Musculoskeletal and joint disorders

Contents:

For full information on treatment, side effects, cautions and contraindications, see electronic British National Formulary (www.bnf.org) or the relevant summary of product characteristics (www.medicines.org.uk).

For information on preparing intravenous medicines for administration, see Medusa Injectable Medicines Guide for the NHS (see Clinical Guidance home page)

1. Rheumatoid arthritis

Rheumatologist referral is required for all patients with suspected rheumatoid arthritis (RA).
Refer urgently if any of the following apply:

- the small joints of the hands or feet are affected
- more than one joint is affected
- there has been a delay of 3 months or longer between onset of symptoms and seeking medical advice.

All patients with newly diagnosed RA should receive treatment with disease-modifying anti-rheumatic drugs (DMARDs) plus short term corticosteroids as soon as possible after diagnosis. **NICE clinical guideline 79** provides further information on the management of rheumatoid arthritis in adults.

i) DMARDs

Most patients require more than one DMARD, either in combination or as sequential monotherapy. For patients receiving monotherapy particular attention should be paid to fast achievement of a clinically effective dose.
An adequate therapeutic trial must be undertaken (i.e. 3 to 6 months) at full dosage to assess efficacy (lower doses are used if limited by toxicity or if disease control is achieved with a lower dose).
Monitor treatment in accordance with shared care guidelines (see below).

Methotrexate is the most commonly used DMARD. To minimise adverse effects the usual starting dose is 7.5mg orally, **once weekly.** Dosage is escalated in accordance with instructions provided by Consultant (see shared care guidelines below). For patients who cannot tolerate oral methotrexate, despite all measures to reduce gastric side effects, subcutaneous dose administration should be considered. (Prescribe 1-litre cytotoxic sharps bins (purple) on FP10 for disposal of used injections).

Folic acid 5mg, orally, on up to 6 days each week (avoiding the day of methotrexate administration) is used to minimise the anti-folate action of methotrexate.

NOTE: All patients prescribed methotrexate must be issued with the National Patient Safety Agency Patient Information Leaflet and Patient-held Monitoring Booklet.

Other DMARDs may be recommended following specialist review. See shared care guidelines for further information:

- **Methotrexate – oral for rheumatological conditions**
- **Methotrexate – subcutaneous for rheumatological conditions**
- **Azathioprine for rheumatological conditions**
- **Ciclosporin for rheumatological conditions**
- **Hydroxychloroquine for rheumatological conditions**
- **Leflunomide for rheumatological conditions**
- **Mycophenolate for rheumatological conditions**
- **Penicillamine for rheumatological conditions**
- **Sodium aurothiomalate for rheumatological conditions**
- **Sulfasalazine for rheumatological conditions**

ii) Corticosteroids

Short term use of corticosteroids is appropriate in newly diagnosed patients to suppress symptoms while starting DMARD therapy. Corticosteroids may also be used to control disease flares.
Osteoporosis prevention must be considered (see **Osteoporosis – management**).

First line
Methylprednisolone acetate 120mg, by IM injection, as a single dose. Repeat after 2 to 3 weeks if required.

For patients with active disease in one or two joints **ONLY**
Triamcinolone acetonide 5 to 40mg (according to joint size), by intra-articular injection (total max 80mg). Dose can be repeated after several weeks if clinically appropriate.

For severe systemic features or vasculitis
Methylprednisolone sodium succinate 500mg to 1g, by IV infusion, as a single dose. Repeat dose daily if necessary as recommended by Consultant Rheumatologists.

If parenteral routes of steroid administration are inadequate or inappropriate
Prednisolone up to 60mg once daily in the morning, orally, as a short course. Response should be reviewed by clinician and dose/duration adjusted accordingly.

For patients in whom DMARDs have failed or are contra-indicated (e.g. due to severe co-morbidities) AND who have been offered biologic therapy:
Continuous, low-dose **prednisolone** therapy (7.5mg daily or lower) can be used.

iii) Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs or cyclo-oxygenase-2 (COX-2) selective inhibitors do not alter disease progression but are often required long term in RA patients to relieve pain and stiffness. There is considerable inter-individual response to NSAIDs: about 60% of patients will respond to any one drug. For those patients who do not respond, consider changing to an NSAID from a different chemical group. Analgesic efficacy can occur in one week, but it can take up to three weeks for the full anti-inflammatory effect of an NSAID to develop.

