CLINICAL GUIDELINE

Acute and Chronic Gout management

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

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Clinical Guideline – Acute and Chronic Gout Management

Section 1 Background to Gout

Introduction
This guideline is intended for use in adult non-pregnant patients with acute or chronic gout receiving treatment in hospital or primary care

Epidemiology
Gout is common;

- affects over 2% of the UK population
- increasing incidence, prevalence and severity
- more common in men

Risk Factors

- Hyperuricaemia – but it is not recommended that asymptomatic hyperuricaemia is treated
- Obesity - aim for Body Mass Index in optimal range – a well-balanced diet and regular exercise should be encouraged.
- Diet - alter diet to avoid purine rich foods (red meat, seafood, fructose)
- Excess alcohol – reduce alcohol (especially beer and spirits)
- Dehydration – important to keep well hydrated
- Medication – review diuretics and consider stopping thiazide diuretic if appropriate.
- Renal impairment
- Metabolic syndrome – hypertension, hyperlipidaemia, diabetes mellitus type 2, treat as appropriate

Diagnosis

Presentation

- Acute attacks usually start very rapidly with pain, redness and swelling
- Typically the first metatarsophalangeal joint is affected
- Almost any joint can be affected
- If gout is left untreated, it is likely to affect more joints over time

Differential Diagnosis

- Septic arthritis
- Pseudo-gout (pyrophosphate arthritis)

Investigations

- Serum urate – this sometimes falls during acute attacks, so if the urate is normal, it should be repeated once the acute attack has resolved
- Urea and electrolytes, liver function tests. Consider glucose/lipids
- Joint aspiration for gram stain, culture and microscopy for urate crystals. This is not needed if the diagnosis has previously been established and there is no suspicion of septic arthritis
- X-ray feet

Education

Patients should receive education on:

- Treating acute attacks as soon as possible
- Modification of lifestyle and risk factors
- Use of urate lowering therapy.

Self-care

During a gout attack, it is important to rest, raise the limb and avoid knocking or damaging the affected joint. Ice packs also help.

Referral to Secondary Care

Most patients are cared for in Primary Care however refer to secondary care if:

- Septic arthritis is suspected, then referral to A&E is required.
- Joint aspiration (for diagnosis, exclusion of sepsis and treatment) is required, then urgent telephone referral to Rheumatology is required – see Appendix 1 for contact details.

Telephone advice from Rheumatologists will often avoid the need for referral

Section 2 Drug Treatment for Acute Gout

Symptoms of an acute attack of gout typically develop over a few hours and last up to 3 to 10 days. If patient is already on allopurinol or febuxostat for chronic gout, DO NOT STOP IT. If possible, stop diuretics. To manage pain and inflammation see below for treatment options. For further information regarding cautions, contraindications and drug interactions refer to BNF and Summary of Product Characteristic.

NSAID
Oral non-steroidal anti-inflammatory drug (NSAID) at maximum dose e.g. naproxen 500mg twice daily unless contraindications, +/- proton pump inhibitor (PPI) for 1 to 2 weeks until the acute attack settles.

Renal impairment: the lowest effective dose should be used for the shortest possible duration. Avoid in eGFR < 30ml/minute. Consider corticosteroid if mild to moderate renal impairment and contact Rheumatology if corticosteroid are still not appropriate – see Appendix 1 for contact details

Colchicine
Alternatively, colchicine 500 micrograms twice daily for up to 6 days can be prescribed. N.B: Licensed courses of colchicine for acute attacks do not exceed 6mg (12 tablets) in total, with 3 days between courses. The use of colchicine is limited by the development of toxicity at higher doses, but it is of value if NSAIDs are contraindicated, not tolerated or ineffective. In patients with heart failure, unlike NSAIDs, it does not induce fluid retention and it can be given to patients receiving anticoagulants.
IMPORTANT NOTE: Patients should be counselled to carefully follow the prescribed dosage and STOP taking colchicine if gastrointestinal upset/diarrhoea. Consider corticosteroid if gastrointestinal upset/diarrhoea and contact Rheumatology if corticosteroid are still not appropriate – see Appendix 1 for contact details

Renal impairment: Should not be used in patients with severe renal impairment (eGFR < 10ml/minute). For mild/moderate renal impairment (eGFR 10 to 50ml/minute) and in the elderly, reduce dose or increase dosage interval.

