

Guidelines



The British Society for Rheumatology Guideline for the Management of Gout

Michelle Hui¹, Alison Carr², Stewart Cameron³, Graham Davenport⁴, Michael Doherty⁵, Harry Forrester⁴, Wendy Jenkins⁵, Kelsey M. Jordan⁶, Christian D. Mallen⁴, Thomas M. McDonald⁷, George Nuki⁸, Anthony Pywell⁵, Weiya Zhang⁵ and Edward Roddy^{4,9} for the British Society for Rheumatology Standards, Audit and Guidelines Working Group

Executive Summary

Scope and purpose of the guideline

Need for a revised management guideline

The British Society for Rheumatology/British Health Professionals in Rheumatology guideline for the management of gout was published in 2007 [1]. A revised and updated guideline is now required because of the availability of new pharmaceutical treatment options; recent increases in the incidence, prevalence and severity of gout [2]; continuing suboptimal management in both primary and secondary care [2, 3]; and better understanding of patient and provider barriers to effective care [4, 5].

Objectives of the guideline

To offer revised and updated, concise, patient-focused, evidence-based, expert recommendations for the management of gout in the UK.

Target audience

To provide assistance to doctors and allied health professionals who treat and manage patients with gout in primary care and hospital practice.

Areas that the guideline does not cover

This guideline does not cover the diagnosis and investigation of gout. This guideline has been reviewed



NICE has accredited the process used by the BSR to produce its guidance for the management of gout. Accreditation is valid for 5 years from 10 June 2013. More information on accreditation can be viewed at www.nice.org.uk/accreditation. For full details on our accreditation visit: www.nice.org.uk/accreditation.

¹Department of Rheumatology, Derby Teaching Hospitals NHS Foundation Trust, Derby, ²Hamell, 1st Floor Dome Building, The Quadrant, Richmond, TW9 1DT UK, ³Renal Medicine, Guy's Campus, Kings College London, London, ⁴Research Institute for Primary Care and Health Sciences, Keele University, Keele, ⁵Academic Rheumatology, University of Nottingham, Nottingham, ⁶Rheumatology, Brighton and Sussex University Hospitals NHS Trust, Brighton, ⁷Medicines Monitoring Unit, Ninewells Hospital and Medical School, Dundee, ⁸Institute for Genetics and Molecular Medicine, University of Edinburgh, Edinburgh and ⁹Haywood Academic Rheumatology Centre, Staffordshire and Stoke-on-Trent Partnership NHS Trust, Stoke-on-Trent, UK

Submitted 18 November 2016; revised version accepted 8 March 2017.

Correspondence to: Edward Roddy, Research Institute for Primary Care and Health Sciences, Keele University, Keele, Staffordshire ST5 5BG, UK. E-mail: e.rodny@keele.ac.uk

and endorsed by the Royal College of General Practitioners.

Key recommendations from this guideline

Management of acute attacks

- (i) Educate patients to understand that attacks should be treated as soon as an attack occurs and ensure that patients are aware of the importance of continuing any established urate-lowering therapy (ULT) during an attack (level of evidence (LoE) IV, strength of recommendation (SOR) 90%).
- (ii) Affected joints should be rested, elevated and exposed in a cool environment. Bed-cages and ice-packs can be effective adjuncts to management (LoE Ib (ice-packs), IV (other), SOR 89%).
- (iii) An NSAID at maximum dose or colchicine in doses of 500 µg bd-qds is the drug of choice when there are no contraindications. Choice of first line agent will depend on patient preference, renal function and co-morbidities. Patients on NSAIDs or cyclooxygenase-2 inhibitors (coxibs) should be co-prescribed a gastro-protective agent. (LoE Ia, SOR 95%)
- (iv) Joint aspiration and injection of a corticosteroid are highly effective in acute monoarticular gout and may be the treatment of choice in patients with acute illness and co-morbidity. A short course of oral corticosteroid or a single injection of an intramuscular corticosteroid is an alternative in patients who are unable to tolerate NSAIDs/colchicine and in whom intra-articular injection is not feasible. Such systemic therapy is also appropriate for oligo- or polyarticular attacks of gout [LoE Ib (oral), III (intra-articular, intramuscular), IV (oligo/polyarticular attacks), SOR 94%].
- (v) In patients with acute gout where response to monotherapy is insufficient, combinations of treatment can be used (LoE IV, SOR 80%).
- (vi) IL-1 inhibitors may be considered in patients who have previously not responded adequately to standard treatment of acute gout [although not approved by the National Institute for Health and Care Excellence (NICE)] [LoE Ib (canakinumab, rilonacept), III (anakinra), SOR 61%].

