Musculoskeletal and Joint Diseases

BNF Chapter 10

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10.1 Drugs used in rheumatic diseases and gout

General advice

Osteoarthritis and soft-tissue disorders

- Refer to NICE NG226 Osteoarthritis and NICE CKS Osteoarthritis.
- Non-drug measures, such as education, weight reduction and exercise, are core treatments in osteoarthritis (OA) and should be offered to everyone. See Versus Arthritis for patient information, musculoskeletal decision support tools and the surgery toolkit.
- There has been a move away from the use of medication to treat chronic pain. Consider signposting/referral to:
    - Relevant support groups e.g. Versus Arthritis (VA) NI provide face to face, telephone and virtual support and pain management courses; Action Mental Health deliver pain management courses across the WHSCT area
    - Better Days Pain Support Programmes run by Healthy Living Centres (HLC). Some centres provide pain support programmes. Refer to the HLC website to find out about the services they offer
    - Online resources such as Live Well with Pain and the Pain Toolkit provide self-management advice for people living with persistent pain
- Do not offer glucosamine, strong opioids or intra-articular hyaluronan injections to manage osteoarthritis.

Low back pain and sciatica

- See NICE NG59 on the management of low back pain and sciatica.
- Consider oral NSAIDs for managing low back pain. Be aware of the risk of harms and limited evidence of benefit from the use of NSAIDs in sciatica.

Rheumatoid arthritis and other inflammatory disorders

- If rheumatoid arthritis is suspected the patient should be referred to Rheumatology for assessment, management and initiation of DMARDs. Patients should **not** be managed by non-specialists.

- Refer to the following websites for further information and guidelines: NICE NG100 Rheumatoid arthritis and British Society for Rheumatology.
- Risks/benefits of treatments should be discussed with patients before commencing. Some charitable/voluntary sector organisations have developed tools for patient communication, e.g. Versus Arthritis and NRAS.

10.1.1. Oral NSAIDs

Note: topical NSAIDs are first line for Osteoarthritis

Choice	Drug
1st choice	Ibuprofen tablets 200mg, 400mg Or Naproxen tablets 250mg, 500mg (plain tablets, not e/c)
2nd choice (if naproxen not tolerated or treatment failure)	2nd line choice is not definitive and will depend on individual patient factors and safety factors of individual NSAIDs. Please see Prescribing Notes below for further information

Prescribing Notes

- In osteoarthritis topical NSAIDs are first choice with oral preparations second line if topical treatment is ineffective or not suitable, see 10.3.2 for formulary choice and NICE NG226 for further information. (*add jump*)
- All NSAIDs should generally be used at the lowest effective dose and for the shortest period of time necessary to control symptoms.
- Differences in anti-inflammatory activity between NSAIDs are small, but there is considerable variation in individual response and tolerance to these drugs. About 60% of patients will respond to any NSAID; of the others those who do not respond to one may well respond to another. See BNF NSAID treatment summary
- Low-dose ibuprofen (≤1200mg per day) is an appropriate first choice oral NSAID in view of its low risk of gastrointestinal (GI) and cardiovascular (CV) side effects. Naproxen is also included as a first choice as it may have a lower CV risk than some other NSAIDs.

- Second line choice is not definitive and will depend on individual patient factors and CV, GI and/or renal safety factors of individual NSAIDs. Refer to NICE CKS for full information
- When considering a second line choice for patients at risk of cardiovascular complications, diclofenac, etoricoxib and high dose ibuprofen ≥2400mg/day) should be avoided.
    - Ibuprofen: People taking ≥2400mg of ibuprofen per day are at higher risk of arterial thrombotic events. No increased risk is seen at doses of up to 1200mg per day. Due to limited data, it is uncertain whether doses between 1200mg and 2400mg are associated with an increased risk
    - If a cox-2 inhibitor is required, celecoxib 100mg twice daily may be considered when the benefits are expected to outweigh the risks, there are insufficient CV safety data for higher doses
- Assess GI risk factors and consider need for gastroprotection– refer to CKS and PrescQIPP

PPI dose for gastroprotection in those who require continued NSAID treatment*

NI Formulary Choices	Dose
Lansoprazole capsules	15-30mg once daily
Omeprazole capsules	20mg once daily

*Prescription directions to include the instruction “while taking [name NSAID]”

- Ibuprofen may interfere with the cardioprotective effects of low dose aspirin when taken concomitantly. Ibuprofen should be taken at least 30 minutes after aspirin ingestion, or at least 8 hours before aspirin ingestion to avoid any potential interaction. Risk may be greater in those taking regular, rather than intermittent, ibuprofen and regular co-prescription should generally be discouraged.