NOTE: Before prescribing an NSAID consider whether the patient has any cardiovascular, gastrointestinal, renal or hepatic risk factors.
For advice on how to select the most appropriate NSAID, see **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) — Prescribing in Inflammatory Arthritis and Osteoarthritis (Adults)**

Formulary choices include:

- **Ibuprofen** 400mg, orally, three times daily; increased if necessary to max. 2.4g daily in 3 to 4 doses
  First choice for patients WITHOUT cardiovascular or gastrointestinal risk factors
- **Naproxen** 250 to 500mg, orally, twice a day
  First choice for patients WITH cardiovascular risk factors
- **Celecoxib** 200mg, orally, daily in 1 or 2 divided doses; increased if necessary to a maximum of 200mg twice daily
  First choice for patients WITH gastrointestinal risk factors ONLY — prescribe with a proton pump inhibitor (PPI)
- **Etoricoxib** 60mg, orally, once a day
  Third choice — before prescribing, note that this drug has ADDITIONAL cardiovascular risks (See MHRA Drug Safety Update for further information) and consider whether a PPI is required.

NOTE: NSAIDs should be prescribed at the lowest effective dose and for the shortest possible duration

When duration of use becomes long term or repeated, add a proton pump inhibitor (PPI)

In secondary care, first choice is:
Omeprazole 20mg, orally, daily
NOTE: All patients with gastrointestinal risk factors should be prescribed a PPI at the same time as starting an NSAID

In primary care, see Scriptswitch for choice of cost effective PPI

iv) Simple analgesics
Simple analgesics such as paracetamol and/or weak opioids should be offered for symptom control and may reduce the need for long term treatment with NSAIDs or COX-2 inhibitors.

First line
Paracetamol 1g, orally, four times daily

If pain uncontrolled consider adding
Codeine 30 to 60mg, orally, up to four times daily (or **dihydrocodeine** 60 to 120mg twice daily using **modified release preparation**); usual max: 240mg in 24 hours.
Or
Tramadol 50 to 100mg, orally, up to four times daily (or 50 to 200mg twice daily using modified release preparation); usual max: 400mg in 24 hours.

Third line (consultant rheumatologist or pain team consultant use only)
In patients with swallowing difficulties who are unable to take standard **oral** medication or in selected patients with compliance issues (e.g. due to requirement for multiple oral medicines **and** problems e.g. gastrointestinal side effects, which cannot be resolved by adjusting medication regime)

Buprenorphine (Butrans®) transdermal patch 5mcg/hr to 40mcg/hr; applied once weekly). Usual dose range in practice is 10–15mcg/hr.

v) Biological therapy (hospital initiation only)

See **Rheumatoid arthritis – Treatment with biologics (secondary care guideline)** for further advice on eligibility criteria and treatment selection.

---

2. Osteoarthritis

For osteoarthritis (OA), regular dosing with simple analgesics such as paracetamol should be used ahead of anti-inflammatory agents wherever possible. A treatment algorithm can be found in **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) — Prescribing in Inflammatory Arthritis and Osteoarthritis (Adults)**

NICE Clinical Guideline 59 provides further information on the care and management of osteoarthritis in adults.

First line
Paracetamol 1g, orally, four times a day

Second line — consider adding
Ibuprofen 5% gel Apply, topically, up to 3 times a day.
Or
Piroxicam 0.5% gel Apply, topically, 3 or 4 times a day.
Or
Movelat gel ®Apply, topically, up to 4 times a day.

In primary care see Scriptswitch for cost effective choices

If pain remains uncontrolled, consider adding
Codeine 30 to 60mg, orally, up to four times daily (or **dihydrocodeine** 60 to 120mg twice daily using **modified release preparation**); usual max: 240mg in 24 hours.
Or
Tramadol 50 to 100mg, orally, up to four times daily (or 50 to 200mg twice daily using modified release preparation); usual max: 400mg in 24 hours.

Third line (consultant rheumatologist or pain team consultant use only)
In patients with swallowing difficulties who are unable to take standard **oral** medication or in selected patients with compliance issues (e.g. due to requirement for multiple oral medicines **and** problems e.g. gastrointestinal side effects, which cannot be resolved by adjusting medication regime)

Buprenorphine (Butrans®) transdermal patch 5mcg/hr to 40mcg/hr; applied once weekly). Usual dose range in practice is 10–15mcg/hr.
Or
Capsaicin 0.025% cream Apply 4 times daily (not more often than every 4 hours). Capsaicin cream may need to be used for 3 to 4 weeks to achieve maximum effect.