Modification of lifestyle and risk factors

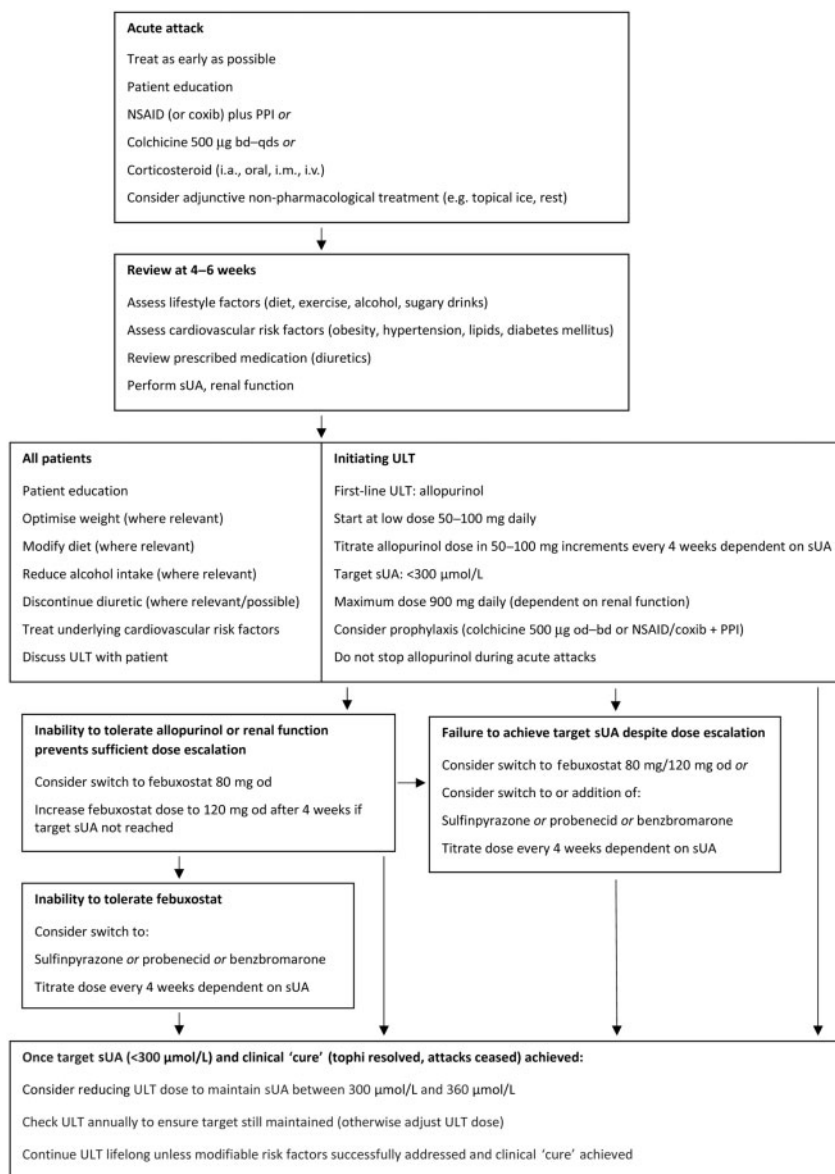
- (i) If diuretic drugs are being used to treat hypertension rather than heart failure, an alternative anti-hypertensive agent can be considered as long as blood pressure is controlled (LoE IV, SOR 91%).
- (ii) All patients with gout should be given verbal and written information about the following: the causes and consequences of gout and hyperuricaemia; how to manage acute attacks; lifestyle advice about diet, alcohol consumption and obesity; and the rationale, aims and use of ULT to target urate levels. Management should be individualized and take into

account co-morbidities and concurrent medications. Illness perceptions and potential barriers to care should be discussed (LoE IIb, SOR 96%).

