Gout: diagnosis and management

Consultation on draft guideline - Stakeholder comments table
13/12/2021 to 02/02/2022

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Society for Rheumatology	Guideline	007	013	It is unclear what is "a healthy, balanced diet"? an example might be helpful to guide the self-management	Thank you for your comment. Referral to NICE guidance Preventing excess weight gain has been included which provides examples of a healthy balanced diet.
British Society for Rheumatology	Guideline	010	004	What if a patient does not respond or contra-indicate to both allopurinol and febuxostat?	Thank you for your comment. In this situation the person should be referred to specialist rheumatology services for further opinion. A Recommendation has been made in 1.6 referral to specialist services.
British Society for Rheumatology	Guideline	010	014	The wording of this sentence in the context of preventing gout flares during initiation of ULT, as duration of NSAID use will be longer than treating a flare, would be better phrased 'Strongly consider using a proton pump inhibitor for people who receive NSAID to prevent gout flares when starting or titrating ULT.'	Thank you for your comment. The wording reflects the strength of the evidence, 'consider' recommendations are based on weaker evidence. We think the current wording is clear.
British Society for Rheumatology	Guideline	011	002 - 003	What about the monitoring serum urate level before reaching the serum urate target? This has not been mentioned in both the treat to target section and the monitoring section?	Thank you for your comment. Monthly serum urate level measurements are recommended to guide ULT treatment in recommendation 1.5.5.
British Society for Rheumatology	Guideline	012	008	Another research question for preventing gout flare is to see whether an up titrated urate lower therapy per se prevents the gout flare, as the current evidence are predominantly based on flares induced by full dose of urate lower therapy.	Thank you for your comment. The committee did consider this and decided it was covered in the evidence for treat to target ULT for managing gout, where trials which assessed the effect of up-titrated ULT on flares were included.
British Society for Rheumatology	Guideline	018	018	Worth commenting about the consideration to commence ULT at the time of the acute flare in discussion with the patient	Thank you for your comment. The section you comment on is regarding follow-up, we have covered this in the rationale for long-term management of gout, as it is better placed there.

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British Society for Rheumatology	Guideline	019	009	The association with diet was also not supported in mendelian randomisation studies	Thank you for your comment.
British Society for Rheumatology	Guideline	020	025	For consistency throughout the document, add hyphen 'cost-effective'	Thank you for your comment. We follow the NICE style guide https://www.nice.org.uk/corporate/ecd1/chapter/using-this-guide and do not use a hyphen for the word cost effective.
British Society for Rheumatology	Guideline	021	021	For consistency throughout the document, add hyphen 'randomised-controlled'	Thank you for your comment. We follow the NICE style guide https://www.nice.org.uk/corporate/ecd1/chapter/using-this-guide and do not use a hyphen between randomised and controlled.
British Society for Rheumatology	Guideline	023	019	For consistency throughout the document, add hyphen 'randomised-controlled'	Thank you for your comment. We follow the NICE style guide https://www.nice.org.uk/corporate/ecd1/chapter/using-this-guide and do not use a hyphen between randomised and controlled.
British Society for Rheumatology	Guideline	024	025 - 026	For consistency throughout the document, add hyphen 'cost-effective'	Thank you for your comment. We follow the NICE style guide https://www.nice.org.uk/corporate/ecd1/chapter/using-this-guide and do not use a hyphen for the word cost effective.
British Society for Rheumatology	Guideline	024	025 - 026	The current wording is very strong regarding the cost-effective aspect of treating. However, the fundamental reason for treating is on clinical grounds. Therefore, suggest '… so offering people ULT is clinically effective and highly likely to be cost-effective compared with offering no treatment.'	Thank you for your comment. This has been updated.
Connect Health	Guideline	003	General	Signs and Symptoms	Thank you for your comment. The recommendations have been amended to assess the possibility of septic

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				Consider alternative diagnosis such as septic joint other than gout with rapid onset of pain and swelling in a single joint with systemic symptoms and pyrexia	arthritis in people presenting with any painful red swollen joint.
Connect Health	Guideline	004	General	Diagnosis Perform joint aspiration only in a sterile and controlled environment, do not perform joint aspiration in primary care or community if septic joint is suspected	Thank you for your comment. Joint aspiration is usually carried out within a rheumatology service rather than primary care and this is described within the committee discussion in evidence review C. Suspected septic arthritis would require immediate referral to secondary care and this is included in the recommendations.
Connect Health	Guideline	004	General	Info & Support Educate patients that sustained high uric acid levels are also associated with metabolic disease and renal stones Provide information on diet and certain food contributions to hyperuricaemia especially alcohol intake	Thank you for your comment. Risk factors such as CKD and hypertension are included in the information and support recommendation. The committee considered renal stones not to be a significant risk factor for gout. Although no evidence was found to support recommending any particular diet, a link to diet and lifestyle and other NICE guidance on preventing excess weight gain has been made. This includes guidance on following a healthy diet, including alcohol consumption.
Connect Health	Guideline	011	General	Referral to Specialist service Do not refer routine gout patients to rheumatology, gout should be managed in primary care. Only refer if the criteria set out are present	Thank you for your comment. A 'do not' recommendation is very strong and is usually based on either very good evidence or something the committee feel very strongly about. The committee felt 'consider' was the better option for this recommendation as there was no evidence and the reasons for referring onwards