If pain is still uncontrolled, consider adding an oral NSAID (use earlier for active inflammation).

NOTE: Before prescribing an NSAID consider whether the patient has any cardiovascular, gastrointestinal, renal or hepatic risk factors.
For advice on how to select the most appropriate NSAID, see **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) — Prescribing in Inflammatory Arthritis and Osteoarthritis (Adults)**

Formulary choices include:

- **Ibuprofen** 400mg, orally, three times daily; increased if necessary to max. 2.4g daily in 3 to 4 doses
  First choice for patients WITHOUT cardiovascular or gastrointestinal risk factors
- **Naproxen** 250 to 500mg, orally, twice a day
  First choice for patients WITH cardiovascular risk factors
- **Celecoxib** 200mg, orally, daily in 1 or 2 divided doses; increased if necessary to a maximum of 200mg twice daily
  First choice for patients WITH gastrointestinal risk factors ONLY — prescribe with a proton pump inhibitor (PPI)

- **Etoricoxib** 30mg, orally, once a day
  Third choice — before prescribing, note that this drug has ADDITIONAL cardiovascular risks and consider whether a PPI is required

NOTE: NSAIDs should be prescribed at the lowest effective dose and for the shortest possible duration

When duration of use becomes long term or repeated, add a proton pump inhibitor (PPI).
In secondary care, first choice is:
Omeprazole 20mg, orally, daily

In primary care, see Scriptswitch for choice of cost effective PPI

For an acute inflammatory flare of symptoms
Triamcinolone acetonide 5 to 40mg (according to joint size), by intra-articular injection (total max 80mg). Dose can be repeated after several weeks if clinically appropriate.

NOTE: There is no place for oral corticosteroid therapy in the treatment of osteoarthritis.

3. Gout — acute

See **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) — Prescribing in Inflammatory Arthritis and Osteoarthritis (Adults)** for more information on cautions, contraindications, risk factors, which NSAID to prescribe and when to use proton pump inhibitors.

NOTE: Before prescribing an NSAID consider whether the patient has any cardiovascular, gastrointestinal, renal or hepatic risk factors.

Decide if PPI cover is indicated
In primary care, see Scriptswitch for choice of cost effective PPI

First line
Naproxen 750mg, orally, as a single dose followed by 250mg three times daily until attack has passed.
Or
Etoricoxib 120mg, orally, once daily for max. 8 days

Second line — if NSAID contra-indicated, not tolerated or inappropriate
Colchicine 1mg, orally, as a single dose followed by 500micrograms 3 or 4 times daily until symptoms relieved. Max. 6mg per treatment course. For dosage in chronic gout, see **4. Gout-chronic**.

Third line — if the above treatment is contraindicated, not tolerated or inappropriate

When only one or two joints are affected:
Triamcinolone acetonide 5 to 40mg (according to joint size), by intra-articular injection (total max 80mg). Dose can be repeated after several weeks if clinically appropriate.

When >2 joints are affected:
Prednisolone 40 to 60mg, orally, once daily for 3 days; then reduce by 10 to 15mg per day every 3 days until discontinuation
Or
Methylprednisolone acetate 120mg, by IM injection, as a single dose

Initiation of hypouricaemic therapy can induce acute gout and is usually delayed until 1–2 weeks after an acute attack has settled. See **4. Gout-chronic**

If a patient is already taking a hypouricaemic drug, it should be continued at the same dose until the acute attack resolves. Consideration may then be given to dose adjustment or drug change.

NOTE: Aspirin prescribed at analgesic doses (ie, 600mg to 2.4g/day) should be avoided where possible as it can cause urate retention. However, low-dose aspirin (75 to 150mg/day) can be continued.

Further information on the management of gout can be found at
http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/m/management_of_gout.pdf

---

4. Gout — chronic

Hypouricaemic treatment should be considered for patients who:

- Experience 2 or more attacks of acute gout per year
- Have tophaceous gout
- Have gouty arthropathy
- Have renal insufficiency
- Have uric acid stones & gout

Initiation of hypouricaemic therapy can induce acute gout and is usually delayed until 1–2 weeks after an acute attack has settled. Anti-inflammatory therapy with either an **NSAID** or **colchicine** (at 500microgram twice or three times daily) should be started at the same time and continued for at least one month after correction of the hyperuricaemia.

