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GUIDELINES

Gout: diagnosis and management—summary of NICE guidance

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What you need to know

- Urate lowering therapy (ULT) should be given using a treat-to-target management strategy (aiming for a serum urate level <360 µmol/L (6 mg/dL)) to provide therapeutic cure
- People without a major cardiovascular disease can be offered either allopurinol or febuxostat as first line treatment.
- When prescribing ULT, it is important to explain to people that treatment is lifelong
- Consider annual monitoring of serum urate level in people with gout who are continuing ULT after reaching their target serum urate level

Gout is a painful and debilitating condition with long term complications, including joint damage and renal stones. Although gout flares are often treated with NSAIDs, colchicine or steroids, those with gout often continue to have flares which could have been prevented with lifestyle modification or urate lowering medication. However, only a third of people with gout receive urate lowering therapies (ULTs), and only a third of those have their serum urate level managed effectively.[1] This article summarises the recommendations from the new National Institute for Health and Care Excellence (NICE) guideline, focusing on the diagnosis and management of gout.[2]

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Diagnosis and assessment

Most people with gout receive a clinical diagnosis in primary care, which is then confirmed by clinical investigation.

Signs and symptoms

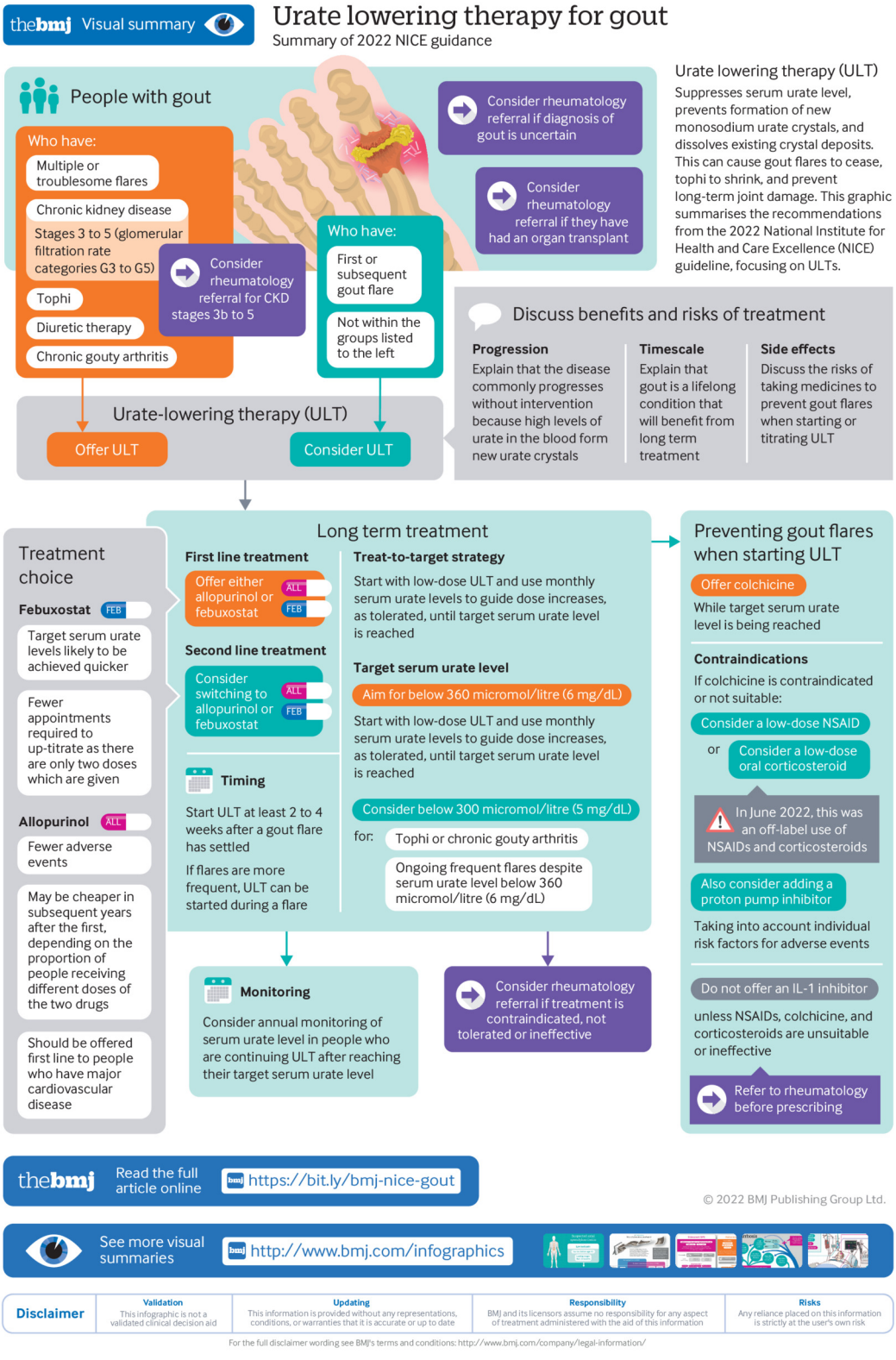
- Suspect gout in people presenting with any of the following:
  - Rapid onset (often overnight) of severe pain together with redness and swelling, in one or both first metatarsophalangeal (MTP) joints
  - Tophi.
- Consider gout in people presenting with rapid onset (often overnight) of severe pain, redness, or swelling in joints other than the first MTP joints (for example, midfoot, ankle, knee, hand, wrist, elbow).
- Assess the possibility of septic arthritis, calcium pyrophosphate crystal deposition, and inflammatory arthritis in people presenting with a painful, red, swollen joint.
- If septic arthritis is suspected, refer immediately according to the local care pathway.
- Consider chronic gouty arthritis in people presenting with chronic inflammatory joint pain.
- In people with suspected gout, take a detailed history and carry out a physical examination to assess the symptoms and signs (see the first recommendation).

