Wales Centre for Pharmacy Professional Education
Canolfan Addysg Fferylliaeth Broffesiynol Cymru

RHEUMATOID ARTHRITIS

Top tips for MURs

- Check that patient understands that there is no cure for rheumatoid arthritis and manage their expectations
- Before discussing drug treatment, ensure that you have a complete list as patient may obtain medication from secondary care (e.g. DMARDs during initiation) or via a homecare provider (e.g. cytokine modulators)
- Advise patient on DMARDs that there will be no immediate therapeutic effect, although after 6-12 weeks (depending on drug) they should start to notice the benefits
- Counsel patient on purpose of each medication and individual monitoring requirements - see below for BNF guidance on the most commonly used DMARDs but the exact monitoring schedule depends on individual patients and is guided by the Shared Care protocol in place in every Health Board*
  - Methotrexate – FBCs, renal and liver function tests within last 2 to 3 months (within last 2 weeks if dose increase or therapy not yet stabilised)
  - Sulfasalazine – FBCs and LFTs monthly for first 3 months, then every three months thereafter
  - Penicillamine – FBCs and renal tests every 1 or 2 weeks for first 2 months or after a dose increase and then every four weeks
  - Hydroxychloroquine – annual visual acuity tests
  - Leflunomide – LFTs every 2 weeks for first six months then every 8 weeks
- Counsel patient on the need to take the disease-modifying or biological drugs regularly and contrast with analgesics and NSAIDs which do not affect the disease process, therefore can be taken in accordance with the level of pain the patient is experiencing (NB this guide does not cover analgesics)
- Check that patient can open the bottle/pop the tablets out of the blister pack. Suggest solutions where appropriate e.g. non clic loc tops
- Advise that patients should speak to the pharmacist before buying OTC medications. If NSAIDs are required with methotrexate, they should be prescribed and the patient should be monitored closely
- Advise patients who are considering becoming pregnant to discuss this with their rheumatology specialist. Methotrexate and leflunomide are teratogenic; effective contraception is essential during treatment and for 3 months after stopping methotrexate and 3 years after stopping leflunamide in women. Men on leflunomide may be advised to have a wash out treatment before trying to father a child
- Advise patients on cytokine modulators to keep Alert Card with them at all times and advise to contact rheumatology specialist team if they get an infection
- Counsel patients on hydroxychloroquine not to take antacids for at least 4 hours before or after to reduce interference with absorption of drug
- Counsel patient on signs / symptoms of complications that need referral (**see red flags overleaf**) and on common side effects (**see side effects overleaf**)
- Advise patient that it is normal to monitor the disease (by measuring C-reactive protein (CRP) and key components of disease activity (using a composite score such as DAS28))
- Advise patient to have annual influenza vaccination
- Report any relevant adverse drug reactions to the Yellow Card Scheme

* Note the monitoring schedule below is for DMARD monotherapy. For combination DMARD therapy please refer to the relevant Shared Care protocol as monitoring schedule is likely to be modified

Pathophysiology of rheumatoid arthritis

Rheumatoid arthritis (RA) is a progressive, systemic inflammatory disorder of the joints characterised by pain, inflammation, joint destruction and loss of joint mobility, which typically affects the small joints of the hands and feet[1]. As it is a systemic disease it can also affect the whole body, including the cardiovascular system, lungs, eyes and small blood vessels (vasculitis)[1]. The exact cause is unknown but it seems to be multi-factorial and immune-mediated[2]. In early rheumatoid arthritis, the synovium becomes inflamed, leading to pain and stiffness[2]. During later disease polymorphonuclear leucocytes, lysosomal and other inflammatory enzymes actively degrade the cartilage and sustained inflammation can lead to the growth of a pannus, (granulation tissue) across the cartilage causing erosion of cartilage and bone surface[2]. This synovial inflammation may subside either spontaneously or because of treatment but if the joint has been damaged, deformities will persist and may worsen, as secondary degenerative changes follow[2].

The drug management of rheumatoid arthritis aims to relieve symptoms, as pain relief is a priority for patients and to modify the disease process, so that radiological progression, which is closely correlated with progressive functional impairment, can be retarded or stopped[1].

