PHARMACOLOGICAL MANAGEMENT OF GOUT

Management of ACUTE gout¹
(If septic arthritis suspected refer urgently to Orthopaedics)

Affected joints should be rested, elevated and kept cool. Consider use of ice packs and bed cages. Start analgesic/anti-inflammatory drug therapy immediately and continue for 1-2 weeks.

- Maximum dose of fast-acting NSAID (refer to Box A below) with PPI for gastro-protection if indicated. If effective, continue the NSAID until 48 hours after the attack has finished (up to 1-2 weeks). As the pain resolves, reduce the dose of the NSAID.

If NSAIDs are contraindicated consider:
- Colchicine 500 micrograms, two to four times a day, until symptoms relieved.²
- For acute gout do not exceed a total dose of 6 mg of colchicine (i.e. up to 6 days with colchicine 500 micrograms twice a day, or up to 3 days with colchicine 500 micrograms four times a day). Course not to be repeated within three days.²
- Reduce dose or increase dosage interval if eGFR 10-50 mL/minute/1.73 m². Avoid if eGFR less than 10 mL/minute/1.73 m².²

In patients with acute gouty mono-arthritis and the above treatments are contraindicated, not tolerated or ineffective consider:
- Corticosteroid (intra-articularly, orally or intramuscularly) (Refer to Box B below).

Do any of the following apply?
- Definite diagnosis of gout following a second or further attacks within one year.
- Presence of tophi.
- Presence of gouty erosive disease.
- Evidence of gout interstitial renal disease.

YES- Consider LONG TERM TREATMENT with uric acid lowering therapy at least one to two weeks after acute attack has resolved.

Initial long-term treatment should be with allopurinol at 100 mg/day preferably after food.² For short term prophylaxis of gout attacks during initial treatment with allopurinol or uricosuric drugs prescribe a low dose NSAID +/- PPI or colchicine 500micrograms twice a day.²

Continue prophylactic therapy against gout attacks until serum uric acid level is less than 300micromol/L (0.3mmol/L)¹ & is stable for a minimum of 4 weeks. There is a risk of precipitating acute attacks for approximately 12 months, therefore duration of prophylactic therapy is a clinical decision.

- Check serum uric acid levels every 4 weeks and increase allopurinol dose by100mg increments not more frequently than every 4 weeks, until therapeutic target is reached [serum uric acid <300micromols/L (0.3mmol/L)]. Usual maintenance dose in mild conditions is 100mg-200mg daily, in moderately severe conditions 300mg-600mg daily and in severe conditions 700-900mg daily. Max dose is 900mg/day. Doses over 300mg daily should be given in divided doses.²
- If allopurinol is not tolerated or is contraindicated consider febuxostat³ (Refer to Box B below) initially at a dose of 80mg daily*** for 2 to 4 weeks. Only increase to 120mg daily if target uric acid level (<300micromol/L, 0.3mmol/L) is not achieved. Prophylactic therapy should be continued for 6 months.⁴

*** The licensed starting dose for febuxostat is 80mg daily, but starting with a lower dose such as 40mg (half of the 80mg tablet) may reduce the incidence of gout flares.

Note: Aspirin in low doses (75-150mg/day) has insignificant effects on plasma urate, but higher doses interfere with uric acid excretion and should be avoided.¹

Recommended Corticosteroid Doses³
Also Consult Product SPCs
Prednisolone oral 20-40mg once a day for 5 days.
One-off intra-articular injection (if only single joint involvement, then this is preferable to oral or IM steroids):
Methylprednisolone 10-80mg, hydrocortisone acetate 12.5-25mg OR triamcinolone acetonide 20-40mg.
Smaller joints: methylprednisolone or hydrocortisone
Larger joints: methylprednisolone or triamcinolone.
One-off IM injection into gluteal muscle: Methylprednisolone 40-120mg OR triamcinolone acetonide 40-80mg. The dose will depend on the size of the joint and the severity of the condition.

Recommended NSAIDs & licensed doses for ACUTE gout. BNF and local formulary recommended products (order of choice):
1) Naproxen tablets: 750mg initially, then 250mg every 8 hours.
2) Indometacin capsules: 50mg 3-4 times a day.
3) Etoricoxib tablets: 120mg once a daily for a maximum of 8 days. Caution in patients at higher risk of cardiovascular disease.² People with gout may be at a higher risk of cardiovascular disease.²

Dealing with flares whilst on uric acid lowering therapy:
- Suppress pain and reduce inflammation.
- Do not interrupt uric acid lowering therapy unless there is a clinical reason (gout flare is not a clinical reason).
- Continued flares of gout despite uric acid levels less than target level (300micromol/L, 0.3mmol/L) for more than 3 months should be referred to rheumatology.

