SUMMARY Rheumatoid arthritis (RA): a collaborative approach to management

Early detection/referral, allowing for prompt DMARD initiation, improves long-term outcomes

Main diagnostic features:

- ✔ Synovitis (tenderness, warmth and erythema, joint swelling, reduced ROM)
  - Often symmetrical, affecting multiple small joints
  - Other differential diagnoses have been excluded
  - Morning stiffness that lasts more than 30 min
  - Pain during squeeze test
- ✔ Symptoms longer than six weeks*
- ✔ RF-positive **and/or** anti-CCP-positive (ideally request both)
- ✔ Elevated CRP **and/or** ESR†

* Earlier if there is a strong family history; † Suspicion of RA usually needs to be documented on the request form for an ESR test to be performed at community labs.

For more information on diagnosing RA, see the "Practice Tool

Other tests to request: FBC, creatinine, LFTs, ANA, urinalysis

X-rays are often recommended as part of the diagnostic work-up, and are important to assess damage and progression, but are not required to make a diagnosis in early-stage RA

See your regional Health Pathway for specific recommendations

DMARD treatment will usually be initiated in secondary care following rheumatology referral or consultation; however, primary care continues to play an important role in the ongoing management, including (but not limited to):

- Monitoring for disease activity/ adverse effects
- Co-ordinating dose adjustments and appropriate DMARD use
- Wider patient care, managing co-morbidities and CVD risk
- Providing symptomatic relief for flares (see next page)

Methotrexate is the first-line DMARD for treating patients with RA

Once weekly dosing – more frequent dosing increases the risk of serious adverse effects
- Increase dose as tolerated; usually guided by rheumatologist

Prescribe folic acid (5 mg, once weekly) alongside methotrexate, taken on a different day e.g. "**M**ethotrexate for **M**onday, **F**olic acid for **F**riday"

Methotrexate is contraindicated during pregnancy
Advise using contraception during and for at least 3 months after treatment with methotrexate in both women and men

Review vaccinations
- Ensure patient is up to date with the National Immunisation Schedule
- Recommend other vaccines e.g. annual influenza vaccine, pneumococcal

Tips to help avoid errors associated with dosing:

- ☐ Confirm that the patient (and/or carer) understands their dosing regimen; specifically that it is once weekly
- ☐ Avoid writing "as directed" on prescriptions
- ☐ Agree on a day of the week to take methotrexate; specify on prescription label in full
- ☐ Only prescribe (and dispense) one tablet strength

	Monitoring (for adverse effects of methotrexate)	**Frequency**	**What to look for**	**Action**
Laboratory tests	Full blood count	Baseline; every 2–4 weeks initially until the dose of methotrexate is stable; then every month to three months thereafter	WBC count <3.5×10⁹/L; neutrophils <2.0×10⁹/L; platelets <150×10⁹/L	Discuss with rheumatologist
			MCV >105 fL	Check vitamin B12, folate and TSH
	Liver function tests		AST, ALT >2× the upper limit of normal	Withhold until discussed with rheumatologist. Also: • Re-check alcohol intake (up to 1–2 standard drinks once or twice a week is acceptable) • Review NSAID use; may cause liver dysfunction • Review other medicine use
			Unexplained decrease in albumin (in absence of active disease)	
	Serum creatinine		Moderate renal function deterioration	Reduce methotrexate dose and address possible causes
			Significant renal function deterioration	Withhold until discussed *with* or referred to rheumatologist
Symptoms/signs	Rash or oral ulceration	**Warn the patient that they need to report any of these symptoms immediately if they occur**		Withhold until discussed with rheumatologist. Oral folinic acid or folinic acid mouthwash may help with mucositis
	Nausea and vomiting, diarrhoea			Discuss with rheumatologist about giving oral methotrexate in three divided doses over 36 hours once a week or giving methotrexate by subcutaneous injection to avoid nausea
	New or increasing dyspnoea or dry cough (pneumonitis)	Baseline chest x-ray and respiratory function tests recommended		Withhold and discuss URGENTLY with rheumatologist. Arrange chest x-ray and respiratory function tests
	Severe sore throat or abnormal bruising			Immediate FBC and withhold until results available. Discuss any unusual results with rheumatologist

Abbreviations: ALT, aspartate transaminase; ANA, antinuclear antibody; AST, aspartate aminotransferase; anti-CCP, anti-cyclic citrullinated peptide/protein antibody; CRP, C-reactive protein; DMARD, disease-modifying anti-rheumatic drug; ESR, erythrocyte sedimentation rate; FBC, full blood count; LFT, liver function test; MCV, mean corpuscular volume; RF, rheumatoid factor positive; ROM, range of motion; TSH, thyroid stimulating hormone; WBC, white blood cell.

Refs: 1. Aletaha D, Smolen JS. JAMA. 2018;320:1360–72. 2. Methotrexate. MedSafe. Available at: https://www.medsafe.govt.nz/profs/PUArticles/December2017/Methotrexate.htm (Accessed Oct, 2020); 3. Drug treatment for rheumatoid arthritis. NICE. Available at: http://pathways.nice.org.uk/pathways/rheumatoid-arthritis (Accessed Oct, 2020).