Lifestyle issues

- Advise patient about the benefits of regular exercise in protecting joints by keeping the muscles strong and signpost to Arthritis Care or Expert Patients Programme
- Advise patients who wish to experiment with their diet that there is no strong evidence their rheumatoid arthritis will benefit, however, they could be encouraged to eat a Mediterranean-style diet
- Advise patient that having rheumatoid arthritis can increase their risk of cardiovascular disease, so discuss lifestyle changes that can reduce this risk
- Patients taking methotrexate should limit their alcohol intake to avoid increasing the risk of liver toxicity. Department of Health guidelines should be considered as an absolute maximum (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Advise patients that there is little evidence for the long-term efficacy of complementary therapies, but if they decide to use them they should continue with their normal treatment. Where this includes medication, check for interactions with their conventional treatment

Compiled: Mair Davies, WCPPE, October 2013
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Quick practice guide for targeted MURs

Red flags that need prompt referral

- Any symptoms of blood dyscrasia (unexplained bleeding, bruising, purpura, sore throat, mouth ulcers, metallic taste, recurrent infections, fever or malaise)
- Any symptoms of hepatotoxicity (nausea, vomiting, abdominal pain, loss of appetite and jaundice)
- Any symptoms of nephrotoxicity (blood in urine, oliguria, nausea, drowsiness, imbalance, fatigue, confusion)
- Any symptoms of ocular toxicity (changes in visual acuity or blurred vision) – particularly with hydroxychloroquine
- Any symptoms of tuberculosis (breathlessness, persistent cough, fatigue, night sweats, weight loss), septicaemia (fever, nausea & vomiting, lethargy, diarrhoea, drowsiness) or hepatitis B (flu-like symptoms, jaundice, nausea)
- Any symptom of depression

How do medications to treat RA work?

DMARDs (Non- biological)	The exact mechanism of action of most DMARDS is uncertain but they suppress the disease process by acting on the immune system to reduce its destructive effects on the joints.
Corticosteroids	Reduce inflammation by inhibiting components of the immune system such as macrophages and cytokines.
Cytokine modulators	Inhibit inflammatory processes at an early stage in the inflammatory cascade, for example by inhibiting TNF , to reduce joint damage. This guide will not cover these drugs in any detail.
NSAIDs	NSAIDs inhibit the enzyme cyclo-oxygenase (COX), which catalyses arachidonic acid to prostaglandins and leukotrienes. This results in reduction of inflammation, reduced temperature and an analgesic effect.
Paracetamol	Proposed mechanisms of action include effects on central prostaglandin inhibition, peripheral bradykinins and serotonergic systems.
Weak opioids	Mimics the action of the naturally occurring pain reducing chemicals called endorphins. It combines with the mu opioid receptors in the brain and spinal cord to block the transmission of pain.

What are the common side effects to look out for?

Drug	Common side effects	Recommendation
Methotrexate (most patients are prescribed folic acid to reduce adverse effects)	Gastrointestinal intolerance	Advise patient that this will normally settle after a few weeks, if persistent refer to prescriber for anti-emetic or dose / route alteration. If currently not taking folic acid refer to prescriber.
	Thinning or hair loss	Advise patient that usually slight and returns to normal on stopping treatment.
	Sore mouth, mouth ulcers	Refer to prescriber as could be a sign of blood dyscasia and folic acid dose may need adjusting. Maintain good oral hygiene.
Sulfasalazine	Gastrointestinal intolerance	Refer to prescriber if not tolerated.
	Colour urine orange and stain contact lenses. Variable degree of male infertility	Advise patient that this is reversible on stopping the medication.
Penicillamine	Nausea	Advise patient to take before food or before going to bed.
	Loss of taste	Advise patient that this is temporary.
	Rashes	Refer to prescriber for possible dose reduction.
Hydroxychloroquine	Gastrointestinal intolerance, headaches and skin rashes	Refer to prescriber if not tolerated.
Leflunomide	Gastrointestinal intolerance, reversible alopecia, rash and hypertension	Refer to prescriber.
Corticosteroids	Osteoporosis, peptic ulceration, diabetes mellitus and hypertension	Refer to prescriber.
Cytokine modulators (etanercept, infliximab, adalimumab, certolizumab, rituximab, tocilizumab etc).	Skin reactions at the site of injection, gastrointestinal disturbance, infections, nausea, fever and headaches.	Refer to prescriber.

Potential serious drug interactions?

Drugs used to treat rheumatoid arthritis interact with many other medications and with each other - **see BNF Appendix 1: Interactions for more detail**

Where can you find more information?

- Musculoskeletal and joint diseases – BNF sub-section 10.1.3
- NICE Clinical Guideline CG79: Rheumatoid arthritis: The management of RA in adults **www.nice.org.uk**
- Arthritis Care which can be found at **www.arthritiscare.org.uk**
- NICE Clinical Knowledge Summary can be found at **http://cks.nice.org.uk/**
- Arthritis Research UK which can be found at **www.arthritisresearchuk.org**

References

1. Rheumatoid arthritis : management of rheumatoid arthritis in adults, NICE clinical guideline CG79,2009
2. Musculoskeletal disorders level 1, CPPE
3. Musculoskeletal disorders – advancing your practice level 2, CPPE,

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