

## Acute Gout Management:

**Start anti-inflammatory/analgesic therapy straight away and continue for 1-2 weeks**  
Affected joints should be rested, elevated and kept cool. Avoid trauma to the affected joint and consider the use of an ice pack or bed-cage. [2] [3]

**1<sup>st</sup> line: NSAIDs** continued for 24-48 hrs after attack has resolved.

There is no evidence to suggest 1 NSAID is more effective than another. NSAIDs benefit from being quick acting but are associated with GI and renal safety concerns.

The British Society for Rheumatology guideline recommends using any NSAID at maximum dose as early as possible. Maximal doses of NSAIDs are considered a risk factor for gastrointestinal effects, therefore co-prescribing of a proton pump inhibitor is recommended for gastric protection. [3] [4]

**OR alternative 1<sup>st</sup> line: Colchicine depending on patient preference, renal function and co-morbidities** - 500 micrograms 2-3 times per day, until symptoms are relieved  
Can be used in patients on warfarin and in patients with heart failure but use is limited by side effects (can cause profuse diarrhoea) and the development of toxicity at higher doses. (See also colchicine [prescribing information](#)) [3]

**2<sup>nd</sup> line: Corticosteroids** [3]

**STAT Intra-articular injection** (Off license use. Suitable for gouty monoarthritis only)

- Methylprednisolone 10-80mg, Hydrocortisone acetate 12.5-25mg or Triamcinolone acetonide 20-40mg

If intra-articular injection is not feasible

- **Oral** -Prednisolone 20-40mg daily for 5 days  
**OR STAT Intramuscular injection** -Methylprednisolone 40-120mg or Triamcinolone acetonide 40-80mg

**In patients with acute gout where response to monotherapy is insufficient, combinations of treatment can be used (most commonly an NSAID combined with another agent).**

**Does the patient have any of the following?** [1]

- Definite diagnosis of gout  $\geq 2$  attacks within 1yr
- Tophi
- Erosive arthropathy (x-ray)
- Uric acid nephropathy or nephrolithiasis
- Polyarticular flare at presentation [5]

**If NO:** Uric acid lowering therapy is not indicated. **If 1<sup>st</sup> attack check serum urate (sUA) 4weeks post flare.**

**Reconsider diagnosis:** refer persistent symptoms without definitive diagnosis secondary care [2]

**If YES: consider LONG TERM TREATMENT with uric acid lowering therapy.**

## Chronic Gout Management

 [2] [5]

(See also allopurinol and febuxostat [prescribing information](#))

- Ensure serum urate (sUA) levels are obtained after the convalescent period (4 weeks post-acute attack)
- Commence **allopurinol 1<sup>st</sup> line** ensuring at least 1-2 weeks have passed from last attack
  - Start at 50-100 mg/day, and titrate to achieve sUA <300  $\mu\text{mol/l}$
  - Recheck sUA 4 weeks after initiation
  - If >300 $\mu\text{mol/l}$  increase to 200 mg/day
  - Recheck sUA after a further 4 weeks
  - If >300 $\mu\text{mol/l}$  increase to 300 mg/day
  - Continue monthly sUA levels, increasing by a further 100mg/day each month until sUA <300  $\mu\text{mol/l}$  or maximum tolerated dose is reached (The BNF max dose = 900 mg per day, [8] but locally it has been agreed that treatment should be reviewed at 600 mg per day)
  - Once sUA target is achieved, annual sUA measurements are recommended
- **Co-prescribe prophylactic colchicine** (500 micrograms once or twice daily for up to 6 months) **or low dose NSAID** (e.g. ibuprofen 200mg twice daily or naproxen 250mg daily with gastroprotection). [3] [4] to prevent an acute gout flare.

**If allopurinol is contraindicated, not tolerated or there is inefficacy despite titration to 600 mg per day.**

- Consider **Febuxostat 2<sup>nd</sup> line** ensuring at least 1-2 weeks have passed from last attack (See also [NICE TA 164](#) and [SPC](#)) [9] [10] [11]
  - The licensed starting dose is 80 mg once daily
  - If after 4 weeks, the sUA is >300  $\mu\text{mol/l}$  then the dose can be increased by 40mg & sUA rechecked in a further 4 weeks
  - Max dose = 120 mg daily
- **Co-prescribe prophylactic colchicine** (500 micrograms once or twice daily for up to 6 months) **or low dose NSAID** (e.g. ibuprofen 200mg twice daily or naproxen 250mg daily with gastroprotection). [3] [4]

**NB: Stop febuxostat immediately if hypersensitivity occurs, do not restart** ([See MHRA warning](#))

**Refer to Secondary Care** [2] [5]

**Immediately if Septic Arthritis is suspected**  
(Please note it is possible for both gout and septic arthritis to co-exist)

**Or by routine referral if:**

- Patient contraindicated to or cannot tolerate allopurinol or febuxostat
- The sUA is unresponsive to uric acid lowering therapy or suffering persistent symptoms despite maximal NSAIDs
- If gout persists despite uric acid levels <300 $\mu\text{mol/l}$
- Patient suffers complications relating to gout e.g. nephropathy
- Patient requires Intra-articular therapy and primary care are not able to provide
- Pregnancy, young onset of primary gout (<30years) or diagnostic uncertainty