Side Effects

- All NSAIDs carry the risk of side effects which can be serious and life-threatening. Although the risk varies between individual NSAIDs, important side effects include:
    - GI (e.g. perforation, ulcer, bleeding)
    - Renal (e.g. deterioration of renal function, renal failure)
    - CV (e.g. stroke, myocardial infarction) *see MHRA.*

Cautions

- Cautions and contra-indications vary between drugs, refer to BNF and/or product literature for full information.
- NSAIDs should be used with caution in the elderly (risk of serious side-effects and fatalities).
- NSAIDs may worsen asthma in patients who are susceptible; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma.
- NSAIDs: potential risks following prolonged use after 20 weeks of pregnancy – see MHRA
    - Systemic (oral and injectable) NSAIDs are contraindicated during the last trimester (after 28 weeks) of pregnancy
    - Avoid prescribing systemic NSAIDs from week 20 of pregnancy unless clinically required and prescribe the lowest dose for the shortest time in these circumstances
- During an acute illness, consider temporarily stopping NSAID in order to reduce the risk of acute kidney injury. See 'sick day rules'. (*Add jump)*
- Avoid use of NSAIDs with severe hypertension, i.e. systolic blood pressure consistently above 170mmHg and /or diastolic blood pressure consistently above 100mgHg
    - Etoricoxib may be associated with severe effects on blood pressure and is therefore contraindicated in patients with BP persistently >140/90mmHg. Hypertension should be controlled before treatment with etoricoxib is started and BP should be monitored within two weeks after initiation, after six weeks and periodically thereafter – see MHRA.

10.1.2 Corticosteroids

10.1.2.1 Systemic corticosteroids

Choice	Drug
1st choice (oral)	Prednisolone tablets 1mg, 5mg (standard release, not e/c) Note: Soluble tablets are high cost
1st choice (parenteral)	Intramuscular depot injection: methylprednisolone acetate (Depo-Medrone®) vials 40mg/mL, 80mg/2mL, 120mg/3mL Or Intramuscular injection: triamcinolone acetonide 40mg/mL (Kenalog® Intra-articular/Intramuscular) Or Intravenous injection: methylprednisolone (as sodium succinate) (Solu-Medrone®) vials 40mg, 125mg, 500mg, 1g: slow intravenous injection or infusion

10.1.2.2 Local corticosteroid injections

Choice	Drug
1st choice	Intra-articular injection: Methylprednisolone acetate (Depo-Medrone®) vials 40mg/mL, 80mg/2mL, 120mg/3mL Or Triamcinoline acetonide (Adcortyl® Intra-articular) injection 50mg/5mL, (Kenalog® Intra-articular) injection 40mg/mL

Prescribing Notes

- There is no consistent evidence for an ideal steroid regimen that is suitable for all patients. Therefore, the approach to treatment must be flexible and tailored to the individual. See NICE CKS.
- Note: the use of enteric-coated formulations of corticosteroid is not recommended for reducing the risk of gastrointestinal bleeding or dyspepsia.
- A Steroid Emergency Card has been developed in response to a National Patient Safety Alert.The alert highlights the dangers associated with adrenal insufficiency for patients taking corticosteroid medication, and recommends that all eligible patients prescribed (or initiated on) steroids are assessed and where necessary issued with a Steroid Emergency Card. Community pharmacies and GP practices can order these from pharmacystationeryorders@hscni.net. For full information see BNF and HSC letter.
- Consider osteoporosis prophylaxis for patients receiving 7.5mg or more of prednisolone daily (or equivalent) for longer than 3 months. For further details refer to NOGG guideline.
- Long-term steroids should be withdrawn gradually.
- The British Society for Rheumatology recommends initiation of low-dose steroid therapy (prednisolone 15mg daily) with gradually tailored tapering in straightforward **polymyalgia rheumatica** (PMR). Refer to guidelines here.