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					may be diverse and not clear-cut. Therefore 'consider' was used to refer to some criteria where gout may not be able to be managed in primary care and therefore patients could be referred onwards.
External expert reviewer	Evidence review C	General	General	There are several references about gout being commonly diagnosed in primary care by a GP. I think that the diagnosis of gout falls within the expertise of other members of the primary care team including Advanced Nurse Practitioners and Physician associates. I would recommend removing any references to the GP doing the diagnosing and instead just state that gout is commonly diagnosed in primary care.	Thank you for your comment. We agree and have amended the text to indicate it is not only GPs who see people with gout in a primary care setting.
External expert reviewer	Evidence review G	058	010	Price of febuxostat 80mg not consistent with other places in evidence reviews - £0.13 here, but £0.10 elsewhere	Thank you for your comments. This has been updated This specific cost was not updated when the unit costs for febuxostat and allopurinol were updated. All costs for allopurinol and febuxostat in the guideline have been updated (17/02/22) and the cost of 80mg febuxostat is now £0.09 per unit.
External expert reviewer	Evidence review G	068	010	Allopurinol is also a once daily dosing at lower doses, only higher doses need to be split. I think this needs to be made clear when discussing adherence	Thank you for your comment. Allopurinol is a once daily dosage for people receiving 100mg and 300mg allopurinol. Therefore, a higher pill burden compared to febuxostat is associated with all doses of allopurinol except 100mg and 300mg. We have clarified this in the committee discussion of the evidence when discussing adherence.
External expert reviewer	Guideline	003	013	I don't think recommendations 1.1.3 or 1.1.5 are helpful, and as such should be removed as they simply bloat the guideline. 1.1.3 clinicians know that septic arthritis is something that needs immediate referral. The guideline doesn't	Thank you for your comment. Because gout can present with a range of symptoms and signs the committee wanted to stress the importance of a holistic clinical assessment as well as serum urate measurement to confirm diagnosis.

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				tell clinicians to refer people with suspected inflammatory arthritis to an appropriate rheumatology service without delay, so why single out the management of septic arthritis? 1.1.5 again, we have to assume clinicians know their job. I think it is insulting and condescending to tell clinicians to take a history and examine patients.	Because septic arthritis is a red flag requiring urgent referral the committee decided to emphasise this by making a recommendation.
External expert reviewer	Guideline	004	002	Recommendation 1.1.6 seems to imply that the urate level should be done during the flare. I wonder whether it would be worth rephrasing. Something like: Measure the serum urate level in people with suspected gout (see recommendation 1.1.1) to confirm the diagnosis (serum urate level of 360 micromol/litre [6 mg/dl] or more). If serum urate is below 360 micromol/litre (6 mg/dl) during a flare and gout is strongly suspected, consider repeating the serum urate level measurement 2 to 4 weeks after the flare has settled to confirm the diagnosis as serum urate can fall during flares.	Thank you for your suggestion. The committee have amended the recommendation to make clearer the if serum urate is below 360micromol/L and gout is strongly suspected to the serum urate level measurement at least 2 weeks after the flare has settled.
External expert reviewer	Guideline	005	002	I suggest changing the word 'treatment' to 'management'. If someone has a flare of gout due to lifestyle, diuretics etc, could it not be that the risk factors could be managed without ULT to stop progression? This line suggests unless a patient with gout is on ULT then then their disease will definitely progress, which is quite a strong assertion.	Thank you for your comment. The committee have reviewed the recommendation and preferred the term 'intervention' to 'management' . The glossary in the methods chapter defines the term as either a drug treatment, surgical procedure, diagnostic test, psychological therapy or public health intervention such as healthy eating. We have amended the wording accordingly.
External expert reviewer	Guideline	005	008	Similar to above. The word 'will' is a strong assertion. Is the evidence clear that everyone on ULT benefits?	Thank you for your comment. The evidence supports the use of ULT and the committee agree gout is a condition that benefits from long-term use. However, we

