Risk

People with inflammatory arthritis are at an increased cancer risk. Many experts worry that taking biologics, particularly TNF inhibitors, could increase this risk.

However, clinical studies suggest that TNF inhibitors do not significantly increase the risk of cancer.

TNF inhibitors do seem to increase the risk of nonmelanoma skin cancer (basal and squamous cell).



Eat a heart-healthy diet.



Limit your alcohol intake.



Be physically active.



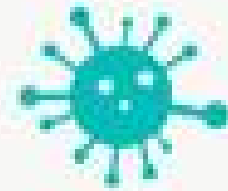
Don't smoke – or use any form of tobacco.



Make your home smoke-free.



Avoid too much sun and use protection.



**Take part in cancer-screening programs.**

# Adverse reactions to drugs

## Yellow card scheme

[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

<https://yellowcard.mhra.gov.uk/>

The screenshot shows the Yellow Card reporting website. The header is yellow with the 'Yellow Card' logo and a search bar. A navigation menu includes links for Home, About Yellow Card, FAQs, Resources, Campaigns, Drug Analysis Profiles, and Contact Us. A banner below the menu states: 'Use the Coronavirus Yellow Card reporting site to report suspected side effects to medicines and vaccines or medical device and diagnostic adverse incidents used in coronavirus treatment.' The main content area is titled 'Welcome to the reporting site for the Yellow Card scheme' and 'Report a suspected problem or incident:'. It features several buttons for reporting: 'COVID-19' (yellow), 'Side effects' (yellow), 'Devices' (blue), 'Defective' (purple), 'Fake' (green), and 'e-cigarette' (orange). A link for 'Not sure which option to select? Help us guide you' is also present. On the right side, there is a section for 'Download the Yellow Card App!' and a 'Sign in / Register' section with fields for email and password, and a 'Login' button. At the bottom, there is a disclaimer: 'We cannot give you medical advice. If you are worried about your health: 1. Talk to your doctor, pharmacist or nurse. 2. Call the NHS. (Telephone 111)'. It also mentions that users can use the NHS 111 British Sign Language service available in their country. A footer note states: 'Always read the patient information leaflet, or instructions supplied with your medicine or medical device. It lists the known side effects or problems and advises you on what to do.'



Drug Information  
**Infliximab**

**INFLIXIMAB**  
is used to treat rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.

**VERSUS ARTHRITIS**



**STOP**



# 5 Tips For Medication Management

**1**

**Understand the Medication**  
Do your own research. Know the name of the medication you or your patient is taking, the dosage, possible side effects and why it has been prescribed.

**3**

**Keep Medical Records**  
Keep a written history of all medications and dosages, immunizations, surgeries, allergies, and a family health record.

**5**

**Be Health-Conscious**  
Inform your doctor about your eating habits, alcohol consumption, smoking, or any other drug use. Make the best choices you possibly can to reduce risk of complications.

**2**

**Follow the Directions**  
Following the directions for medication prescriptions will increase effectiveness. Make sure that you or your patient takes the appropriate dosage and at the correct time. In terms of complications, certain foods and other drugs should be avoided while taking some prescriptions.

**4**

**Watch for Changes**  
Be aware of any social, sleeping, work, or diet changes that you or your patient experiences on new medications. Symptoms and side effects can be minor and disappear within a few weeks or they can continue and present severe issues.



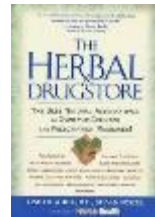
**Drug Allergy**

**PATIENT ALERT CARD**

**XELJANZ<sup>®</sup>**  
(tofacitinib citrate)

▼ New medication product is subject to additional monitoring. The well observed identification of new safety information. You can help by reporting any side effects you may get. If you get any side effects, talk to your doctor, pharmacist or nurse. Reporting form and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store. Any suspected adverse reaction may also be reported to Pharm Meds Information on 01204 616161.