**In Addition to Acute Management**

- **Assess lifestyle factors** and provide advice. E.g. reduce alcohol intake (particularly beer) and intake of purine rich foods (shellfish & meat) [2] Click on the relevant link for patient information on [6]:
  - [Gout](#)
  - [Diet](#)
  - [Related health problems](#)
  - [Treatments](#)
- **Treat cardiovascular risk factors and review annually:** There is a connection between sUA levels and CV disease, with high sUA being part of metabolic syndrome. Additionally components of metabolic syndrome are independent risk factors for gout [2] [3]
- **Consider drug induced gout:**
  - Low dose aspirin** (75-150mg/day) can interfere with uric acid excretion and use is a risk factor for incident gout. [3]
  - Review antihypertensives:** Diuretics (Inc. thiazide), B-blockers, ACE inhibitors and non-losartan angiotensin II receptor blockers increase sUA. Losartan and calcium channel blockers decrease sUA. [7]

**DO NOT interrupt uric acid lowering therapy unless there is a clinical reason Gout flare is NOT a clinical reason)** [2]

**Table 1: Renal Dose Adjustments** [2] [8] [11] [12] [14]

<b>Allopurinol</b> (increase dose by 50mg increments until target sUA reached)	Max. 100 mg daily, increased only if response inadequate; in severe impairment, reduce daily dose below 100 mg, or increase dose interval; if facilities available, adjust dose to maintain plasma-oxipurinol concentration below 100 micromol/litre.
<b>Colchicine</b>	eGFR 10-50: Reduce dose or increase interval eGFR < 10: Do not use <b>Note: colchicine is contraindicated if administered with p-glycoprotein or CYP3A4 inhibitors in renal impairment</b>
<b>Febuxostat</b>	No dose adjustment is necessary in mild or moderate impairment. Efficacy and safety have not been fully evaluated in patients with eGFR <30 – use with caution
<b>NSAIDs</b>	Avoid if possible/use with caution in renal impairment

## Supporting Information

Gout is the most common inflammatory arthritis in the UK and mainly diagnosed and managed in primary care. The clinical course of gout is largely predictable and divided into three stages. [1]

### Stage 1: Asymptomatic Hyperuricaemia

sUA levels rise but no clinical features of gout are present.

### Stage 2: Acute Gout and “intercritical periods”

sUA reaches saturation, monosodium urate (MSU) crystals are precipitated and deposited in joints causing an inflammatory response and painful arthritis. Attacks are self-limiting and followed by asymptomatic “intercritical” periods before the next flare.

### Stage 3: Chronic Tophaceous Gout

Crystal deposits in the joints and surrounding soft tissue. Symptoms are persistent.

**Diagnosis [1]:** sUA is the most important risk factor for gout, but should only be considered in combination with other clinical features, since on its own it does not confirm or exclude a diagnosis of gout. Many patients with hyperuricaemia do not develop gout, and sUA can be normal during an acute attack.

**Acute Gout Diagnosis:** Acute joint pain is the most common presenting complaint. Joints affected include the big toe (up to 78% of 1<sup>st</sup> attacks) foot, ankle, knee, wrist, finger, and elbow.

Urate crystals in fluid aspirated from the affected joint is the “gold standard” for diagnosis, but in reality, this test is only applied to a minority of patients and most patients are diagnosed clinically.

**Features which strongly predict a diagnosis of gout are [1]:**

- First metatarsophalangeal (MTP) joint involvement
- Rapid onset of severe joint pain (over 6-12 hrs)
- Joint swelling and tenderness
- Overlying erythema
- Self-limiting with complete resolution
- Tophus (proven or suspected)

Laboratory and radiological investigations are not necessary as sUA is often normal during an attack, and x-rays are unlikely to be helpful

**Chronic Gout Diagnosis:** In between attacks MSU crystals will be seen in joint fluid providing definitive diagnosis.

In the absence of this, **the following features are strong predictors of gout [1]:**

- History of classical acute attacks
- Presence of tophi
- Asymmetrical swelling within a joint, or subcortical cysts without bony erosions on x-ray
- Double contour sign” (hyperechoic band seen parallel to the edge of the joint line) on ultrasound – N.B. not available in all regions.

## Prescribing Information. Please Refer to Individual [SPCs](#) for Full Details

### Allopurinol [8]

**Renal impairment:** Dose adjustment required see [Table 1](#).

**Side Effects:** Most common are rash and GI intolerance. [1]

**Pruritic maculopapular skin rashes** may occur in up to 10% of people who take allopurinol, the rash can be the 1<sup>st</sup> sign of a severe but rare hypersensitivity syndrome. Patients should be advised to stop allopurinol immediately and seek medical advice promptly. When the rash is gone if the rash was mild allopurinol can be gradually reintroduced, if the rash recurs immediately discontinue the allopurinol.