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				I don't think it is. I would suggest changing 'will' to 'can' or 'may'	have changed the wording to remove the word will in response to your comment.
External expert reviewer	Guideline	008	015	Recommendation 1.5.4 may read better if it was prefixed with something like 'Ideally,' or 'Preferentially,'	Thank you for your comment. This is not in line with NICE terminology.
External expert reviewer	Guideline	010	007	The subtitle is confusing. Consider changing to 'Preventing gout flares during ULT initiation'	Thank you for your comment. We agree and have made this change.
External expert reviewer	Guideline	010	014	I'm sure you discussed this, but why is a PPI not recommended when corticosteroiods are used? I understand for short courses in the flare treatment recommendation, but here the steroid may be used for several weeks to months, so I would think co-prescribing a PPI would be good practice, even if low dose. I know doses aren't mentioned in guidelines, but in this case, I wonder whether we need to stipulate 'low-dose' corticosteroid as we don't want people taking 30mg daily for several weeks-months	Thank you for your comment. The committee agree and corticosteroids have been added to the PPI recommendation. NICE guidelines do not usually provide information on dosages and refer to the BNF and SPC for guidance on prescribing medication. Dosage for Colchicine is provided in the BNF. The committee consider clinicians would know to prescribe a lower dose but have added this for NSAIDs and corticosteroids.
External expert reviewer	Guideline	017	019	I don't think intra-articular and IM steroids are 'commonly' used in practice. Is this a typo? I would say 'sometimes'	Thank you for your comments. This has been amended as suggested.
Keele University	Evidence review I	009	012	Should reference 31 actually be 32? It is 32 earlier in section 1.1.4.1 and also table in 2.	Thank you for your comment. This has been corrected.
Keele University	Evidence review I	020	003	Table 8 title is missing.	Thank you for your comment. This has been added.
Keele University	Evidence review I	023	010	The sample size is stated as n=50 but in table 2 sample size stated as n=120.	Thank you for your comment. This has been deleted.
Keele University	Guideline	029	021 - 022	This part of the guideline states '…..flares. They can be prevented by a combination of lifestyle modification (such as losing weight)…' But there is a lack of strong evidence from RCTs showing that	Thank you for your comment. We agree this is misleading and have removed this sentence.

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				lifestyle/losing weight prevents flares and thus guidelines state elsewhere 'People should also be advised that excess weight, obesity or excessive alcohol consumption may exacerbate gout flares'.	
NHSEI	Guideline	005	022	The date 2022 is in the future but the full sentence is in past tense. "In June 2022, this was an off-label use of oral corticosteroid" appears to be a typo, can this be reviewed	Thank you for your comment. This will be correct for publication in June 2022.
NHSEI	Guideline	006	007	The date 2022 is in the future but the full sentence is in past tense. "In June 2022, this was an off-label use of oral corticosteroid" appears to be a typo, can this be reviewed	Thank you for your comment. This will be correct for publication in June.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	005	022	Is this a typo as June 2022 hasn't happened yet.	Thank you for your comment. This will be correct for publication in June 2022.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	008	001 - 012	Section 1.5 Conflicting statements ; 1.5.1 states ULT as a treat to target for people with "multiple or troublesome flares" yet in 1.5.2 states discuss the option of ULT using T2T for people experiencing the FIRST or subsequent flare. Not clear when to use ULT.	Thank you for your comment. We have added a link 'see recommendation 1.5.4 on when to start ULT.' Recommendation 1.5.2 is for people who have had one or more gout flares in order to treat symptoms and discuss the option of ULT, unless they are part of the groups in 1.5.1, where a treat to target ULT is offered as there is more evidence for treating these groups but others are still likely to benefit from treatment.
Primary Care Rheumatology &	Guideline	008 - 010	General	1.5 Things become less clear for me here. Should ULT be offered in patients experiencing their first flare, or	Thank you for your comment. The wording of the recommendation has been amended to make clearer discussion about the option of taking ULT should take

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Musculoskeletal Medicine Society				should they be offered NSAID/Colchicine/corticosteroid and monitor?	place with people who have had a first or subsequent flare. If ULT treatment is chosen this should start at least 2-4 weeks after a flare has settled.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	010	001 - 003	**1.5.9** Regarding Allopurinol use in those at higher risk of CVD,is it not the case that most,if not all,patients with a diagnosis of gout are at higher risk of CVD a) by virtue of their phenotype which predispose them to CVD in the first place, & b) the fact that they have an inflammatory arthropathy ? If so,then Allopurinol should be first line for ALL newly diagnosed unless they have some obvious contra-indication	Thank you for your comment. The committee agreed that many people with gout are at increased of cardiovascular disease because of prevalent traditional cardiovascular risk factors such as hypertension and hyperlipidaemia, but this is not the case for all people with gout. The extent to which other factors such as hyperuricaemia or chronic inflammation contribute to cardiovascular disease in people with gout is unclear. The current SPC states pre-existing CV disease is a caution for using febuxostat, but it is not a complete contra-indication. Febuxostat may be an option for those without pre-existing major CV disease, including those with CV risk factors, especially those for whom allopurinol is unsuitable. Current SPC advice for this patient group is for treatment with Febuxostat to be exercised cautiously and they should be monitored regularly. Hence the committee's recommendation that allopurinol or febuxostat can be used first line is in accordance with this Drug Safety Update.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	010	004 - 006	**1.5.10** Regarding the introduction of a secondary treatment if a target is not reached,after what period of time are we talking ? Is 12 weeks too soon ,and is the secondary treatment in lieu of,as I suppose,or in addition to,the first treatment choice?	Thank you for your comment. Monthly serum urate level measurements are recommended to guide ULT treatment. A link to this recommendation has been added. The wording of the recommendation has been amended to make clear the second–line treatment is instead of the first drug tried.