  [*Based on limited evidence and the experience and opinion of the Guideline Committee (GC)*]

Diagnosis

- Measure the serum urate level in people with symptoms and signs of gout to confirm the clinical diagnosis (serum urate level ≥360 µmol/L (6 mg/dL)). If serum urate level is <360 µmol/L during a flare and gout is strongly suspected, repeat the serum urate level measurement at least two weeks after the flare has settled.
- Consider joint aspiration and microscopy of synovial fluid if a diagnosis of gout remains uncertain or unconfirmed.
- If joint aspiration cannot be carried out or the diagnosis of gout remains uncertain, consider imaging the affected joints with x ray, ultrasound scanning, or dual-energy computed tomography (CT).

  [*Based on the experience and opinion of the GC*]



Information and support

People with gout (and their families and carers) require information and support to understand their condition and provide self management options to ensure efficacy of long term treatment.

- Provide tailored information to people with gout and their family members or carers (as appropriate) at the time of diagnosis and during subsequent follow-up appointments.
- Explain:

- The symptoms and signs of gout
- The causes of gout
- That the disease progresses without intervention because high levels of urate in the blood lead to the formation of new urate crystals
- Any risk factors for gout they have, including genetics, excess body weight or obesity, medicines they are taking, and comorbidities such as chronic kidney disease (CKD) or hypertension
- How to manage gout flares and the treatment options available
- That gout is a lifelong condition that benefits from long term urate lowering therapy (ULT) to eliminate urate crystals and prevent flares, shrink tophi, and prevent long term joint damage
- Where to find other sources of information and support such as local support groups, online forums, and national charities.

[*Based on low to high quality qualitative studies and the experience and opinion of the GC*]

Treatment for gout flares

Recurrent flares are a common manifestation of gout, which can be severely painful and sudden in onset. Treatment is required to provide rapid relief from the joint pain and inflammation.

- Offer a non-steroidal anti-inflammatory drug (NSAID), colchicine, or a short course of an oral corticosteroid for first line treatment of a gout flare, taking into account the person's comorbidities, co-prescriptions, and preferences.
- Consider adding a proton pump inhibitor for people with gout who are taking an NSAID to treat a gout flare.
- Consider an intra-articular or intramuscular corticosteroid injection to treat a gout flare if NSAIDs and colchicine are contraindicated, not tolerated, or ineffective.

[*Based on the experience and opinion of the GC*]

Diet and lifestyle

There is no standardised advice for diet and lifestyle modification in gout, and the current evidence base to support specific dietary interventions is limited.

- Explain to people with gout that there is not enough evidence to show that any specific diet prevents flares or lowers serum urate levels. Advise them to follow a healthy, balanced diet.
- Advise people with gout that excess body weight or obesity, or excessive alcohol consumption, may exacerbate gout flares and symptoms.

