

# Disease-modifying antirheumatic drugs (DMARDs) for rheumatoid arthritis<sup>1-5</sup>

Drug (Brand name) and dose	Contraindications	Toxicities that need monitoring	Monitoring
<b>Conventional DMARDs</b>			
<p><b>Methotrexate</b> (Ledertrexate, Methoblastin) 5–10 mg orally <b>once a week</b>, increase by 2.5–10 mg every 4–6 weeks to maximum 15–25 mg <b>once a week</b> Use with folic acid 5 mg orally once or twice a week (preferably not on day of methotrexate)</p>	Hypersensitivity to methotrexate, severe renal or hepatic disease, infection, myelosuppression, neoplastic disorder, alcohol dependence, poor nutrition, immunodeficiency syndrome, peptic ulceration or ulcerative colitis, pregnancy or lactation	Myelosuppression, abnormal LFTs, hepatotoxicity, nephrotoxicity, interstitial pneumonitis, pulmonary fibrosis	<ul style="list-style-type: none"> <li>Hepatitis B and C serology (high-risk patients) and chest X-ray at baseline</li> <li>FBC, LFTs and urinalysis at baseline, monthly for the first 6 months, then every 1–2 months</li> <li>FBC and LFTs at least monthly if used with leflunomide, or with sulfasalazine and hydroxychloroquine</li> </ul>
<p><b>Sulfasalazine</b> (Pyralin EN, Salazopyrin EN) 500 mg orally daily, increase by 500 mg a week to maximum 3 g daily in divided doses</p>	Hypersensitivity to salicylates or sulfonamide derivatives	Myelosuppression, abnormal LFTs	<ul style="list-style-type: none"> <li>FBC and LFTs at baseline, monthly for the first 3 months, then every 3 months</li> </ul>
<p><b>Hydroxychloroquine</b> (Plaquenil) 400–600 mg orally daily in divided doses for 1–3 months (maximum 6 mg/kg/day), then 200–400 mg daily</p>	Hypersensitivity to quinolines, retinopathy, pregnancy	Retinal toxicity, haemolysis	<ul style="list-style-type: none"> <li>Ophthalmological review at baseline, then every year</li> <li>FBC after 1 week of treatment</li> </ul>
<p><b>Leflunomide</b> (Arabloc, Arava) 100 mg orally once daily for 3 days, then 10–20 mg once daily</p>	Hypersensitivity to leflunomide, renal or hepatic impairment, infection, history of toxic epidermal necrolysis or erythema multiforme (e.g. Stevens–Johnson syndrome), myelosuppression, immunodeficiency, pregnancy	Myelosuppression, abnormal LFTs, hepatotoxicity, severe skin reactions, interstitial pulmonary disease	<ul style="list-style-type: none"> <li>Hepatitis B and C serology (high-risk patients) at baseline</li> <li>FBC and LFTs at baseline, monthly for the first 6 months, then every 1–2 months</li> </ul>
<p><b>Azathioprine</b> (Azahexal, Azamun, Azapin, Imuran, Thioprine) 1 mg/kg orally daily, increase by 0.5 mg/kg/day over several weeks to maximum 2.5 mg/kg/day</p>	Hypersensitivity to azathioprine or mercaptopurine, porphyria, neoplastic disorder, infection	Myelosuppression, hepatotoxicity, nephrotoxicity	<ul style="list-style-type: none"> <li>Urinalysis at baseline</li> <li>FBC and LFTs at baseline, every 1–2 weeks during dose adjustment, then every 1–3 months</li> </ul>
<p><b>Cyclosporin</b> (Cicloral, Cysporin, Neoral, Sandimmun) 2.5–3 mg/kg orally daily in divided doses for 6 weeks, increase by 0.5–1 mg/kg daily every 1–2 months to maximum 5 mg/kg/day</p>	Hypersensitivity to cyclosporin, renal impairment, uncontrolled hypertension, malignancy, infection	Nephrotoxicity, hypertension, hyperkalaemia, abnormal LFTs	<ul style="list-style-type: none"> <li>Creatinine and blood pressure at baseline, every 2 weeks until dose is stable, then every 1–3 months</li> <li>FBC, LFTs and serum potassium at baseline, then periodically</li> </ul>