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Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	011	004 - 011	1.6 I find this point rather strange having always been taught that you should check a serum urate when the patient is not having an attack as it can be paradoxically lowered. Has the advice regarding this changed? If so, I think this should be clarified as I'm sure I'm not the only person reading this who will find it odd. If the advice has not changed, surely it is not "cost effective" to either the patient or the NHS to do a test during a flare when you may end up having to repeat it 2-4 weeks later? Particularly given the fact that we have just experienced a blood bottle shortage.	The committee agrees that the serum urate level can be paradoxically lower if measured during a flare. However, it was recognised that in clinical practice, the flare is often the most convenient time to check the serum urate level as that is when the patient has presented. If the serum urate level is elevated when measured during a flare this supports the diagnosis of gout. However, the committee felt it important to provide guidance for the situation where the serum urate level has been checked during a flare and is not high enough to support a diagnosis of gout.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	General	General	The Diagnosis and information/Support sections are very clear.	Thank you for your comment.
Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	General	General	• Are there any factors that influence choosing an intramuscular or intraarticular injection?	Thank you for your comment. No evidence was found to support one route over another. The choice of route medication would be determined by individual presentation of gout and in consultation with the patient.

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Primary Care Rheumatology & Musculoskeletal Medicine Society	Guideline	General	General	When to refer to Rheumatology is not very clear.	Thank you for your comment. Most people with gout will be cared for within primary care services. Indications for referral to specialist services would include when the diagnosis of gout is uncertain, if treatments are contraindicated, not tolerated or response to treatment is inadequate. People with other conditions requiring input by a specialist such as CKD stages 3b to 5. The committee consider the recommendation to be clear.
Royal College of General Practitioners	Guideline	004	002 - 007	Can the committee consider adding to line 5 "if gout is strongly suspected and the serum urate level is below 360mmol/L during a flare, or if blood testing is not available/ possible during the acute flare, to measure the serum urate 2-4 weeks after the flare…" The likelihood of patients being able to, with the 1-5 days of their acute flare being able to book and have a blood test taken in primary care is low, it is therefore important that clinicians are aware that if they are unable to obtain the blood testing during the acute flare that the test can be taken after 2 weeks.	Thank you for your comment. The recommendation has been amended to make clearer if serum urate is below 360mmol/L and gout is strongly suspected to repeat the serum urate level measurement at least 2 weeks after the flare has settled.
Royal College of General Practitioners	Guideline	005	008 - 010	The statement which suggests all patients, even those with a single episode of gout will benefit from long term ULT is not aligned to recommendations 1.5.1 and 1.5.2 which are much more selective regarding those who will benefit from the treatment. Can the committee review this to ensure consistency throughout? Can we suggest "gout is a lifelong condition that in *most* people will benefit from…"	Thank you for your comment. Without intervention gout will continue to progress due to high levels of urate leading to the formation of crystals. The committee have reviewed the recommendation and have amended the wording to recommend intervention to manage the condition. This maybe lifestyle or drug therapies. The evidence supports the use of ULT and the committee agree gout is a condition that benefits from long-term use.

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					However, we have updated the wording of the recommendation in response to your comment to remove 'will'.
Royal College of General Practitioners	Guideline	006	007	In June 2022. Can we ask should this be January 2022 or is June 2022 the publication date of the guidance? If June is correct, please ensure that this is still correct at the time of publication.	Thank you for your comment. This will be correct for publication in June 2022.
Royal College of General Practitioners	Guideline	008	001	Please see point 2 above. This statement does not align with the initial recommendation that states all people will benefit from ULT	Thank you for your comment. We have changed the initial recommendation to 'gout is a lifelong condition that benefits from long-term ULT' in response to your comment.
Royal College of General Practitioners	Guideline	008	005 - 006	From our review of the evidence review, it appears that CKD and diuretics are included as risks because they increase the chance of future flares. Can the committee consider the following amendment to ensure clinicians and patients know why this is added here? "CKD 3-5 as they are at increased risk of future flares" (ideally with a quantifier). This would avoid a misunderstanding on the part of the clinician that ULT improves outcomes for people with CKD and people being recommended treatment on that basis alone which is particularly important in those with lower risk CKD 3a.	Thank you for your comment. The committee discussion within the guideline review E 'Which people with gout should be offered a urate-lowering therapy?' details that 'people on diuretics are prone to significant hyperuricaemia and frequent flares owing to the effect of diuretics in reducing renal urate excretion. The committee noted people with CKD or on diuretics tend to have more flares than people with normal renal function due to reduced urate excretion leading to more severe hyperuricaemia and greater monosodium urate crystal formation.' As the increased risk of flares in these populations are described in the rationale and impact section of the guideline the committee did not think that this detail was required in the recommendation.
Royal College of General Practitioners	Guideline	008	007	From our review of the evidence review, it appears that CKD and diuretics are included because they increase the chance of future flares.	Thank you for your comment. The rationale and impact section of the guideline explains people on diuretic therapy are at an increased risk of flares. The committee discussion within the guideline review E