[*Based on a limited number of high to very low quality RCTs and the experience and opinion of the GC*]

Management of gout with urate lowering therapies

Gout is a long term condition in which an elevated serum urate level leads to monosodium urate crystal formation, and consequently recurrent flares of severe joint pain and inflammation, tophi, and chronic arthritis. Progression, if left untreated, commonly causes more frequent flares and development of tophi and chronic arthritis. Urate lowering therapy suppresses the serum urate level, prevents formation of new monosodium urate crystals and dissolves existing crystal deposits, causing gout flares to cease, tophi to shrink, and prevents long term joint damage. The evidence review for the guideline found a treat-to-target strategy showed clinical benefit and was cost-effective compared with usual care. Treat-to-target was beneficial for quality of life, pain, joint swelling and tenderness, and reducing adverse events compared with usual care. There was some uncertainty around effect sizes, and the amount of evidence was limited, but, overall, the evidence was supportive of a treat-to-target strategy, which aligned with the Guideline Committee's experience. Because of the uncertainty around effect sizes it was difficult to determine a number needed to treat (NNT).

The committee noted that treatment with urate lowering therapy (ULT) for gout is suboptimal, with only around a third of people with gout receiving ULT. Treat-to-target with ULTs is considered best practice, compared with only treating symptoms. Employing a treat-to-target management strategy results in more people achieving target serum urate levels, resulting in fewer flares in the long run, resulting in less cost impact for the NHS and improvements in people's quality of life. Achieving target serum urate levels and sustaining these targets will likely result in fewer people having permanent joint damage which has a high cost impact.

Febuxostat was found to be more effective than allopurinol at reducing flares and lowering serum urate, but allopurinol was found to have fewer adverse events. A costing analysis indicated there were minimal cost differences in the first year of treatment between allopurinol and febuxostat when following a treat-to-target management strategy. The Guideline Committee acknowledged that the cost of febuxostat may be higher in subsequent years, but this was highly dependent on the proportion of people receiving different doses of allopurinol and febuxostat. The more people who received a higher dose of febuxostat (120 mg), the more likely febuxostat will be more expensive in subsequent years. The committee did, however, note that the price of 120 mg febuxostat is likely to fall given that it is now a generic drug. The committee also noted that fewer appointments are required to up-titrate people taking febuxostat as there are only two doses which are given (80 mg and 120 mg), compared with a possible nine doses of allopurinol. Target serum urate levels are likely to be achieved more quickly for people receiving febuxostat. However, people are likely to experience a greater number of flares initially after starting febuxostat.

- Offer ULT, using a treat-to-target strategy, to people with gout who have:
  - Multiple or troublesome flares
  - Chronic kidney disease (CKD) stages 3 to 5 (glomerular filtration rate (GFR) categories G3 to G5)
  - Diuretic therapy
  - Tophi
  - Chronic gouty arthritis.
- Discuss the option of ULT, using a treat-to-target strategy, with people who have had a first or subsequent gout flare who are not within the groups listed above.
- Offer either allopurinol or febuxostat as first line treatment when starting treat-to-target ULT, taking into account the person's comorbidities and preferences.
- Offer allopurinol as first line treatment to people with gout who have major cardiovascular disease (for example, previous myocardial infarction or stroke, or unstable angina).
- Aim for a target serum urate level <360 µmol/L (6 mg/dL).

- Start with a low dose of ULT and use monthly serum urate levels to guide dose increases, as tolerated, until the target serum urate level is reached.
- Ensure people understand that ULT is usually continued after the target serum urate level is reached and is typically a lifelong treatment.
- Start ULT at least two to four weeks after a gout flare has settled. If flares are more frequent, ULT can be started during a flare.
- Consider annual monitoring of serum urate level in people with gout who are continuing ULT after reaching their target serum urate level.

  [*Based on evidence from very low to high quality randomised controlled trials and the experience and opinion of the GC*]

Preventing gout flares when starting or titrating urate lowering therapy

- Discuss with the person the benefits and risks of taking medicines to prevent gout flares when starting or titrating ULT.
- For people who choose to have treatment to prevent gout flares when starting or titrating ULT, offer colchicine while the target serum urate level is being reached. If colchicine is contraindicated, not tolerated, or ineffective, consider a low dose NSAID or a low dose oral corticosteroid.