**Interactions:** Allopurinol potentiates the anticoagulant effect of [warfarin](#) (increase monitoring during dose titration). Do not co-prescribe with [azathioprine](#) (it inhibits the metabolism of azathioprine, leading to accumulation of toxic metabolites). [1]

**Do not start during an acute attack** ensure at least 1-2 weeks have passed before initiation, (can prolong the attack indefinitely). Continue if an attack develops whilst already on treatment and treat attack separately. [3]

Allopurinol doses >300mg should be given in divided doses (maximum 300mg in a single dose).

### Febuxostat [11]

**Cautions:** Max 80mg daily in mild liver impairment (no information available in moderate-severe liver impairment) Use with caution in patients with thyroid disorders, ischaemic heart disease and/or heart failure. [1]

**Side Effects:** Most common are GI, abnormal LFTs and oedema.

**Serious hypersensitivity reactions**, including Stevens-johnson syndrome and acute anaphylactoid/shock reactions have been reported, mostly during the 1<sup>st</sup> month of therapy. Treatment should be stopped immediately if signs of hypersensitivity reactions occur and treatment must not be restarted. <sup>8</sup> [See MHRA warning](#)

**Interactions:** Avoid concomitant use with azathioprine and mercaptopurine

**Do not start during an acute attack** ensure at least 1-2 weeks have passed before initiation, (can prolong the attack indefinitely). Continue if an attack develops whilst already on treatment and treat attack separately. [3]

### Colchicine [12]

**Dose and duration of treatment: For acute attacks**, this guidance recommends 500mcg 2-3 times daily, until symptoms are relieved. This is lower than the dose listed in the SPC, because there is trial and clinical practice evidence that the higher dosing regimen is frequently associated with diarrhoea and other toxic side effects, and not significantly more effective than low-dose colchicine. [13] If colchicine is used for treatment of an acute attack, it can be continued as **prophylactic treatment** at a reduced dose of 500mcg twice daily upon initiation of uric acid lowering therapy and used for up to 6 months.

**Renal impairment:** Dose adjustment required see [Table 1](#).

**Cautions:** Increased risk of toxicity in elderly and debilitated patients. Avoid in patients with blood disorders.

**Side Effects:** Use is limited by side effects and toxicity at higher doses. Can cause profuse diarrhoea, nausea, vomiting and abdominal pain.

## References

- [1] Collaboration of Keele University, Primary Care Rheumatology Society and the British Society for Rheumatology, "INSPIRE Gout Guidelines," August 2012.
- [2] NICE, "Clinical Knowledge Summaries (CKS). Management of Gout (last revised February 2018)," [Online]. Available: <https://cks.nice.org.uk/gout>. [Accessed 25 September 2018].
- [3] Hui M et al, "The British Society for Rheumatology Guideline for the Management of Gout," *Rheumatology*, 2017.
- [4] NICE, "Clinical Knowledge Summaries (CKS), NSAIDs - prescribing issues (last revised July 2015)," [Online]. Available: <https://cks.nice.org.uk/nsaids-prescribing-issues>. [Accessed 25 September 2018].
- [5] Lancashire Care NHS Foundation Trust, "Shared Care Guideline," p. Version 1, December 2014.
- [6] UK Gout Society, "Patient Information Leaflets: "All about Gout and other health problems"; "All about gout and Treatments"; "All about Gout and diet"," [Online]. Available: <http://www.ukgoutsociety.org>.
- [7] Choi et al, "Antihypertensive drugs and risk of incident gout among patients with hypertension: population base case-control study," *BMJ*, vol. <http://www.bmj.com/content/344/bmj.d8190> , 2012.
- [8] Electronic Medicines Compendium, "Summary of Product Characteristics Allopurinol 100mg tablets," Accord Healthcare Limited, 12 10 2007. [Online]. Available: <https://www.medicines.org.uk/emc/product/6007/smpc>. [Accessed 25 September 2018].
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- [10] MHRA, "Drug Safety Update: Febuxostat and hypersensitivity reactions.," 2012. [Online]. Available: <https://www.gov.uk/drug-safety-update/febuxostat-adenuric-stop-treatment-if-signs-or-symptoms-of-serious-hypersensitivity>. [Accessed 25 September 2018].
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- [12] Electronic Medicines Compendium, "Summary of Products Characteristics Colchicine 500 mcg tablets," Wockhardt UK Ltd, 12 December 1982. [Online]. Available: <https://www.medicines.org.uk/emc/product/6415>. [Accessed 25 September 2018].
- [13] American College of Physicians, "Management of Acute and Recurrent Gout: A Clinical Practice Guideline From the American College of Physicians," *Ann Intern Med*, vol. 166, pp. 58-68, 2017.
- [14] Royal Pharmaceutical Society, British National Formulary 76, London: Pharmaceutical Press, 2018.

**The format of this guideline is based on the 2014 Pharmacological Management of Gout, Mersey Area Joint Medicine Guideline**

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Version Control	Date	Amendments Made
1.0	12 <sup>th</sup> November 2015	First Version Approved
1.1	14 <sup>th</sup> January 2016	Updated – Non-losartan angiotensin II blockers increase Serum Uric Acid

1.2	December 2018	Uric acid level updated in line with BSR recommendations. Renal and NSAID dosing information updated.
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