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				We believe that there should be a note added to make clinicians aware that diuretic therapy raises urate and increases the risk of further flares, and that consideration should be made for stopping or swapping diuretic therapy where possible and re-measuring urate thereby avoiding cascade prescribing.	'Which people with gout should be offered a urate-lowering therapy?' details that 'people on diuretics are prone to significant hyperuricaemia and frequent flares owing to the effect of diuretics in reducing renal urate excretion. The committee noted people with CKD or on diuretics tend to have more flares than people with normal renal function due to reduced urate excretion leading to more severe hyperuricaemia and greater monosodium urate crystal formation.' We cannot comment on stopping or swapping diuretic therapy as we have not looked at the evidence for this.
Royal College of General Practitioners	Guideline	010	007	This title could be misinterpreted as "when to initiate ULT". Can we suggest an alternative title please: "Preventive treatment options for gout flares caused by initiation of ULT"	Thank you for your comment. The committee considered your suggestion but have opted for the shorter title preventing gout flares..
Royal College of General Practitioners	Guideline	010	010 - 013	Can the committee consider clarifying whether the recommended doses when using these drugs for this purpose are the same dose as used for the treatment of flares?	Thank you for your comment. NICE guidelines do not usually provide information on dosages and refer to the BNF and SPC for guidance on prescribing medication. Dosage for Colchicine is provided in the BNF. BNF advice is to prescribe at the lowest possible dose for the shortest possible time. The committee consider clinicians would know to prescribe a lower dose but have added this for NSAIDs and corticosteroids
Royal College of Nursing	Guideline	005	022	June 2022 (is this meant to be June 2021?)	Thank you for your comment. This will be correct for publication in June 2022.
Royal College of Nursing	Guideline	006	007	June 2022 (is this meant to be June 2021?)	Thank you for your comment. This will be correct for publication in June 2022.
Royal College of Nursing	Guideline	007	014	Should we be signposting people to Drink Aware DoH https://www.drinkaware.co.uk/ ?	Thank you for your comment. Referral to NICE guidance Preventing excess weight gain has been included which provides guidance on alcohol

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					consumption. Therefore, we do not think signposting to this is required.
Royal College of Nursing	Guideline	General	General	Clinical practice includes patients with Gout- unwarranted Variance noted in how individual patients diagnosed and treated in Urgent Care - Out of Hours	Thank you for your comment. Publication of new NICE guidance on the diagnosis and treatment of gout will hopefully reduce current variance.
Royal College of Nursing	Guideline	General	General	Clear describer for how diagnosis is obtained in primary care	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Clear list of diagnostic investigations and best outcome referrals given	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Clear treatment options for treatment and need for more comparative research provided, therefore leaving room for discussion and collaborative decision making during the consultation.	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Clear guidance for both acute and chronic presentations - as well as potential differentiation	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Clear reasoning to support guidance throughout the document	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Clear acknowledgment that with refractory patients who need a secondary care opinion on suspected/confirmed gout that they may well be waiting longer than usual due to widespread backlog pressures on rheumatology units from Covid.	Thank you for your comment.
Royal College of Physicians and Surgeons of Glasgow	Comments form question	001	Question 1	1. **Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why**. The biggest impact on practice is likely to be from more definitive and updated diagnosis and treatment initiation. The challenges arise from offering patients	Thank you for your comments. Comments will be considered by NICE where relevant support activity is being planned.

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				with hyperuricemia/gout regular follow-up (e.g. annual review) outside of their acute flares. The other continuing challenge has always been supervision and guidance regarding titration of allopurinol (particularly increasing the dosage beyond 300mg or follow-on instructions to re-check serum uric acid and initiate urate-lowering therapy in primary care. The challenges fall to primary care predominantly but also to rheumatology departments who aim to follow-up these patients long-term in the more complex cases. Both primary and secondary care will struggle to adhere to guidance, primarily due to capacity issues within the NHS especially following the Pandemic crisis.	
Royal College of Physicians and Surgeons of Glasgow	Comments form question	001	Question 2	**2. Would implementation of any of the draft recommendations have significant cost implications?** Use of IL-1 inhibitors (in rare cases) has a significant and disproportionate cost implications as alluded to in the draft guideline already. There is also the cost implication of aiming to offer these increasing number of patients' regular follow-up (either in primary or secondary care). There are indirect costs associated with key co-morbidities related to gout, including the cost of type II diabetes mellitus (and its widespread complications), cardiovascular disease and other features of the metabolic syndrome.	Thank you for your comments. Comments will be considered by NICE where relevant support activity is being planned. We acknowledge the use IL-1 inhibitors have significant cost implications. However, the recommendations made for the use of IL-1 inhibitors are reflective of current practice and therefore will not increase resources The guideline recommends considering a follow-up appointment after a gout glare and annual monitoring once a person has achieved target serum urate levels. Although no health economic evidence was found for these two review questions, we anticipate the recommendations made will likely be cost effective. The committee anticipated that offering a follow-up appointment would be a cost-effective use of resources

