Rheumatologic Pharmacology & DMARDs

A Clinical Guideline Synthesis for Australian Practice

Australian Clinical Context

~2% prevalence of Rheumatoid Arthritis in the general population.

Higher prevalence, earlier onset, and greater severity in Aboriginal and Torres Strait Islander communities.

Access to advanced bDMARDs/tsDMARDs is PBS-gated: prescription strictly requires documented failure or intolerance of conventional therapies.

The DMARD Universe Taxonomy

csDMARDs
Conventional Synthetic

- Methotrexate (Anchor)
- Sulfasalazine
- Leflunomide
- Hydroxychloroquine

bDMARDs
Biologics

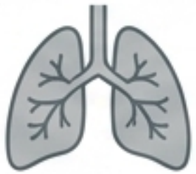
- **TNF:** Adalimumab, Etanercept, Infliximab
- **IL-6:** Tocilizumab, Sarilumab
- **IL-17:** Secukinumab, Ixekizumab
- **IL-23:** Guselkumab, Risankizumab

tsDMARDs
Targeted Synthetic (JAKi)

- Tofacitinib
- Baricitinib
- Upadacitinib

PBS Sequencing Constraint: csDMARD failure is mandatory before biologic or tsDMARD initiation.

The Pre-Treatment Safety Gateway



Tuberculosis (TB)

Test: IGRA ± CXR (No TST on biologics).
Action: If latent, commence prophylaxis (e.g., isoniazid 6–9 months) before threshold.

Hepatitis B & C

Test: HBsAg, core/surface Abs, HCV RNA.
Action: DAA therapy or antiviral prophylaxis (entecavir) before threshold.

Strongyloides

Test: Serology (critical in QLD/NT/Pacific demographics).
Action: Ivermectin 200 mcg/kg daily x 2 days to prevent **fatal** hyperinfection.

Live Vaccines

Test: Assess status (MMR, Yellow Fever).
Action: Administer prior; **strictly contraindicated** once on therapy.

TREATMENT THRESHOLD: Do NOT
Do NOT initiate bDMARD/tsDMARD therapy until cleared.

Methotrexate: The Foundational Anchor

Clinical Parameters

Target Dose: 15–25 mg/week (Oral or Subcutaneous).

Optimization: Subcutaneous route offers better bioavailability and less GI side effects.

Toxicity Management: Hold therapy if LFTs >3x ULN or if significant cytopenias occur.

CRITICAL SAFETY ALERT: Methotrexate is **strictly ONCE WEEKLY.** Daily dosing is a potentially fatal prescribing error. **Never prescribe on the same day as folic acid.**

The Conventional Synthetic Arsenal (csDMARDs)

Sulfasalazine

Dosing: Start 500 mg daily, titrate to max 3 g/day (in divided doses).
Monitoring: FBC and LFTs required initially, then 3-monthly.
Note: Adequate fluid intake is highly required.

Leflunomide

Dosing: Maintenance dose of 10–20 mg daily.
Monitoring: Blood pressure, FBC, and LFTs.
Alert: Teratogenic (Category X). Requires rapid washout with cholestyramine if cessation is needed.

Hydroxychloroquine (HCQ)

Dosing: ≤5 mg/kg actual body weight daily (typically 200–400 mg).
Monitoring: High risk of irreversible retinal toxicity.
Action: Requires baseline ophthalmology exam and annual exams after 5 years of use.
Note: Safe for use in pregnancy.

Biologic DMARDs: Cytokine Targets

TNF Inhibitors

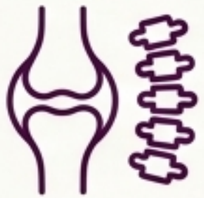
Adalimumab **Etanercept** **Infliximab**

First-line biologics post-csDMARD failure. Significant risk of serious bacterial infections and TB reactivation. Avoid in severe heart failure (NYHA III/IV).

IL-6 Inhibitors

Tocilizumab **Sarilumab**

Clinical Trap: Masks severe infection by artificially suppressing CRP and fever. Clinicians must actively monitor lipids and watch for gastrointestinal perforation.



IL-17 Inhibitors

Secukinumab **Ixekizumab**

Heavy utilization in the treatment pathways for Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS).