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 at extremes of age.
Drug Interactions: Colchicine should also only be used with caution and at low doses in patients taking drugs that are potent inhibitors of cytochrome P450 3A4 (e.g. cimetidine, clarithromycin, erythromycin, fluoxetine, ketoconazole, protease inhibitors, tolbutamide) or p- glycoprotein (e.g. clarithromycin, ciclosporin, erythromycin). Caution is also required when using colchicine in patients receiving statins, particularly in those with renal impairment, as there are case reports of myopathy and rhabdomyolysis following combined use of colchicine and statins. See BNF and SPC for further information on interactions.

Corticosteroid
It is recommended that a short course of oral corticosteroid or single injection of intramuscular corticosteroid can be used in people unable to tolerate NSAIDs or colchicine and where intra-articular injection is not feasible. Although no studies on the optimum dose and duration of oral corticosteroids for gout are available, a suggested dose of oral prednisolone 30-35 mg once a day for 3-5 days is based on a recommendation from the European League against Rheumatism Allopurinol (European Alliance of Association of Rheumatology) guideline. If intramuscular corticosteroid is considered discuss with Rheumatology – see Appendix 1 for contact details.

+/- Joint aspiration/ intra-articular injection

+/- Joint aspiration/ intra-articular injection of a corticosteroid in mono-articular gout after infection excluded by negative synovial fluid culture (e.g. methylprednisolone or triamcinolone) - discuss with Rheumatology (see Appendix 1 for contact details).

Review
Review at 4 to 6 weeks – assess lifestyle and cardiovascular risk factors, undertake medication review, measure serum uric acid level and renal function

Section 3 Drug Treatment for Chronic Gout

Just over half of all people with gout (62%) experience a repeat attack within a year. Two methods are used to prevent further attacks of gout - making lifestyle and risk factor changes to reduce uric acid levels, and medication to reduce uric acid levels.

Medication to reduce uric acid levels - what is the aim?

- To prevent further acute attacks of gout. Warn the patient that attacks may continue until serum urate lowering therapy is established
- To reduce the size of tophi
- To reduce joint damage

Serum Urate Target Level

Aim for initial serum urate ≤ 300 micromol/L. Until the target is achieved, the patient will require serial monitoring of serum urate. Annual serum urate monitoring is encouraged, particularly if recurrent acute attacks. After some years (at least 3 years) of successful treatment, when tophi have resolved and the patient remains free of symptoms, the dose of urate lowering therapy can be adjusted to maintain the serum urate at or below a less stringent target of 360 micromol/L. The aim is to avoid further crystal deposition and the possibility of adverse effects that may be associated with a very low serum urate level. Studies have shown a possible association between low serum urate levels and progression of neurodegenerative disorders.

Who to treat with serum urate lowering therapy?

Urate lowering therapy should be discussed and offered to all patients who have a diagnosis of gout, particularly advised in patients with the following:

- recurring attacks (≥ 2 acute attacks in 12 months)
- tophi
- chronic gouty arthritis
- joint damage
- renal impairment (eGFR < 60ml/min)
- a history of urolithiasis
- diuretic therapy use
- primary gout starting at a young age (under 40 years)
- very high serum urate **> 500 micromol/L.**

Drug Treatment for Chronic Gout

Commencement of urate lowering therapy is best delayed until after the acute inflammation settles as it is better to discuss when the patient is not in pain. Therefore, urate lowering therapy is usually started 1 – 2 weeks after the acute attack has settled to lower serum urate levels and reduce risk of further acute attacks, and continued indefinitely. However, if attacks are so frequent to make this difficult, urate lowering therapy may be started during acute inflammation, providing treatment for acute gout also given.

The treatment options below outline dosing advice, with some guidance provided on renal impairment, cautions and drug interactions, however for further information refer to BNF and Summary of Product Characteristic.

Allopurinol

Allopurinol is the recommended first line drug, initially 100mg daily, dose to be taken preferably after food.

Renal impairment: Start with 50mg daily or 100mg on alternate days in renal impairment. From the BNF, in renal impairment the maximum recommended dose is 100mg daily, increased only if response is inadequate. Do not increase allopurinol above 100mg daily if eGFR < 30ml/minute without discussion with Rheumatology or Renal. Lowering the starting dose of allopurinol appropriate to the level of renal function reduces the risk of allopurinol hypersensitivity, and subsequent gradual increase in the dose based on renal function results in reduction of serum urate to target levels without increase in toxicity. In patients with renal impairment, smaller increments (50 mg) should be used and the maximum dose will be lower, but target urate levels should be the same.