Giant cell arteritis

- **Giant cell arteritis** (GCA) is a medical emergency and patients should be urgently referred to a specialist ideally for same day evaluation. Patients in whom GCA is strongly suspected should be immediately treated with high-dose glucocorticoids (40-60mg prednisolone per day). If same day specialist evaluation is not available primary care providers should initiate glucocorticoids alongside an urgent referral. For further information see BRS guideline
- Immediate referral to Ophthalmology is essential if there is visual loss for consideration of IV methylprednisolone.

10.1.3 Drugs that suppress the rheumatic disease process (specialist treatments)

- Disease Modifying Anti-Rheumatic Drugs (DMARDs) on the AMBER list are initiated by specialists in secondary care and can be prescribed by GPs under a shared care arrangement. Refer to the Red Amber List for further details including shared care guidelines as appropriate. Note shared care guidelines are updated regularly and paper copies should not be relied on.
- Biological therapies and JAK inhibitors are RED list treatments for specialist use only.

10.1.4 Gout

Acute Gout

Choice	Drug	Dosage
1st choices	NSAID (see 10.1.1 *add link* for choices, consider gastroprotection) or Colchicine tablets 500 micrograms	See BNF See BNF
2nd choice	Prednisolone 5mg [off label]	A short course such as 30-35 mg once a day for 3-5 days* **other regimens may be used*

Prescribing Notes

- Prescribe as per NICE NG219 Gout: diagnosis and management recommendations. See NICE visual summaries and also NICE CKS: Gout and BMJ Gout: diagnosis and management – summary of NICE guidance
- Acute episodes should be treated as soon as possible. Patients can be given a supply of acute treatment and advised to start it if they feel an attack coming on.
- Assess lifestyle and comorbidities (including cardiovascular risk factors and CKD).
- Aspirin is not indicated for acute attacks of gout.

Cautions

- Colchicine has a narrow therapeutic window and is extremely toxic in overdose. Patients at particular risk of toxicity are those with renal or hepatic impairment, gastrointestinal or cardiac disease, and patients at extremes of age - see MHRA.
- Refer to 10.1.1 [add jump] for NSAID prescribing notes.

Prevention of recurrent attacks – Urate Lowering Therapy (ULT)

Choice	Drug
Formulary choices	Allopurinol tablets 100mg, 300mg or Febuxostat f/c tablets 80mg, 120mg

Prescribing Notes

- Prescribe as per NICE NG219 Gout: diagnosis and management recommendations. See NICE visual summaries and also NICE CKS: Gout and BMJ Gout: diagnosis and management – summary of NICE guidance
- Offer allopurinol first line in people who have major cardiovascular disease
- Assess lifestyle and comorbidities (including cardiovascular risk factors and CKD)
- ULT should not be started during an acute attack, as it will increase its intensity. Usually wait at least 2 to 4 weeks after an acute episode before starting ULT. Once ULT is commenced it is continual (typically lifelong) and must **not** be stopped during acute gout flares.
- Discuss the benefits and risks of taking medicines to prevent gout flares when starting or titrating ULT
    - For people who choose to have treatment to prevent gout flares when starting or titrating ULT, offer colchicine while the target serum urate level is being reached.
    - If colchicine is contraindicated or not suitable, consider a low dose NSAID or a low dose oral corticosteroid (note off-label use of NSAID and corticosteroids). Consider adding a PPI, taking into account individual risk factors
- Analgesic doses of aspirin should be avoided. Low dose aspirin has the potential to precipitate gout; it should be reviewed and continued if indicated.

Cautions

- Allopurinol can cause rashes, including the rare and potentially life-threatening Allopurinol Hypersensitivity Syndrome (AHS). Monitor closely for hypersensitivity syndrome when therapy is initiated.
- Caution is required if prescribing febuxostat in patients with pre-existing major cardiovascular disease, particularly in those with evidence of high urate crystal and tophi burden or those initiating urate lowering therapy- see MHRA. Febuxostat should be stopped if signs or symptoms of serious hypersensitivity (e.g. serious skin reactions or systemic hypersensitivity) occur, see MHRA.

Renal Impairment

- Allopurinol should be used with caution (risk of accumulation) – refer to BNF re dose adjustments. The British Society of Rheumatology (BSR) give further recommendations on starting doses according to GFR to reduce the risk of allopurinol hypersensitivity– refer to table 2 in BSR guideline
- Febuxostat requires no dose adjustment in mild or moderate renal impairment. Caution in severe renal impairment (creatinine clearance <30mL/min).