PP-XEL-GBR-2043 | January 2020



# Injection Phobia and Injection site pain





## Tips for Overcoming Fear of Self-Injection

Take deep  
breaths

Ask a loved  
one for help

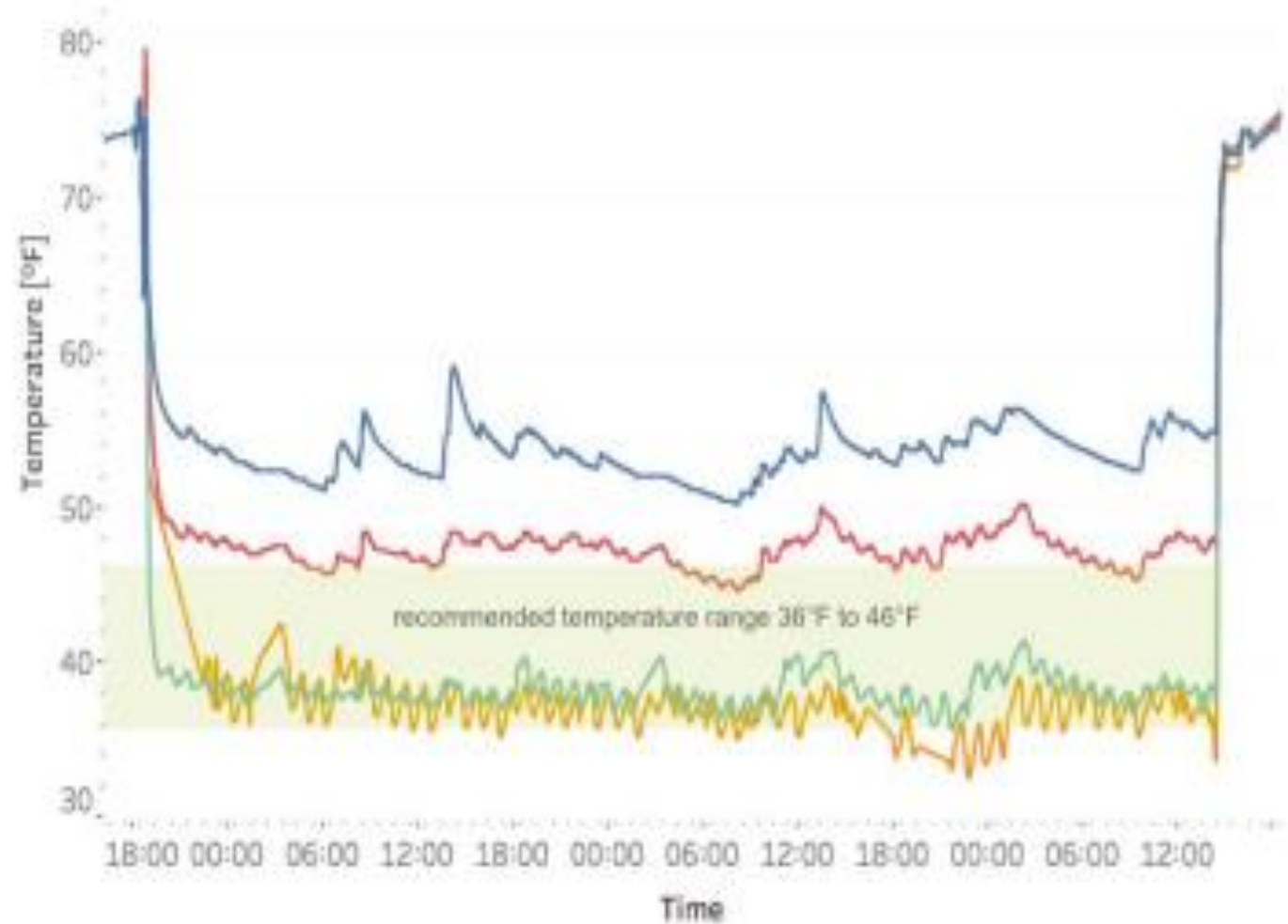
Practice with an  
empty syringe

Ask about an  
autoinjector

Don't inject the  
same site each time



# Storage most injectable (2°C-8°C/36°F-46°F)



# Removal from Fridge



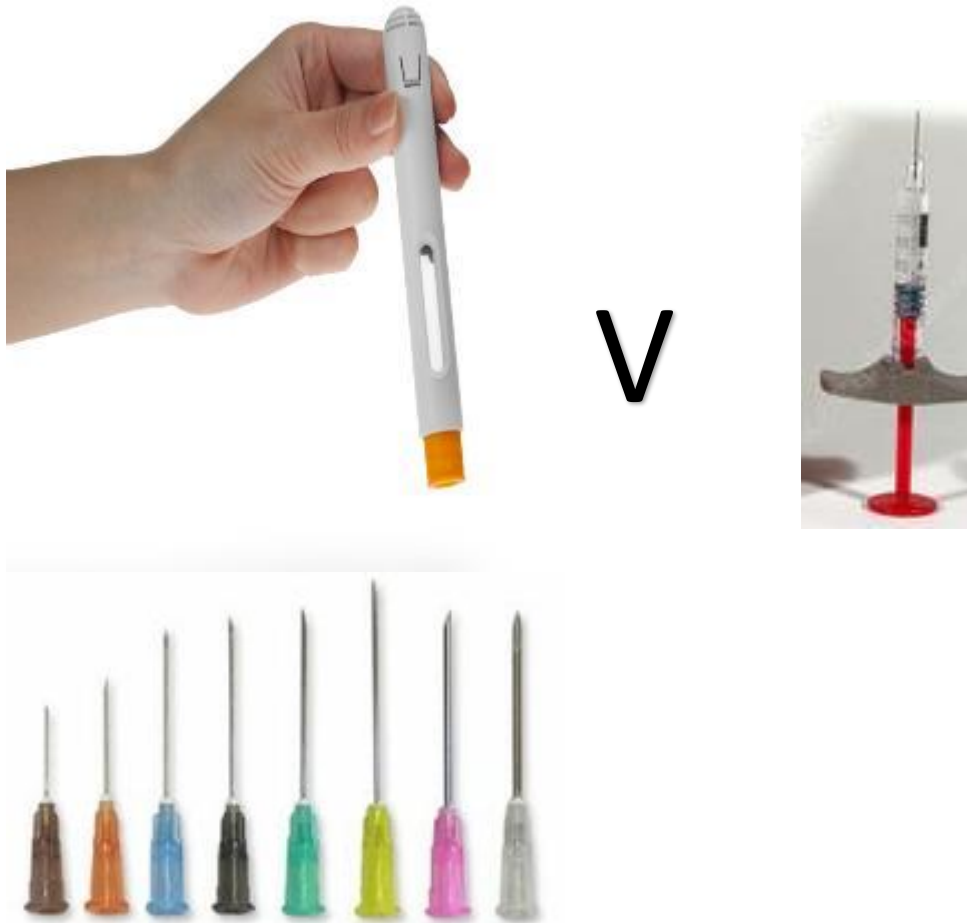
# Select right time for yourself



# V



# Most Biologic Therapies for Ankylosing Spondylitis are Auto injectors

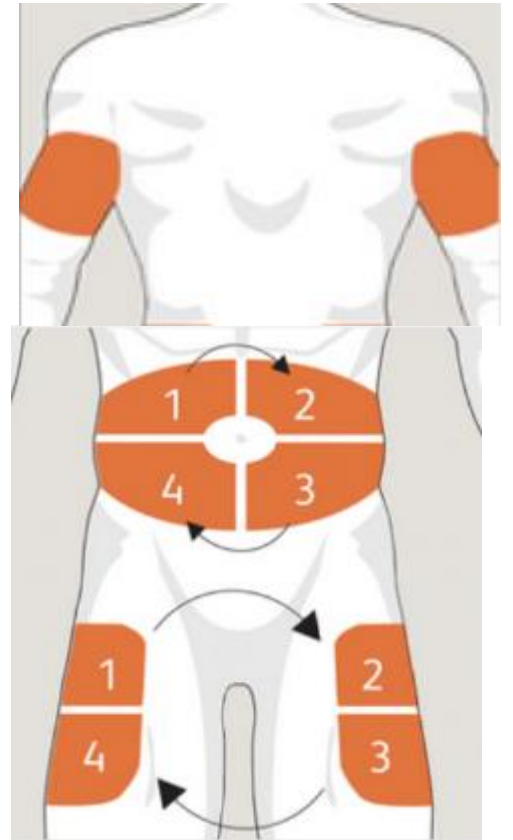
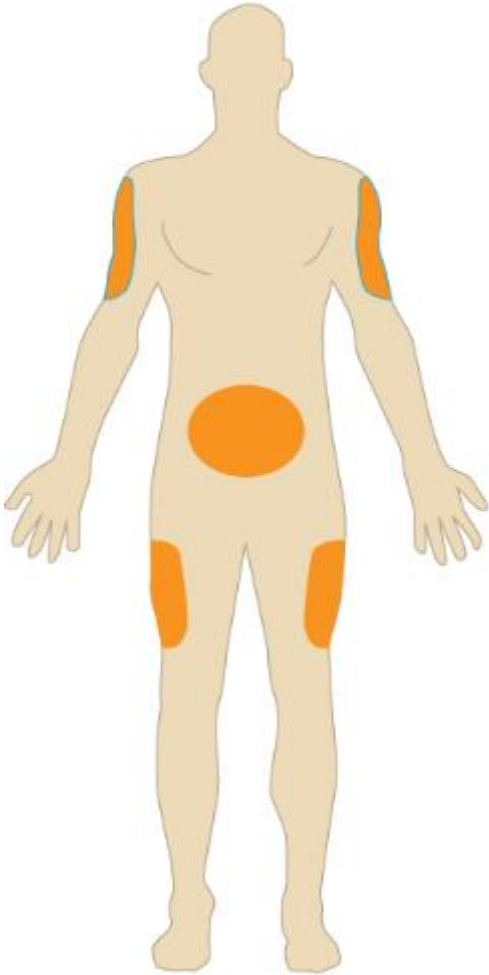