Drug Interactions: There have been rare reports of increased effect of warfarin and other coumarin anticoagulants when co-administered with allopurinol, therefore, all patients receiving anticoagulants must be carefully monitored. See BNF and Summary of Product Characteristic for full list of interactions in relation to allopurinol section

Skin rashes: may occur in up to 10% of people and could be a first sign of severe but rare hypersensitivity reaction. Patients should be advised to stop allopurinol immediately and seek medical advice promptly. After recovery from mild reactions, allopurinol tablets may, if desired, be re-introduced at a small dose and gradually increased. If the rash recurs allopurinol tablets should be permanently withdrawn as more severe hypersensitivity may occur.
Review: Every 4 weeks check the serum urate level, and escalate the dose of allopurinol by 100mg daily at monthly intervals to target serum urate level. Usual maintenance dose of allopurinol is 300mg per day (maximum 900mg daily in divided doses, preferably after food,). Once this target is achieved, it often takes up to a year or two before all crystals have dissolved and no further attacks occur, and the less stringent serum urate target can be applied. The medication will then usually be life-long.
Screening: Screening patients of Korean, Han Chinese and Thai descent for HLA-B*5801 before considering ULT with allopurinol has been recommended [35] because of the high frequency (6–12%) of this allele in these ethnic groups compared with <2% in Caucasian populations. Patients with this allele have a much higher risk of hypersensitivity reaction and allopurinol should be avoided.

Febuxostat
If the patient is intolerant of allopurinol (side effects of high dose can include severe rash), allopurinol is contraindicated or in symptomatic patients whose uric acid levels have failed to respond adequately despite optimal dosing of allopurinol, then try febuxostat 80mg daily. Ideally start febuxostat after acute attack has settled unless attacks are so frequent to make this difficult. Increase dose after 4 weeks to 120mg daily if necessary to achieve serum urate target level.
Renal impairment: Consult with Rheumatology if eGFR <30ml/minute for treatment alternatives – see appendix 1 for contact details.
Cautions: Maximum dose of 80mg daily in mild liver impairment (no information available in moderate-severe liver impairment). Use with caution in patients with thyroid disorders. Use with caution in pre-existing major cardiovascular disease.

Serious hypersensitivity reactions: Stevens-Johnson syndrome and acute anaphylactoid / shock reactions have been reported, mostly during the first month of therapy. Patients should be advised of the signs and symptoms of severe hypersensitivity; febuxostat must be stopped immediately if these occur (early withdrawal is associated with a better prognosis), and must not be restarted in patients who have ever developed a hypersensitivity reaction to febuxostat. Most cases occur during the first month of treatment; a prior history of hypersensitivity to allopurinol and/or renal disease may indicate potential hypersensitivity to febuxostat.

Prophylactic NSAID or colchicine
The initiation of urate lowering therapy may precipitate an acute attack of gout, and therefore an NSAID or colchicine should be used as a prophylactic during initial urate lowering therapy. There is limited evidence available about prophylactic medication and duration, and treatment choice often depends on co-morbidities and contraindications to medicines. The BNF recommends that low dose NSAID e.g. naproxen 250mg twice daily +/- PPI, or colchicine e.g. 500micrograms once or twice daily can be considered as short term prophylaxis for at least one month after hyperuricaemia has been corrected (usually for first 3 months) to avoid precipitating an acute attack. If an acute attack develops during treatment, then the urate lowering therapy should continue at the same dosage and the acute attack treated in its own right.

References

1. Hui, M., Carr, A., Cameron, S., et al. (2017) The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology 56(7), 1-20
2. BNF (2017) British National Formulary. 74th edn. London: British Medical Association and Royal Pharmaceutical Society.
3. National Institute for Health and Care Excellence (NICE). Clinical Knowledge Summaries: Gout. https://cks.nice.org.uk/topics/gout/: Accessed 09022021
4. Richette, P., Doherty, M., Pascual, E., et al. (2017) 2016 updated EULAR evidence- based recommendations for the management of gout. Annals of the Rheumatic Diseases 76(1), 29-42.

Appendix 1: Telephone Contact Details for Rheumatology Teams

New Stobhill Hospital	0141 355 1521 or 1062
Glasgow Royal Infirmary	0141 451 5384
Gartnavel General Hospital	0141 211 3057 or 0141 531 3720
New Victoria Hospital	0141 347 8058
Queen Elizabeth University Hospital	0141 451 6081
Royal Alexandra Hospital	0141 314 9557
Inverclyde Royal Hospital	01475 504561