Box A

Box B

Recommended NSAIDs & licensed doses for ACUTE gout. BNF and local formulary recommended products (order of choice):

1) Naproxen tablets: 750mg initially, then 250mg every 8 hours.
2) Indometacin capsules: 50mg 3-4 times a day.
3) Etoricoxib tablets: 120mg once a daily for a maximum of 8 days. Caution in patients at higher risk of cardiovascular disease.² People with gout may be at a higher risk of cardiovascular disease.²

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(or earlier if there is significant new evidence relating to this recommendation)
Supporting information

Gout is a disorder caused by deposition of urate crystals in joints and other tissues. There are four clinical stages: (i) asymptomatic hyperuricaemia; (ii) acute gouty arthritis; (iii) intercritical gout (intervals between acute attacks); and (iv) chronic tophaceous gout. Estimated prevalence of gout 1.5% of the population (1,500 per 100,000). 81% of these are eligible for urate-lowering drugs. Estimated male to female ratio is 3.6 to 1.

A significant proportion of the population have a high serum uric acid concentration, but comparatively few people present with clinical symptoms related to gout. 40% of people experiencing an acute attack of gout have a normal serum uric acid concentration. A relationship with symptoms is likely above a serum uric acid concentration 360micromol/L(0.36mmol/L).

A reduction in the serum uric acid concentration below the 'saturation point' (approx 360micromol/L= 0.36mmol/L= 6mg/dL) is necessary to avoid precipitation of uric acid crystals in tissues in the long term. For the management of recurrent, intercritical and chronic gout the plasma urate should be maintained below 300micromol/L(0.3mmol/L). NICE estimate that 3% of people will be intolerant of allopurinol or have a contraindication.

Colchicine dose for acute gout

The BNF reflects the advice in the British Society for Rheumatology and British Health Professionals in Rheumatology Guideline for the Management of Gout (2007) and further expert advice that for the treatment of acute gout, colchicine should be given no more frequently than 2–4 times daily. This dose is preferred to the licensed dose of every 2–3 hours because, while remaining effective, it is less likely to cause side-effects. Colchicine is not an analgesic and has no effect on blood concentrations of uric acid, or on the excretion of uric acid. It is thought that it reduces the inflammatory reaction to urate crystals. Colchicine has a narrow therapeutic margin, and overdosage may be serious. The most frequent adverse effects of oral colchicine are those involving the gastrointestinal tract and may be associated with its antimitotic action. Diarrhoea, nausea, vomiting, and abdominal pain are often the first signs of toxicity and are usually an indication that colchicine therapy should be stopped or the dose reduced. Treatment should be started as soon as possible and an effect may be expected within 12 hours.

Allopurinol and skin rash

Pruritic maculopapular skin rashes may occur in up to 10% people who take allopurinol — a rash can be the first sign of a rare hypersensitivity reaction. Patients should be advised to stop allopurinol immediately and seek medical advice promptly. When the rash has gone if it was mild, gradually reintroduce the allopurinol. If the rash recurs, immediately discontinue the allopurinol. Overall, adverse effects are rare but their incidence (particularly rashes) is higher in the presence of renal impairment.

Febuxostat and hypersensitivity reactions

Febuxostat treatment should be stopped immediately if signs or symptoms of serious hypersensitivity reactions occur – early withdrawal is associated with a better prognosis. If a patient has ever developed a hypersensitivity reaction with febuxostat, including Stevens-Johnson syndrome, febuxostat must not be re-started at any time. Most cases of hypersensitivity to febuxostat occur during the first month of treatment. Patients should be advised of signs and symptoms of severe hypersensitivity or Stevens-Johnson syndrome; these include: infiltrated maculopapular eruption, generalised or exfoliative rashes, skin lesions, facial oedema, fever, haematologic abnormalities such as thrombocytopenia, a single or multiple organ involvement (liver and kidney including tubulointerstitial nephritis), progressive skin rashes associated with blisters or mucosal lesions and eye irritation, a prior history of hypersensitivty to allopurinol and/or renal disease may indicate potential hypersensitivity to febuxostat.

Injectable corticosteroids

Intramuscular corticosteroids are not specifically licensed for the treatment of gout. Triamcinolone acetonide or methylprednisolone can be given as a one-off deep intramuscular injection to relieve the symptoms of gout. In order to avoid the danger of subcutaneous fat atrophy, the corticosteroid should be deeply injected into the gluteal muscle. Intra-articular corticosteroids are not specifically licensed for the treatment of gout. Atrophy of subcutaneous tissues and local skin depigmentation may occur from peri-articular leakage of corticosteroid. The risk is greatest if large or repeated doses of a long-acting, potent corticosteroid are given.

Consult BNF and/or relevant SPCs for further information on contraindications/cautions and adverse effects for medicines used for gout.

References:
2. Electronic BNF. Last accessed 08/12/2015: https://www.medicinescomplete.com/mc/bnf/current/
4. SPC for allopurinol (Zyloric®) 100mg & 300mg tablets by A. Menarini Farmaceutica Internazionale SRL. EMC last updated 13th August 2015. http://www.medicines.org.uk/emc/search
5. Clinical Knowledge Summaries (CKS), Management of Gout. Last revised April 2015. Gout - NICE CKS
7. SPC for allopurinol (Zyloric®) 100mg & 300mg tablets by Aspen. EMC last updated 13th August 2015. http://www.medicines.org.uk/ark/7e125320d6ebf2f5a7f7943e30f1f436
10. NICE TA281, April 2013. Canakinumab for treating gouty arthritis attacks and reducing the frequency of subsequent attacks.