# Injection site selection

## When injecting

Avoid the bellybutton and waistline areas.

Stay away from body areas with scar tissue, stretch marks, visible blood vessels and any areas that are tender, red, or bruised.



To limit pain, bruising, and scarring, don't give the injection in the same place every time. Instead, rotate injection sites regularly. Each time, you should be at least an inch or two away from the previous injection site. A calendar or smartphone can help you keep track of injection sites.



# Numb the Injection Site

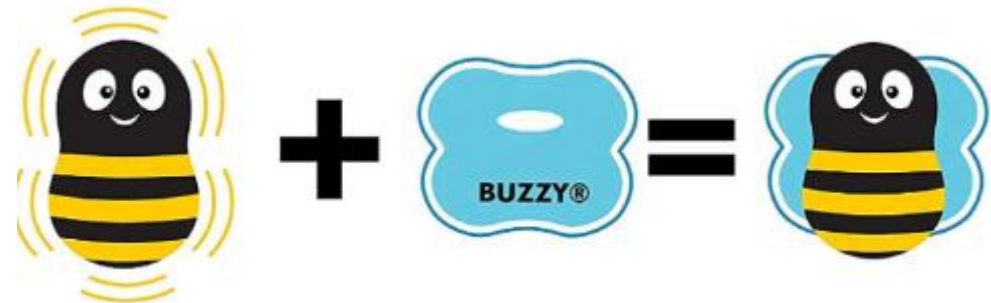
If you are worried about pain and discomfort during the injection, take some time to numb the area before injecting.



One of the easiest ways to do this is with an ice cube  
Prescription topical anaesthetic cream containing lidocaine



Another option is trying a tool called [Buzzy](#).  
This device combines ice and vibration to initiate non-pain nerve signals that get sent to the brain. Because the brain is receiving all of these overwhelming messages, pain signals can't be singled out and are, therefore, dulled.



Citrated V Non Citrated Injections

# Injection site reactions



Ask your local chemist about



# When to talk about switching medication ?