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					as this provides people an opportunity to initiate ULT, if clinically appropriate, and discuss the management of gout. The committee concluded that annual monitoring once people achieve target serum urate levels would be cost effective due to the number of flares prevented in the long-run as a result of annual monitoring. The committee qualitatively discussed the costs and benefits of both interventions compared to usual practice and concluded both interventions would likely be cost effective. We have not explicitly noted the potential indirect cost savings associated with reduced comorbidities in the committee discussion of the evidence sections for this guideline. However, we acknowledge that improved treatment of gout may also lead to indirect cost savings associated with comorbidities.
Royal College of Physicians and Surgeons of Glasgow	Comments form question	001	Question 3	3. **What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)** The Department of Health patient literature needs to be adjusted (it promotes diet rather than drug treatment). There needs to be specific education focussed at primary care and community pharmacy to alter current practices of detection, monitoring and prevention. There is a particular issue where colchicine prescriptions are limited incorrectly. There is a need for additional resources/capacity which is difficult to address definitively.	Thank you for your comments. Comments will be considered by NICE where relevant support activity is being planned.

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Royal College of Physicians and Surgeons of Glasgow	Comments form question	001	Question 4	4. **Please tell us if there are any particular issues relating to COVID-19 that we should take into account when finalising the guideline for publication.** Primary care has been nationally tasked with dealing with only 'urgent' problems at the current time. Although acute gout is an urgent problem, acute and chronic gout, may be and are often overlooked in terms of necessity for diagnosis and regular review. This may result in a delay in diagnosis, failure to commence or titrate serum urate lowering therapy, further disease flares and potential for joint damage and renal damage, more time off work and multiple other further consequences.	Thank you for your comments. Comments will be considered by NICE where relevant support activity is being planned.
Royal College of Physicians and Surgeons of Glasgow	Guideline	003	003	Gout is quite frequently overlooked as a possible diagnosis and patients may have the disease for many years. The significant morbidity cause by the disease is often under-recognised. In young and mid adulthood one acute joint may the presenting feature. As the individual ages multiple joints may be involved and the symptoms become less intense. In fact, it is not uncommon for tophaceous gout to present with minimal symptoms.	Thank you for your comment. Gout can present differently within age groups. The committee agree a detailed history and thorough examination of symptoms and signs is required and have reflected this within the recommendations.
Royal College of Physicians and Surgeons of Glasgow	Guideline	004	002	The current British Society for Rheumatology Guideline considers the level of urate likely to cause crystal formation in a supersaturated medium is 420umol/l. This is within the normal range for many laboratories. Reduction of this level to 360umol/l will increase the number of patients with levels consistent with gout. However, the rationale does not appear to be discussed in the linked documents.	Thank you for your comment. We are unable to find any mention of the level of urate likely to cause crystal formation in the current British Society for Rheumatology gout management guideline. The threshold of 420micromol/L does not appear to be mentioned. The physiological saturation threshold of urate in body tissues is generally considered to be

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				Many laboratories do not routinely measure urate in their profiles. It is a specific request. There is a danger of over reliance on blood results and not as quite rightly stated a combination of clinical history, examination and blood tests. Recommendation 1.1.6 implies a raised serum urate in context of acute arthritis confirms diagnosis of gout. This most likely with 1st MTP joint inflammation presentation. It is less likely with other joints and multiple joints. As stated above the whole picture must be considered.	between 360 and 420 micromol/L, and patients certainly present with urate levels in the high 300s. The committee agree gout is diagnosed by taking a detailed history, doing a physical examination and measuring serum urate levels with a blood test. The recommendation has been amended to make clearer it is the symptoms and signs of gout as well as the serum urate measurement that is used to make a clinical diagnosis. This is discussed in the rationale and impact section of the guideline and committee discussion in evidence review B and C.
Royal College of Physicians and Surgeons of Glasgow	Guideline	004	008	We consider that the firm diagnosis of gout is important as it may infer lifelong treatment. Joint aspiration should be strongly recommended.	Thank you for your comment. A detailed history and thorough clinical examination of symptoms and signs along with measurement of serum urate levels is usually adequate to confirm a diagnosis

