Lancashire & South Cumbria Medicines Management Group

Gout Management Summary Guidelines

Version 1.4 – September 2023

Introduction



VERSION CONTROL		
Version	Date	Amendments made
1.0	November 2015	First Version Approved
1.1	January 2016	Updated – Non-losartan angiotensin II blockers
		increase Serum Uric Acid
1.2	December	Uric acid level updated in line with BSR
	2018	recommendations. Renal and NSAID dosing
		information updated.
1.3	March 2023	Updated in accordance with NICE guidance update
		(June 2022). AG.
1.4	September	Formatting undated
	2023	Formatting updated.

Contents

- 1. Acute Gout Management -Page 3
- 2. Chronic Gout Management Page 4
- 3. Supporting information Page 5
- 4. References Page 6

©Midlands and Lancashire Commissioning Support Unit, 2023.

The information contained herein may be superseded in due course. All rights reserved. Produced for use by the NHS, no reproduction by or for commercial organisations, or for commercial purposes, is allowed without express written permission.

Midlands and Lancashire Commissioning Support Unit, **Jubilee House,** Lancashire Business Park, Leyland, PR26 6TR **Tel:** 01772 644 400 | www.midlandsandlancashirecsu.nhs.uk

Gout Management Summary Guidelines



Acute Gout Management (confirm diagnosis by measuring serum urate level)

Anti-inflammatory/analgesic therapy - 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. [14] [3]

1st line (depending on patient preference/co-prescriptions/co-morbidities)

NSAID at maximum dose until 24-48 hrs after attack has resolved. NSAIDs benefit from being quick acting but are associated with GI and renal safety concerns. Co-prescribing of a proton pump inhibitor is recommended for gastric protection [3] [4]

Or

Colchicine - 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 and the development of toxicity at higher doses. (See also colchicine prescribing information) [3]

Or

Oral Corticosteroids - Prednisolone 10-20mg daily for 5 days

2nd line: Intra-articular or intramuscular 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

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).

Refer to Secondary Care [14]

[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 <300μmol/l
- Patient has CKD stages 3b to 5
- Patient had an organ transplant
- 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. follow a healthy, balanced diet, avoid excessive alcohol consumption. Click on the relevant link for patient information on [6]:
 - o Gout
 - o Related health problems
 - o **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
- 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]

Gout Management Summary Guidelines

Chronic Gout Management

Lancashire & South Cumbria Medicines Management Group

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

- Multiple or troublesome flare (≥2 attacks within 1yr)
- Tophi
- Chronic gouty arthritis / erosive arthropathy (x-ray)
- CKD stages 3 to 5
- Diuretictherapy [5]

Uric acid lowering therapy is not indicated. If 1st attack check serum urate (sUA) 4 weeks post flare

Reconsider diagnosis: refer persistent symptoms without definitive diagnosis secondary care [14]

Yes

Consider LONG TERM TREATMENT (life long) with uric acid lowering therapy.

No

OR

Ensure serum urate (sUA) levels are obtained after the convalescent period (2-4 weeks post-acute attack)

Commence **allopurinol** ensuring at least 2-4 weeks have passed from last attack

- Start at 50-100 mg/day, and titrate to achieve sUA <360 μmol/l
- Recheck sUA 4 weeks after initiation. If >360µmol/l increase to 200 mg/day
- Recheck sUA after a further 4 weeks. If >360μmol/l increase to 300 mg/day
- Continue monthly sUA levels, increasing by a further 100mg/day each month until sUA <360 µmol/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)
- If tophi/chronic gouty arthritis/frequent flares, consider a sUA level below 300 µmol/l.

NB Offer allopurinol as first-line treatment to people with gout who have major cardiovascular disease

Consider as alternative 1st line Febuxostat ensuring at least 2-4 weeks have passed from last attack (See also NICETA 164 and SPC) [9] [10] [11]

- The licensed starting dose is 80 mg once daily
- If after 4 weeks, the sUA is >360 μmol/l then the dose can be increased by 40mg & sUA rechecked in a further 4 weeks
- Max dose = 120 mg daily
- Conduct annual CV risk assessment

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

When initiating allopurinol/febuxostat co-prescribe prophylactic colchicine (500 micrograms once or twice daily for up to 6 months)

OR if colchicine is contraindicated/not tolerated/ineffective consider short term low dose NSAID (e.g. ibuprofen 200mg twice daily or naproxen 250mg daily with gastroprotection) or short term low dose corticosteroid (e.g. prednisolone 10-20mg daily). [3] [4]

Once sUA target is achieved, consider annual sUA measurements

DO NOT interrupt uric acid lowering therapy unless there is a clinical reason Gout flare is NOT a clinical reason) [14]

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

Allopurinol (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.
Colchicine	eGFR 10-50: Reduce dose or increase interval eGFR < 10: Do not use Note: colchicine is contraindicated if administered with p-glycoprotein or CYP3A4 inhibitors in renal impairment
Febuxostat	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
NSAIDs	Avoid if possible/use with caution in renal impairment

Gout Management Summary Guidelines -

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

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 its 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. In people with suspected gout, take a detailed history and carry out a physical examination to assess the symptoms and signs.

NICE recommends confirming clinical diagnosis by measuring serum urate level (>360 μmol/l). If < 360 μmol/l during flare and gout still strongly suspected repeat level 2 weeks after flare has settled. If gout diagnosis uncertain/unconfirmed consider joint aspiration and microscopy of synovial fluid (or x-ray/ultrasound/ dual energy CT if joint aspiration is not

Acute Gout Diagnosis: Acute joint pain is the most common presenting complaint. Joints affected include the big to e (up to 78% of 1st 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 metatars ophalangeal (MTP) joint involvement
- Rapid onset (often overnight) of severe joint pain (over 6-12 hrs)
- Joint swelling and tenderness
- Overlying erythema
- Self-limiting with complete resolution
- Tophus (proven or suspected)

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 <u>Table 1</u>. 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 1st 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 2-4 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 1st month of therapy. Treatment should be stopped immediately if signs of hypersensitivity reactions occur and treatment must not be restarted. 8 See MHRA warning Interactions: Avoid concomitant use with azathioprine and mercaptopurine

Do not start during an acute attack ensure at least 2-4 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 500micrograms 2-3 times daily, until symptoms are relieved (maximum 6mg per course). 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 500micrograms twice daily upon initiation of uric acid lowering therapy and used for up to 6 months.

Renal impairment: Dose adjustment required see <u>Table 1</u>.

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, "NG 219 Gout: diagnosis and management (last revised June 2022)," [Online]. Available: https://www.nice.org.uk/guidance/ng219/chapter/Recommendations. [Accessed 10 August 2022]. [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 April 2020)," [Online]. Available: https://cks.nice.org.uk/nsaids-prescribing-issues. [Accessed 10 August 2022].
- [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 10 August 2022].
- [9] NICE Technology appraisal guidance, "Febuxostat for the management of hyperuricaemia in people with gout [TA164]," 17 December 2008. [Online]. Available:
- https://www.nice.org.uk/guidance/ta164. [Accessed 25 September 2018].
- [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].
- [11] Electronic Medicines Compendium, "Summary of Product Characteristics Adrenuric 80mg film coated tablets," A. Menarini Farmaceutica Internazionale SRL, 21 April 2008. [Online]. Available: https://www.medicines.org.uk/emc/product/487/smpc. [Accessed 10 August 2022].
- [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 10 August 2022].
- [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, 2022.