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SUMMARY Rheumatoid arthritis (RA): a collaborative approach to management

Symptomatic relief for patients with RA flares

Medicines to acutely manage pain and inflammation are often given when DMARDs are being initiated ("**bridging**") or when flares occur – use for the **shortest period of time** possible

Mild disease activity?

A **NSAID** alone may be sufficient

- ✔ NSAIDs can usually be **co-prescribed with methotrexate for RA**
- ✔ Paracetamol can also be used for additional pain relief, if required
- ✘ **Avoid opioids** as an analgesic

More severe disease activity?

Corticosteroids can be used for more severe disease, or if patients respond insufficiently to NSAIDs alone

- **Usually oral or a one-off intra-muscular injection** for acute symptoms
- **Intermittent intra-articular injections** may be useful if one or two joints are affected, or for problematic joints

Optimising the long-term treatment of patients with RA

The long-term objective is remission; defined as the *sustained* absence of joint pain, swelling, and morning stiffness, with normalised inflammatory marker levels

Possible markers to assess changes in disease activity include:

- ✔ Tender joint counts/ swollen joint counts
- ✔ Level of pain or discomfort; effect on daily function/QOL
- ✔ Laboratory testing, particularly CRP levels
- ✔ Imaging of affected joints, e.g. with x-ray, ultrasound, MRI

Methotrexate alone is only sufficient for disease control for

1 in 4 patients

Alternatives to methotrexate monotherapy

Treatment	When might it be used?	Notes	Monitoring **Note:** specific requirements will be directed by the rheumatologist
Leflunomide	• Alone or in combination with methotrexate when it is contraindicated, not tolerated, or ineffective • Often the first choice alternative to methotrexate	• Comparable efficacy to methotrexate • Contraindicated during pregnancy; contraception is required during use and after until serum levels are not detectable (which may take several months to years due to the long half-life; a washout is possible if required) • Advise limited alcohol consumption	• Similar to methotrexate; particularly liver monitoring • Also ensure blood pressure is closely monitored at each visit as leflunomide can increase blood pressure
Sulfasalazine	• Alone or in combination with methotrexate when it is contraindicated, not tolerated, or ineffective • Patients with mild RA • Patients with liver disease • Patients who are pregnant (or planning); there is a theoretical risk of neonatal haemolysis in third trimester; prescribe folic acid throughout pregnancy	• Is a yellow-orange colour which may affect the colour of urine, tears, sweat and soft contact lenses • Ensure patients drink ≥2L fluid/daily • Can cause reversible oligospermia • May take ≥1–2 months to improve symptoms	• Similar to methotrexate • Small risk of severe neutropenia
Hydroxy-chloroquine	• Alone or in combination with methotrexate when it is contraindicated, not tolerated, or ineffective • Patients with very mild RA • Patients who are pregnant (or planning pregnancy)	• Increased risk of cardiomyopathy and QT prolongation and damage to the retina • May cause photosensitivity of skin • Dose based on body-weight; may take ≥2–3 months to improve symptoms	• A baseline ophthalmological review is essential; if normal examination and low risk (age <60 years, no liver disease, no retinal disease), 5 yearly visual acuity test; if high risk, annual visual acuity test is needed • Consider performing baseline ECG
Dual or triple combination treatment	• When monotherapy alone is ineffective • Some patients with a high level of disease activity will be moved straight to triple therapy if methotrexate alone is ineffective (vs dual therapy)	• The most effective triple combination is methotrexate, sulfasalazine and hydroxychloroquine	• As directed by rheumatologist
Biologics e.g. adalimumab, etanercept, rituxumab	• Special Authority criteria requires that the patient has trialled optimal dosing* of methotrexate, triple combination treatment, as well as an additional DMARD first; in addition, the patient needs to meet a specific threshold of disease activity and duration (see medicine-specific Special Authority criteria for more details) • Do not give live vaccines to patients receiving biologics		

* Optimal dosing refers to when the patient has not responded to at least three months of oral or parenteral methotrexate at a dose of at least 20 mg weekly or a maximum tolerated dose.

Abbreviations: DMARD, disease modifying anti-rheumatic drug; NSAID, non-steroidal anti-inflammatory drug; QOL, quality of life; RA, rheumatoid arthritis.

Refs: 1. NZ Formulary. NZF v100. Available from: www.nzf.org.nz (Accessed Oct, 2020); 2. Aletaha D, Smolen JS. JAMA. 2018;320:1360–72; 3. Singh JA, Saag KG, Bridges S, et al. Arthritis Care Res. 2016;68:1–25; 4. Drug treatment for rheumatoid arthritis. National Institute for Health and Care Excellence (NICE). Available at: http://pathways.nice.org.uk/pathways/rheumatoid-arthritis (Accessed Oct, 2020).

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