- (iii) In overweight patients, dietary modification to achieve a gradual reduction in body weight and subsequent maintenance should be encouraged. Diet and exercise should be discussed with all patients with gout, and a well-balanced diet low in fat and added sugars, and high in vegetables and fibre should be encouraged: sugar-sweetened soft drinks containing fructose should be avoided; excessive intake of alcoholic drinks and high purine foods should be avoided; and inclusion of skimmed milk and/or low fat yoghurt, soy beans and vegetable sources of protein, and cherries in the diet should be encouraged [LoE I (vitamin C and skimmed milk), III (others), SOR 92%].
- (iv) Patients with gout and a history of urolithiasis should be encouraged to drink >2 l of water daily and avoid dehydration. Alkalinization of the urine with potassium citrate (60 mEq/day) should be considered in recurrent stone formers (LoE IV, SOR 57%).
- (v) Cardiovascular risk factors and co-morbid conditions such as cigarette smoking, hypertension, diabetes mellitus, dyslipidaemia, obesity and renal disease should be screened for in all patients with gout, reviewed at least annually and managed appropriately (LoE III, SOR 90%).

Optimal use of urate-lowering therapies

- (i) The option of ULT should be explained to patients when the diagnosis is confirmed and they are being given information about gout. Patients should be fully involved in the decision as to when to commence ULT. The importance of taking ULT regularly and continually to prevent the return of gout attacks should be explained. Patients should be supported during the process of lowering their serum uric acid (sUA) levels as it can cause an increase in gout flares during this time (LoE Ib, SOR 94%).
- (ii) ULT should be discussed and offered to all patients who have a diagnosis of gout. ULT should particularly be advised in patients with the following: recurring attacks (≥ 2 attacks in 12 months); tophi; chronic gouty arthritis; joint damage; renal impairment (estimated glomerular filtration rate (eGFR) <60 ml/min); a history of urolithiasis; diuretic therapy use; and primary gout starting at a young age [LoE Ia (attacks, tophi, chronic gouty arthritis, joint damage, renal impairment), III (urolithiasis), IV (diuretics, young age), SOR 95%].
- (iii) Commencement of ULT is best delayed until inflammation has settled as ULT is better discussed when the patient is not in pain (LoE IV, SOR 94%).
- (iv) The initial aim of ULT is to reduce and maintain the sUA level at or below a target level of 300 µmol/l to prevent further urate crystal formation and to dissolve away existing crystals. The lower the sUA the

Fig. 1 Algorithm for the management of gout

coxib: cyclooxygenase-2 inhibitor; PPI: proton pump inhibitor; sUA: serum uric acid; ULT: urate-lowering therapy.

greater the velocity of crystal elimination. After some years of successful treatment, when tophi have resolved and the patient remains free of symptoms, the dose of ULT can be adjusted to maintain the sUA at or below a less stringent target of 360 µmol/L to avoid further crystal deposition and the possibility of adverse effects that may be associated with a very low sUA [LoE III (sUA target <300 µmol/L), IV (subsequent dose adjustment to sUA <360 µmol/L), SOR 97%].

- (v) Allopurinol is the recommended first-line ULT to consider. It should be started at a low dose (50–100 mg daily) and the dose then increased in 100 mg increments approximately every 4 weeks until the sUA

target has been achieved (maximum dose 900 mg). 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 [LoE Ib (dose escalation), III (dose adjustment for renal function), SOR 97%].