Drug (Brand name) and dose	Contraindications	Toxicities needing monitoring	Monitoring
<b>Conventional DMARDs (cont'd)</b>			
<b>Sodium aurothiomalate, injectable gold</b> (Mycocrisin) 1–5 mg intramuscularly, increase gradually at weekly intervals to 10 mg, 15 mg, 25 mg and 50 mg once a week, then reduce to every 2–4 weeks	Serious toxicity with gold, renal or hepatic impairment, history of myelosuppression or severe haematological disorders, severe or chronic skin conditions, systemic lupus erythematosus	Myelosuppression, proteinuria, hepatotoxicity, exfoliative dermatitis, interstitial pneumonitis, pulmonary fibrosis	<ul style="list-style-type: none"> <li>FBC, LFTs and urinalysis at baseline, every 1–2 weeks for the first 5 months, then monthly</li> <li>FBC and urinary protein excretion before each injection</li> </ul>
<b>Auranofin, oral gold*</b> (Ridaura) 6 mg orally daily, if no response after 6 months increase to maximum 9 mg daily in divided doses *Not commonly used in rheumatoid arthritis	As for injectable gold	As for injectable gold, but generally less toxic	<ul style="list-style-type: none"> <li>FBC, LFTs and urinalysis at baseline then every 1–3 months</li> </ul>
<b>Penicillamine*</b> (D-Penamime) 125 mg orally daily, increase by 125 mg daily every 6–8 weeks to maximum 1.5 g daily in divided doses *Not commonly used in rheumatoid arthritis	Hypersensitivity to penicillamine, haematological or renal toxicity with penicillamine, systemic lupus erythematosus	Myelosuppression, proteinuria, nephrotoxicity, hepatotoxicity	<ul style="list-style-type: none"> <li>FBC and urinalysis at baseline, every 2 weeks until dose is stable, then every 1–3 months</li> </ul>
<b>Biological DMARDs</b>			
<b>TNF-alpha inhibitors</b> <b>Etanercept</b> (Enbrel) 50 mg subcutaneously once a week or 25 mg twice a week (3–4 days apart) <b>Infliximab</b> (Remicade) 3mg/kg by intravenous infusion, repeated after 2 and 6 weeks, then every 8 weeks <b>Adalimumab</b> (Humira) 40 mg subcutaneously every 2 weeks May increase to 40 mg once a week in patients not taking methotrexate <b>IL-1 receptor antagonist</b> <b>Anakinra</b> (Kineret) 100 mg subcutaneously once daily	Hypersensitivity to biological DMARD, use of anakinra if hypersensitivity to <i>Escheria coli</i> -derived proteins, concomitant use of TNF-alpha inhibitors and anakinra, previous untreated tuberculosis, septic arthritis (within 12 months), recurrent chest infections or bronchiectasis, infected prosthesis, acute or chronic active hepatitis B or C infection, live vaccination, indwelling urinary catheter, multiple sclerosis or demyelinating disease, malignancy (< 10 years, apart from fully resected basal cell carcinoma > 5 years), congestive heart failure, chronic cutaneous ulceration, pregnancy or lactation Withhold treatment during severe intercurrent infection, malignancy, surgery, congestive heart failure, pregnancy and lactation.	Infusion or injection site reactions, serious infection, reactivation of tuberculosis (pulmonary or extra-pulmonary), lymphoproliferative disease, demyelinating disease, systemic lupus erythematosus, exacerbation of congestive heart failure, blood dyscrasias, hepatotoxicity	<ul style="list-style-type: none"> <li><b>Long-term safety is not yet established; monitor for all rare but serious toxicities</b></li> <li>Hepatitis B and C serology and screen for tuberculosis at baseline</li> <li>FBC and LFTs at baseline, monthly for 6 months then every 3–6 months (more often if used with other DMARDs)</li> <li>Monitor for reactivated tuberculosis during first 2–5 months of treatment</li> <li>Monitor for signs of heart failure and pulmonary sepsis at every visit</li> <li>Serology if exposure to chickenpox or shingles occurs during treatment</li> </ul>

Abbreviations: FBC = full blood count, IL = interleukin, LFTs = liver function tests, TNF = tumour necrosis factor

## References

1. Therapeutic Guidelines: Rheumatology, Version 1. 2006.
2. Australian Medicines Handbook, 2006.
3. Lu TY-T, Hill C. Aust Prescr 2006;29:67–70.
4. Scott D, Kingsley G. N Engl J Med 2006;355:704–12.
5. Australian Rheumatology Association. APLAR J Rheumatol 2006;9:123–6.

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