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				We highlight the importance of false negative aspirates: *e.g.* If the clinical presentation is consistent with gout and the synovial fluid analysis fails to demonstrate crystals, the synovial fluid analysis result can be falsely negative. Crystal examination depends on access to a polarising microscope. In many hospitals this is in the Cytology Laboratory which may not offer an acute service. Examination for crystals is highly dependent of pH and temperature. Delay in examination will lead to false negative results. One should continue with treatment based on the overall clinical presentation.	of gout. If the diagnosis is not confirmed via this method or there is uncertainty, then the committee agree joint aspiration would need to be considered. This would usually be carried out within a rheumatology service rather than primary care, as it requires specialist facilities and expertise as you describe. This is described in more detail within the committee discussion in evidence review C.
Royal College of Physicians and Surgeons of Glasgow	Guideline	005	004	The association of elevated serum uric acid and features of the metabolic syndrome, including the risk of type II diabetes mellitus and adverse cardiovascular outcomes needs to be included. There is a need to be vigilant in assessing for these factors.	Thank you for your comment. Please refer to recommendation 1.3.6, where we suggest a follow-up appointment to measure the serum urate level and to assess lifestyle and comorbidities (including cardiovascular risk factors).
Royal College of Physicians and Surgeons of Glasgow	Guideline	005	017	Colchicine is commonly used for treatment of acute flares. However, the dosage is variable. Many pharmacists limit course to eight or ten tablets (0.5mg) which is not appropriate and not the practice of most rheumatologists and was a recommendation in the BNF. There is also a tendency to be given an excessive dose during 24 hours. Colchicine can be given for long periods safely in low dosage without side effects (usually diarrhoea). A reasonable regimen is 0.5mg bd or tds for up to seven days or longer if necessary. In polyarticular flares or presentations a short course of oral corticosteroids may be more effective.	Thank you for your comment. 'The committee recognises that there is variation in the doses of colchicine used for flare management in clinical practice and that although the recommended dose regime in the BNF permits some flexibility, longer courses than those advocated in the BNF are sometimes used. However, NICE guidelines do not usually provide specific information on drug doses

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Royal College of Physicians and Surgeons of Glasgow	Guideline	006	003	If available, ACTH can be used in acute gout treatment in those who do not tolerate or refractory to conventional treatments? Parenteral treatment can be used in patients who have had abdominal surgery and cannot take oral drugs.	Thank you for your comment. This is not included within the scope and therefore we cannot provide any guidance on it.
Royal College of Physicians and Surgeons of Glasgow	Guideline	006	013	Splinting may be helpful in addition to ice packs.	Thank you for your comment. Splinting was not included in the protocol for this question, therefore we cannot comment on it. The Committee did not include it in the protocol as splinting would only really be relevant to hand/wrist involvement, which is less common than involvement at other sites. It can be difficult to apply a splint to a joint affected by a gout flare as the joint is usually very swollen and tender.
Royal College of Physicians and Surgeons of Glasgow	Guideline	007	010	It is also appropriate to suggest avoiding dehydration. The advice of not using dietary manipulation is appropriate. However, it may be appropriate to avoid high-purine foods such as shellfish or offal (accepting there is no good quality evidence to support this advice).	Thank you for your comment. The evidence was weak in this area and the committee were unable to recommend any specific diet or avoidance of certain foods and instead recommended a balanced diet.
Royal College of Physicians and Surgeons of Glasgow	Guideline	008	003	Generally speaking, it has been customary to use a urate of 500umol/l or above as a criterion. In addition, there is no mention of its use as a prophylactic treatment in those undergoing chemotherapy such that the purine load will increase.	Thank you for your comment. The committee are not aware of the urate level criteria of 500micromol/l. As the guideline does not cover chemotherapy, we are unable to comment on its use in this scenario.
Royal College of Physicians and Surgeons of Glasgow	Guideline	008	014	We agree that lifelong therapy with monitoring is appropriate. It is extremely common for therapy to be stopped in primary care either by a GP or community pharmacist.	Thank you for your comment.
Royal College of Physicians	Guideline	008	015	Flares are common in the first three months of treatment particularly with introduction of allopurinol.	Thank you for your comment. A link to the recommendations on preventing flares during the initiation and titration of ULT has been added.

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and Surgeons of Glasgow				A first line drug such as NSAID or Colchicine is commonly recommended in the first three months.	
Royal College of Physicians and Surgeons of Glasgow	Guideline	009	005	The current UK recommendation of a target of 300umol/l or below has been in place since 2008. The EULAR recommendation is 360. However most British authorities use the BSR guidance. There is no clear rationale for this change in this guidance and in the supporting evidence. In practice many patients on treatment with a level between 300 and 360umol/l will continue to have attacks. It is slightly odd that the guidance suggests using the same value for diagnosis and target dose for therapy. We draw attention that the target level of treatment falls within the 'normal range' in most laboratory reference ranges. Therefore clinicians must be wary to that a urate level within the normal range can still be well above the target (and diagnostic) level in patients with known gout.	Thank you for your comment. The rationale behind the committees decision to recommend a target serum urate level below 360µmol/L (6 mg/dl) is explained in the rationale and impact section of the guideline and in the discussion of evidence review K best serum urate level target. The committee agreed that a serum urate level of <360µmol/L (6mg/dl) would be appropriate as it is more attainable and requires lower doses of ULT, which may improve patient adherence. The committee also acknowledged a target of below 360µmol/L reflected practice within primary care and disagreed with the statement that 'most British authorities follow the BSR guidance' since the BSR national audit of gout management by rheumatologists published in 2018 found that only 25% of people with gout seen in rheumatology clinics in the UK had achieved a serum urate level below 300µmol/L after 12 months. The committee also disagreed that many patients on treatment with a level between 300 and 360µmol/l will continue to have attacks. Reducing urate below 360 does bring about flare cessation in many patients and recommendation 1.5.7 provides flexibility to lower urate below 300 in people continue to have ongoing frequent flares despite achieving the 360µmol/litre. The cost of achieving a target serum urate level of less than 360µmol/L will also likely be lower than a target of less than 300µmol/ due to fewer appointment costs and blood tests.