- (vi) Febuxostat can be used as an alternative second-line xanthine oxidase inhibitor for patients in whom allopurinol is not tolerated or whose renal impairment prevents allopurinol dose escalation sufficient to achieve the therapeutic target. Start with a dose of 80 mg daily and, if necessary, increase after 4 weeks to 120 mg daily, to achieve therapeutic target (LoE Ia, SOR 90%).

- (vii) Uricosuric agents can be used in patients who are resistant to, or intolerant of, xanthine oxidase inhibitors. The preferred drugs are sulfinpyrazone (200–800 mg/day) or probenecid (500–2000 mg/day) in patients with normal or mildly impaired renal function, or benzbromarone (50–200 mg/day) in patients with mild to moderate renal insufficiency (LoE Ia, SOR 92%).
- (viii) Losartan and fenofibrate should not be used as a primary ULT but where treatment for hypertension or dyslipidaemia, respectively, is required, they may be considered as they have a weak uricosuric effect. Vitamin C supplements (500–1500 mg daily) also have a weak uricosuric effect (LoE III, SOR 89%).
- (ix) A uricosuric agent can be used in combination with a xanthine oxidase inhibitor in patients who do not achieve a therapeutic serum urate target with optimal doses of monotherapy (LoE III, SOR 88%).
- (x) Colchicine 500 µg bd or od should be considered as prophylaxis against acute attacks resulting from initiation or up-titration of any ULT and continued for up to 6 months. In patients who cannot tolerate colchicine, a low-dose NSAID or coxib, with gastro-protection, can be used as an alternative providing there are no contraindications (LoE Ib, SOR 86%).

The full guideline, available at *Rheumatology* online, contains specific recommendations for management of gout in special groups: patients with renal sufficiency, severe refractory tophaceous gout and in pregnancy. Figure 1 illustrates the suggested care pathway.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: W.Z. reports grants from Arthritis Research UK, Health Technology Assessment, National Institute for Health Research and honoraria for consultations from AstraZenica, Daiichi Sankyo, Biobarica,

Hisun and Grunenthal outside the submitted work. M.D. has received honoraria for ad hoc advisory boards relating to osteoarthritis and gout from Ardea Biosciences, AstraZenica, Nordic Biosciences and Roche; AstraZenica are funding a Nottingham University investigator-led non-drug study on gout. G.N. was a member of the Independent Disease Monitoring Committee for trials of lesinurad (Ardea/AstraZenica), and has received honoraria for advisory boards from Gruenenthal and Menarini, and research funding from Menarini for the FAST trial. T.M.M. is/has been principle investigator on trials paid for by Pfizer, Novartis, Ipsen, Teijin and Menarini, received consulting or speakers fees from Pfizer, Novartis, Takeda, Shire and Lundbeck and their department holds research grants from Novartis, Pfizer, Amgen, Ipsen, Teijin and Menarini. K.M.J. has received educational sponsorship and funding for UK Gout Society in capacity as Trustee. G.J.D. has received ad hoc advisory board honoraria from AstraZenica. All other authors have declared no conflicts of interest.

References

- 1 Jordan KM, Cameron JS, Snaith M *et al*. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of gout. *Rheumatology* 2007;46:1372–4.
- 2 Kuo CF, Grainge MJ, Mallen C, Zhang W, Doherty M. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. *Annals Rheum Dis* 2015;74:661–7.
- 3 Roddy E, Zhang WF, Doherty M. Concordance of the management of chronic gout in a UK primary-care population with the EULAR gout recommendations. *Ann Rheum Dis* 2007;66:1311–5.
- 4 Spencer K, Carr A, Doherty M. Patient and provider barriers to effective management of gout in general practice: a qualitative study. *Ann Rheum Dis* 2012;71:1490–5.
- 5 Rees F, Jenkins W, Doherty M. Patients with gout adhere to curative treatment if informed appropriately: proof-of-concept observational study. *Ann Rheum Dis* 2013;72:826–30.