  [*Based on very limited number of moderate to low quality randomised controlled trials and the experience and opinion of the GC*]

Referral to specialist services

- Consider referring a person with gout to a rheumatology service if:
  - The diagnosis of gout is uncertain
  - Treatment is contraindicated, not tolerated, or ineffective
  - They have CKD stages 3b to 5 (GFR categories G3b to G5)
  - They have had an organ transplant.

  [*Based on the experience and opinion of the GC*]

Implementation

Challenges to implementing this guidance include informing patients and healthcare professionals of the shift in practice to prescribing ULT using a treat-to-target management strategy and time constraints within appointments in primary care. Although treat-to-target ULT and increased levels of monitoring and follow-up may lead to an initial increase in service delivery, long term management for people with gout will improve, resulting in less and more predictable demand for services in the future.

Future research

The Guideline Committee prioritised the following questions for further research:

- In people with gout (including people with gout and chronic kidney disease (CKD)), what is the clinical and cost effectiveness of colchicine compared with corticosteroids for managing gout flares?
- In people with gout (including people with gout and CKD), what is the clinical and cost effectiveness of non-steroidal anti-inflammatory drugs or corticosteroids for preventing gout flares when starting or titrating urate lowering therapy?
- What is the clinical and cost effectiveness and patient acceptability of different approaches to follow-up, including provision of patient information and managing gout flares?
- In people with gout (including people with gout and CKD), what is the most clinically and cost effective frequency of serum urate level monitoring when target serum urate level is reached?

Guidelines into practice

- When and how will you offer treat-to-target urate lowering therapy (ULT) to people with multiple troublesome flares, tophi, chronic kidney disease, diuretic therapy, or chronic gouty arthritis, with the aim of achieving a target serum urate level <360 µmol/L?
- How will you provide annual monitoring of serum urate level for people with gout who are continuing ULT after reaching their target serum urate level?

How patients were involved in the creation of this article

Committee members involved in this guideline update included lay members, who contributed to the formulation of the recommendations summarised here.

Further information on the guidance

This guidance was developed by the National Guideline Alliance in accordance with NICE guideline methodology (https://www.nice.org.uk/process/pmg20/chapter/introduction). A guideline committee (GC) incorporating healthcare professionals and two lay members identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworking-group.org) for intervention reviews; GRADE CERQual (www.cerqual.org) for qualitative reviews; QUADAS for diagnostic reviews, and QUIPS for prognostic reviews. These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or, when evidence was not found, based on their experience and opinion using informal consensus methods.

Original costing analyses were undertaken in priority areas not sufficiently addressed by the published cost effectiveness literature. Costing analyses were undertaken instead of cost effectiveness analyses due to a lack of appropriate data to adequately model long term outcomes. The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the GC took all comments into consideration when producing the final version of the guideline. NICE will conduct regular reviews after publication of the guidance, to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

Contributors: All authors confirm that they meet all four authorship criteria in the ICMJE Uniform requirements. JN and AB reviewed the evidence and assessed the data within the article. ER and AD interpreted the evidence and generated the recommendations. All authors drafted and revised the content of the article and approved the final version and agree to be accountable for the accuracy and integrity of the work. JN is the guarantor for this article.

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The members of the Guideline Committee were (shown alphabetically): Alastair Dickson, Sam Finnekin (until July 2021), Hugh Gallagher, Hilton Hirst, Luckshmana Jeyaseelan (co-opted member), Kelsey Jordan, Mohammed Rafiq, Edward Roddy (topic advisor), Sarah Ryan, Aung Soe (chair), Jane Taylor, and Lorraine Watson (co-opted member).

Members of the NICE technical team were (shown alphabetically): Alexandra Bonnon (health economist), Amber Hernaman (project manager), Sophia Kemmis-Betty (senior health economist), Sedina Lewis (senior research fellow until December 2020), Julie Neilson (senior research fellow), Gill Ritchie (guideline lead), Joseph Runicles (information specialist) and Audrius Stonkus (research fellow until June 2021).

1 Russell MD, Rutherford AI, Ellis B, etal. Management of gout following 2016/2017 European (EULAR) and British (BSR) guidelines: An interrupted time-series analysis in the United Kingdom. *Lancet Reg Health Eur* 2022;18:100416. doi: 10.1016/j.lanepe.2022.100416. pmid: 35814340

2 National Institute for Health and Care Excellence. Gout: diagnosis and management (NICE guideline NG219). 2022. https://www.nice.org.uk/guidance/ng219.