10.1.5 Other drugs for rheumatic diseases

Prescribing Notes

- Prescribing of glucosamine or chondroitin products is not supported by DoH or NICE due to insufficient evidence for efficacy, see Limited Evidence List and Stop List

10.2 Drugs used in neuromuscular disorders

10.2.1 Fibromyalgia

Prescribing notes

- Fibromyalgia is a type of chronic primary pain. Chronic primary pain has no clear underlying condition or is out of proportion to any observable injury or illness.
- Recommended management options are mainly non-pharmacological – see 4.7.2 [add jump] and NICE NG193
- Antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine or sertraline) can be considered even in the absence of depression. Note this is off-label use.
- **Do not initiate** opioids, NSAIDs, paracetamol, antiepileptic drugs (including gabapentinoids), antipsychotics, benzodiazepines, local anaesthetics, corticosteroid +/- local anaesthetic trigger point injections or ketamine
- See also 4.7.2 [add jump] for the management of chronic secondary pain e.g. low back pain or osteoarthritis

10.2.2 Skeletal muscle relaxants

Choice	Drug
1st choice	Baclofen tablets 10mg; oral solution 10mg/5mL
2nd choice	Diazepam tablets 2mg, 5mg, 10mg; solution for injection amps 10mg/2mL

Prescribing Notes

- This section of the formulary is to inform choices for approved indications for muscle relaxants i.e.
    - spasticity associated with neurological disorders or damage

- relief of chronic skeletal muscle spasm associated with disorders of the spine or other spinal lesions
- Muscle relaxants are not indicated for spasm or pain associated with injury, fibromyalgia, sciatica or pain with a different aetiology

- For spasticity associated with MS see NG220 Multiple sclerosis in adults: management.
- The underlying cause of spasticity should be treated and any aggravating factors (e.g. pressure sores, infection) remedied.
- Baclofen and tizanidine's initiation and discontinuation should be gradual, refer to product literature for full information.
- Diazepam should be used only if there is clinical evidence of muscle spasm that is painful or causing disability; discontinue after a maximum period of 5-7 days.
- Prescribing of methocarbamol is not supported – it is a drug of limited clinical value and is classified by the BNF as 'less suitable for prescribing'. It is included in the HSC Limited Evidence and Stop List.

Cautions

- See here for cautions when prescribing benzodiazepines.

10.2.3 Nocturnal Leg Cramps

Prescribing Notes

Quinine

- Quinine is very toxic in overdosage and accidental fatalities have occurred. Trials show patients experience only one less episode per week taking quinine compared with placebo and that cramp duration is not significantly affected. **It is not recommended for treating idiopathic leg cramps due to poor benefit-to-risk ratio.** See MHRA
- Prescribers are advised to only consider quinine:

  - when cramps are very painful or frequent
  - when other treatable causes of cramp have been ruled out
  - when non-pharmacological measures (e.g. passive stretching exercises) have been ineffective
- Monitor closely during early treatment for adverse effects including unpredictable, serious and life-threatening thrombocytopenia, cinchonism (even at therapeutic doses) and hypoprothrombinaemia.
- Treatment should be stopped if there is no benefit after an initial trial of four weeks. If treatment continues, benefit should be assessed every 3 months. In patients taking quinine long term, a trial discontinuation should be considered- Quinine Prescribing Review Tool.
- Quinine should be used with caution in people with risk factors for QT prolongation, taking other medicines that could prolong the QT interval or in those with atrioventricular block. For further details see MHRA.

10.3 Drugs used for the treatment of soft-tissue disorders and topical pain relief

10.3.2 Rubefacients, topical NSAIDs, capsaicin, and poultices

Choice	Drug
1st choice	Ibuprofen 5% gel

Prescribing Notes

- In Osteoarthritis (OA), topical NSAIDs are a first-choice treatment and should be offered to people with knee OA and considered for OA of other joints. Topical NSAIDs should be considered before oral NSAIDs.
- All topical NSAIDS are considered equally efficacious **therefore Ibuprofen 5% gel should be prescribed as the 1st line NSAID gel of choice.**

- Patients should be advised against excessive exposure to sunlight to the area treated in order to avoid possibility of photosensitivity. Those who use topical ketoprofen should avoid direct sunlight and sunbeds, see MHRA.
- The evidence available does not support the use of topical rubefacients in acute or chronic musculoskeletal pain.

Editorial note: on conclusion of chapter review complete summary sheet and tagging updates.