Patients should be treated to achieve target serum urate concentration <300micromol/L.

Further information on the management of gout can be found at
http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/m/management_of_gout.pdf

First line
Allopurinol 100mg, orally, once daily as initial dose. After 4 weeks check serum urate concentration and, if necessary, adjust dose. Maximum 900mg daily (doses >300mg daily should be divided). Monitor renal function.

If renal function is impaired, decrease dose according to creatinine clearance (CrCl):
CrCl = 10 to 20mL/minute: 100 to 200mg daily

CrCl = <10mL/minute: 100mg on alternate days (max: 100mg daily)

Second line — for patients intolerant of allopurinol or in whom it is contra-indicated
Febuxostat 80mg, orally, once daily. Increase to 120mg daily after 2 to 4 weeks of treatment if serum urate concentration remains above target.
NOTE: Manufacturer recommends the use of either an NSAID or colchicine for 6 months after initiation of febuxostat to prevent precipitation of an acute attack.

In most cases febuxostat will be initiated following specialist rheumatology review and recommendation but it is also suitable for initiation and monitoring in primary care.
http://www.nice.org.uk/nicemedia/pdf/TA164Guidance.pdf

Second line — for patients who are under-excretors of uric acid and in those resistant to or intolerant of allopurinol
Sulfinpyrazone 100 to 200mg, orally, once daily with food (or milk). After 4 weeks check serum urate concentration and, if necessary, adjust dose (max: 800mg daily). Monitor renal function. On achieving target, consider dose reduction (maintenance dose may be as low as 200mg daily).
NOTE: Fluid intake of at least 2 litres per day is recommended to achieve adequate urinary excretion of the raised urate load and to reduce the risk of urate crystallisation and deposition in the kidneys. Alkalinization of the urine may also be required.

NOTE: Sulfinpyrazone is ineffective in patients with renal failure and should be avoided when creatinine clearance is <20mL/minute.

Sulfinpyrazone can be used with allopurinol for patients who have not responded to monotherapy.

5. Juvenile-onset idiopathic arthritis

This section is under development.

Tocilizumab is available for initiation by consultant rheumatologists ONLY provided it is prescribed in accordance with NICE technology appraisal 238 **(www.nice.org.uk/ta238).**

Abatacept, adalimumab, etanercept and tocilizumab is available for initiation by consultant rheumatologists ONLY provided it is prescribed in accordance with NICE technology appraisal 373 **(https://www.nice.org.uk/guidance/ta373).**

6. Psoriatic arthritis

This section is under development.

Etanercept, infliximab and **adalimumab** are available for initiation by consultant rheumatologists ONLY in accordance with NICE technology appraisal 199 (http://www.nice.org.uk/guidance/ta199)

Golimumab is available for initiation by consultant rheumatologists ONLY provided it is prescribed in accordance with NICE technology appraisal 220 **(www.nice.org.uk/ta220).**

Certolizumab is available for initiation by consultant rheumatologists ONLY provided it is used after other medicines that have a positive NICE TA have been considered and that it is used in accordance with criteria set out in NICE technology appraisal 199 **(http://www.nice.org.uk/guidance/ta199).**

Ustekinumab is available for initiation by consultant rheumatologists ONLY provided it is prescribed in accordance with NICE technology appraisal 340 **(https://www.nice.org.uk/guidance/ta340).**

Apremilast is available for initiation by consultant rheumatologists ONLY provided it is prescribed in accordance with NICE technology appraisal 433 **(https://www.nice.org.uk/guidance/ta433).**

7. Ankylosing spondylitis

This section is under development.

Adalimumab, certolizumab, infliximab, golimumab and **etanercept** are available for initiation by consultant rheumatologists ONLY provided they are prescribed in accordance with NICE technology appraisal 383 **(https://www.nice.org.uk/guidance/ta383).**

Secukinumab is available for initiation by consultant rheumatologists ONLY provided they are prescribed in accordance with NICE technology appraisal 407 **(https://www.nice.org.uk/guidance/TA407)**