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					The serum urate level values for diagnosis are 360µmol/L or more whereas the target level is below 360µmol/L and therefore the committee disagree they are the same. The committee agreed that the saturation threshold of urate in body tissues at which monosodium crystals start to form lies within the normal range in most clinical laboratories, supporting our decision to include a threshold for diagnosis.
Royal College of Physicians and Surgeons of Glasgow	Guideline	009	012	Current NICE advice is that Allopurinol must be given prior to Febuxostat.	Thank you for your comment. The Guideline will replace current recommendations for allopurinol and febuxostat.
Royal College of Physicians and Surgeons of Glasgow	Guideline	010	001	1.5.9 Infers an ongoing and valid association between Febuxostat and adverse cardiovascular outcomes (presumably from CARES trial 2018) - Is this the basis for this advice here? There are now data against this association *e.g.*, FAST trial showed non-inferiority of febuxostat compared to allopurinol with a primary cardiovascular endpoint.	Thank you for your comment. The guidance is in line with MHRA recommendations for prescribing. The SPC has been updated following the FAST trial, CV disease is not a contra-indication, but have advised treatment for this patient group should be exercised cautiously and they should be monitored regularly**.** Please see https://www.medicines.org.uk/emc/
Royal College of Physicians and Surgeons of Glasgow	Guideline	010	009	Prophylaxis is most commonly missed part of management. Use of low dose colchicine or NSAID is effective in preventing attacks during instigation of ULT. Long term use of colchicine is often prevented by local policies. The BNF is unclear on its use for Prophylaxis (does not mention what is meant by	Thank you for your comment. A recommendation has been made for colchicine to be offered while the target serum is being reached.

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				"short term"). There is literature of this drug being used for long periods for gout.	
Royal College of Physicians and Surgeons of Glasgow	Guideline	General	General	The Royal College of Physicians and Surgeons of Glasgow although based in Glasgow represents Fellows and Members throughout the UK. While NICE has a remit for England, many of the recommendations are applicable to all devolved nations including Scotland. They should be considered by the relevant Ministers of the devolved governments. The College welcomes this guidance on Gout including diagnosis and management. It recognises Gout as an important cause of morbidity and disability which is often treated sub-optimally and badly reviewed within primary and secondary care. This review is timely.	Thank you for your comment.
UK Gout Society	Guideline	004	002 - 007	The serum urate level does not confirm or refute a diagnosis of gout. It is frequently misleading. We are concerned that this will lead to doctors and others relying on the urate to make a diagnosis.	Thank you for your comment. The recommendation has been amended to make clearer it is the symptoms and signs of gout as well as the serum urate measurement that is used to make a clinical diagnosis.
UK Gout Society	Guideline	006	009 - 012	Please remember that colchicine is also an IL-1 inhibitor - this should be reworded to specify the IL-1 inhibitors such as Anakinra or Canakinumab that you suggest should not be offered.	Thank you for your comment. The committee are not aware of clinicians regarding colchicine as an IL-1 inhibitor. The SPCs state the mode of action is unclear and the exact mechanism of action of Colchicine in gout is not known. Therefore, the committee don't agree that colchicine is generally known as an IL-1 inhibitor and think the recommendation is clear. Canakinumab is the onlyILl-1 inhibitor licenced for use in gout.

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UK Gout Society	Guideline	010	004 - 006	It is regrettable that you do not mention Benzbromarone as a second line therapy - We note that you do mention the use of prednisolone as an off-label treatment for gout flares - this is well established, as is the use of Benzbromarone and its use by rheumatology units should be recognised by NICE.	Thank you for your comment. Benzbromarone is for specialist use only and this is why it is not included within the recommendation. Where allopurinol or febuxostat are contraindicated, the person should be referred to rheumatology for further opinion. A recommendation has been made to refer to rheumatology services if response to treatment has not been adequate or treatment is not tolerated.
UK Gout Society	Guideline	027	011	1.6.1 NB: The Society regularly receives enquiries from patients requesting direct referral to specialist gout services as they do not feel their GP is knowledgeable enough regarding their gout, there has been little resolution of symptoms, or they do not tolerate their treatment and are seeking further help. All enquiries are asked to recontact to their GP for help - and patient information sheets are also provided.	Thank you for your comment. The recommendation offers guidance to GPs and other health professionals in when to refer a person with gout to specialist services.

**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*