NHS
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Clinical Commissioning Group

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Teaching Hospitals
NHS Foundation Trust

Referral Support Service

Renal

REO6 Hyperuricaemia in patients with stage 3 to 5 CKD

Who is the advice for?

This advice is intended to be specific for adults hyperuricaemia and with stage 3-5 chronic kidney disease (i.e. an eGFR <60 ml/minute, but not on dialysis or transplanted).

York and Scarborough biochemistry department quote a normal range for serum urate of:

Male:	200-430 micromol/L
Female:	140-360 micromol/L

What should I do about a high serum urate in an adult with stage 3 to 5 CKD?

1) There is no need to routinely measure serum urate in adults with CKD.
2) There is no evidence that lowering serum urate alters progression of CKD, renal prognosis or mortality in people with CKD. This has now been investigated in a number of randomised controlled trials.
3) Gout is more common in people with CKD.

Uric acid is the end product of purine metabolism. In humans, the kidney is the only route through which uric acid can be removed from the body. As GFR declines, serum urate will rise. Most adults with CKD will have an elevated serum urate.

The main indications to measure serum urate will be following an episode of acute gout or the presence of gouty tophi. Acute gout is sometimes a clinical diagnosis, but the gold standard diagnostic test is based on the finding of urate crystals in synovial fluid following joint aspiration.

Serum urate has little value in the diagnosis of gout, regardless of kidney function. See the RSS guidance on gout. It is not helpful in people with CKD, because most people with CKD have an elevated serum urate for the reason outlined above.

When should I prescribe treatment (a xanthine oxidase inhibitor) to lower serum urate in an adult with stage 3 to 5 CKD?

First treat the acute gout. Acute gout is usually treated with one of the following:

1) Non-steroidal anti-inflammatory drugs are not recommended by the local the renal team.

   Colchicine 0.5mg twice a day. Higher doses in renal failure are dangerous. Use a maximum of 6mg per course and do not repeat treatment within three days. Be familiar with NICE guidance on colchicine. **Colchicine** has a narrow therapeutic index and is extremely toxic in overdose. Colchicine can be used in CKD, but it is important to avoid diarrhoea especially in someone taking diuretics and/or medications that block the renin angiotensin aldosterone system (e.g. ACE-inhibitors; A2RBs; spironolactone). Diarrhoea can precipitate acute on chronic kidney injury in this setting.

2) NICE CKS guidance is not specific about the use of **prednisolone** in patients with CKD. A short course of oral corticosteroids can be considered. Locally, consultant experience is

that **prednisolone 20 mg once a day** for 5 to 7 days is often very effective although the British Society for Rheumatology suggest higher doses for longer but this is not supported locally. Care should be taken to monitor for increasing blood pressure and or fluid retention.

OR

3) A single intramuscular corticosteroid injection (**depomedrone 40mg**) can be considered in people who cannot tolerate colchicine, and if intra-articular injection is not possible or multiple joints are affected.

Urate lowering therapy should be started 1–2 weeks after the inflammation has settled

NICE say urate lowering therapy should be considered in anyone with an episode of gout and should be strongly offered to patients if

- there have been two or more attacks in a year,
- tophi are present, there is radiographic evidence of erosion,
- renal impairment (eGFR <60) - the local renal team would not start urate lowering therapy after a single episode of gout
- uric acid stones
- in patients on long term diuretic therapy.

Therapy should be aimed at suppressing serum urate to below 300 micromol/L

Allopurinol remains the first line treatment, including in adults with CKD. The prescribing clinician needs to explain potential side effects, including the risk of an acute flare of gout, skin rash and neutropenia.

Febuxostat can be used in those who are intolerant to allopurinol.

Prophylaxis should be prescribed to prevent an acute flare of gout during the initiation of allopurinol. **Colchicine 0.5 mg once or twice a day** for 10 to 14 days can be used if this is well tolerated. Although unlicensed for gout the hospital's renal department suggest an alternative, that they use is a single dose of **intramuscular depomedrone** (e.g. 40 mg, unlicenced) or **oral prednisolone 10 to 15 mg once a day** for 10 to 14 days.

Allopurinol should be prescribed as follows in CKD:

TABLE 2 Starting regime of allopurinol according to glomerular filtration rate

Estimated GFR ml/min/1.73 m^2	Allopurinol starting dose
<5	50 mg/week
5–15	50 mg twice weekly
16–30	50 mg every 2 days
31–45	50 mg/day
46–60	50 mg and 100 mg on alternate days
61–90	100 mg/day
91–130	150 mg/day
>130	200 mg/day

From Stamp LK *et al.* Starting dose is a risk factor for allopurinol hypersensitivity syndrome: a proposed safe starting dose of allopurinol. *Arthritis Rheumatol* 2012;64:2529–36. Copyright © 2012 by John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc. GFR: glomerular filtration rate.

(From British Society of Rheumatology Guideline for the Management of Gout, 2017)

The dose of allopurinol should be increased until serum urate is less than 300 micromol/L. Experience in York is that most people with CKD will tolerate dose titration at 2 weekly intervals. Although NICE recommend titrating dose every 4 weeks the experience in York renal department is that most people with CKD will tolerate dose titration at two weekly intervals which focuses action on getting to the right dose faster and more effectively.

References

NICE Clinical Knowledge Summary on Gout (accessed 17/1/22) published February 2018
British Society of Rheumatology Guideline for the Management of Gout, 2017

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