IL-23 Inhibitors

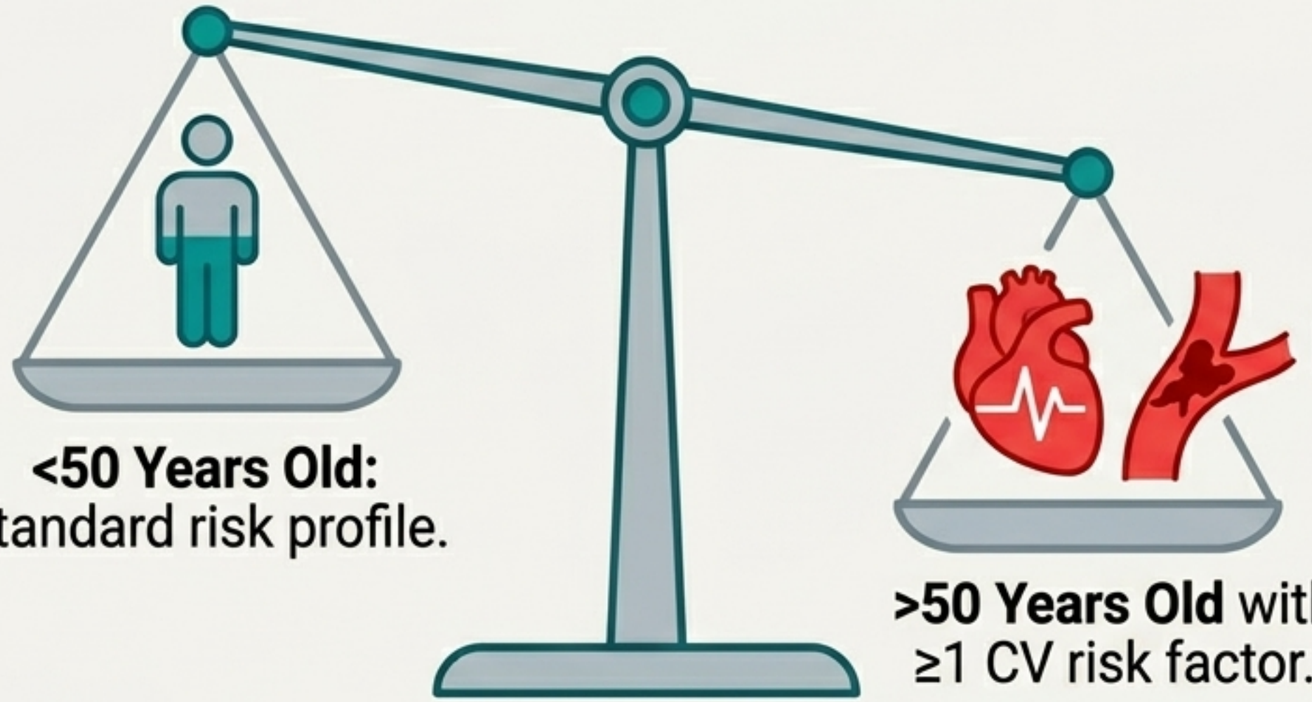
Guselkumab **Risankizumab**

Highly targeted agents, primarily utilized within the Psoriatic Arthritis (PsA) demographic.

Targeted Synthetics: JAK Inhibitors

Tofacitinib **Baricitinib** **Upadacitinib**

Oral agents requiring strict renal dose adjustments.



<50 Years Old:
Standard risk profile.

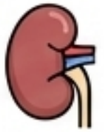
>50 Years Old with ≥1 CV risk factor.

BOXED WARNING:

In **patients >50 with CV risks,** JAK inhibitors carry an increased risk of **Major Adverse Cardiovascular Events (MACE)**, **Venous Thromboembolism (VTE)**, and **malignancy** compared to TNF inhibitors. Use only after TNFi failure in this cohort.

Vaccination Gateway: High risk of Herpes Zoster. Recombinant zoster vaccine (Shingrix®) is strongly recommended BEFORE initiating therapy in patients ≥50.

The Routine Monitoring Matrix

Biological Test	Frequency	Drug Triggers	Action Thresholds
 **FBC**	Every 3 months	MTX, LEF, SSZ, JAKi	Hold therapy if WCC <3.5 or Platelets <100.
 **LFTs (ALT/AST)**	Every 3 months	MTX, LEF, SSZ	Hold if >3x Upper Limit of Normal (ULN); recheck in 2–4 weeks.
 **eGFR / Creatinine**	Every 3–6 months	All DMARDs, csDMARDs, bDMARDs, tsDMARDs	Adjust dose strictly per specific product characteristics.
 **Lipids**	Baseline, 3 months, then annually	IL-6 inhibitors, JAK inhibitors	Manage per standard Cardiovascular risk protocols.
 **Blood Pressure**	Every clinical visit	JAK inhibitors, Leflunomide	Manage hypertension proactively.

Special Populations: Diagnostic Stoplight Matrix

Pregnancy & Breastfeeding	Renal Impairment (<30 eGFR)	Hepatic Impairment
Safe: HCQ, Sulfasalazine (Note: male partners must stop SSZ 3 months pre-conception).		
Caution: TNF inhibitors (stop by 20 weeks unless Certolizumab pegol).	**Caution:** MTX (dose reduce if eGFR 30–50).	**Caution:** TNF inhibitors (rare hepatotoxicity).
Avoid: Methotrexate, Leflunomide (Category X teratogens).	**Avoid:** MTX, NSAIDs, Baricitinib, Tofacitinib.	**Avoid:** MTX (in alcohol use disorder/active disease), Leflunomide (if ALT >2x ULN).

Culturally Safe Care: First Nations Health Context