SUMMARY

NHS Fife Gout Management Guidelines

Diagnosis of Acute Gout

1. A painful red hot swollen joint develops over 2-3 hours and resolves within 2 weeks
2. 90% of first gout attacks are monoarticular and most occur in the big toe
3. Gout attacks may occur when the serum uric acid is normal.

Management of Acute Gout

1. NSAIDs (with PPI) are the treatment of choice when not contraindicated
2. Colchicine is slower to act
3. Analgesics can be added
4. Corticosteroids are highly effective and can be substituted for NSAIDS or added to colchicine
5. Stop thiazide or loop diuretics only if being used to treat hypertension.

Management of Chronic Gout

1. Urate lowering therapy is indicated when patients have clinical evidence of urate overload
2. Delay starting urate lowering therapy until 1-2 weeks after the signs of inflammation have resolved
3. The therapeutic goal of urate-lowering therapy is to achieve a uric acid level < 0.3 mmol/L
4. Allopurinol can be started at a dose of 50-300mg daily. Urate should be checked in 4 weeks and if it remains > 0.3 mmol/L then allopurinol dose should be increased by 100mg. Urate should be repeatedly checked 4 weekly and allopurinol dose increased by 100mg until urate is < 0.3 mmol/L or a maximum dose of 900mg (severe disease) is reached. Doses over 300mg daily given in divided doses
5. Colchicine 0.5 mg bd is given for 6-12 months after starting Allopurinol to reduce the number of acute attacks that are known to occur in the first year of urate lowering therapy
6. Sulphinpyrazone, Febuxostat or Benzbromarone are alternatives to Allopurinol. The latter two should be initiated in a specialist setting.

Patient Education and Lifestyle Advice

1. All patients should receive education and lifestyle advice. See NHS Fife Patient Gout Information Leaflet or patients may visit www.arc.org.
Management of Acute Gout [1]

1. Affected joint(s) should be rested and anti-inflammatory and analgesic drug therapy commenced immediately, and continued for 1-2 weeks. Bed cages and ice packs can be effective adjuncts to therapy.

2. A non-selective oral NSAID e.g. diclofenac, indometacin or naproxen at maximum dose is the drug of choice +/- a PPI when not contraindicated. Etoricoxib +/- PPI may be prescribed if at least two non-selective NSAIDs +/- PPI are ineffective or not tolerated. Treatment should be continued until symptoms have resolved.

3. Co-prescription of a gastroprotective agent e.g. omeprazole or lansoprazole, is now recommended in all high risk patients prescribed a non-selective NSAID or a COX-2 selective agent [2].

4. Colchicine can be an effective alternative but is slower to work than NSAIDs. To minimise risk of diarrhoea doses of 500micrograms two to four times daily should be used. Treatment should be continued until symptoms have resolved or diarrhoea or vomiting occurs.

5. Allopurinol **should not** be commenced during an acute attack. Allopurinol should be continued in patients already established on it, and the acute attack treated as above.

6. Opioid analgesics can be used in addition to or instead of NSAIDs or colchicine.

7. Intra-articular corticosteroids are highly effective in acute gouty monoarthritis and can be used in addition to or instead of NSAIDs or colchicine when ineffective or not tolerated.

8. Oral, IM or IV corticosteroids can be used instead of NSAIDs. Oral, IM or IV corticosteroids can be used in addition to colchicine in those refractory to treatment. Oral Prednisolone 10-30mg /day for up to two weeks or Depomedrone 120mg IM stat may be used.

**Gout Diagnosis Facts**

- A typical gout attack is the development of a painful red hot swollen joint over a 2-3 hour period. Attacks usually resolve within 2 weeks even when untreated.
- The differential diagnosis includes septic arthritis.
- 90% of first gout attacks are monoarticular and most occur in the big toe.
- The skin around the affected joint may be red and look like cellulitis.
- Gout attacks may occur when the serum uric acid is normal.
9. If thiazide or loop diuretics are being used to treat hypertension, alternative agents should be considered. In patients with cardiac failure diuretics should be continued [3].

Table 1.

<table>
<thead>
<tr>
<th>Management of Acute Gout: Key facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line treatment</td>
</tr>
<tr>
<td>NSAID +/- PPI</td>
</tr>
<tr>
<td>Reduce or discontinue loop or thiazide diuretics if possible</td>
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Figure 2. Gout crystals

Figure 3. Gout Erosions

Management of Chronic Gout [1,4]

1. The therapeutic goal of urate-lowering therapy is to achieve a uric acid level < 0.3 mmol/L [1,5]
2. Urate lowering therapy is indicated in patients that have had 2 or more acute gout attacks, chronic gouty arthritis, tophi or radiographic changes of gout (Figs. 3 & 4)
3. Commencement of uric acid lowering therapy should be delayed until 1-2 weeks after the signs of inflammation have subsided
4. Allopurinol is usually started at a dose of 100mg daily. Urate should be checked in 4 weeks and if urate remains > 0.3 mmol/L then allopurinol dose should be increased by 100mg. Urate should be repeatedly checked every 4 weeks and allopurinol dose increased by 100mg until urate is < 0.3 mmol/L
or a maximum dose of 900mg (severe disease) is reached. Doses over 300mg daily should be given in divided doses

5. If allopurinol toxicity occurs, uricosuric agents such as sulfinpyrazone (200-800mg/day) can be used in patients with normal renal function but are not used in patients with urolithiasis

6. Febuxostat is a new non-purine xanthine oxidase inhibitor that has been shown to be more effective in reducing serum urate levels than allopurinol 100-300mg daily. The effect of febuxostat has not been compared with higher doses of allopurinol. Febuxostat is a more costly second line gout treatment that should be prescribed with the recommendation of a Rheumatologist [6,7]

7. Benzbromarone (50-300mg/day available on a named patient basis) is an unlicensed uricosuric agent that can be used in patients with low creatinine clearance. It is ineffective when the eGFR is less than 15mL/min

8. During the first 6-12 months of urate-lowering therapy patients are at increased risk of acute gout attacks [3]. Prophylaxis of acute attacks can be achieved using colchicine 0.5mg twice daily [8]

9. The recommended duration of prophylactic colchicine or NSAIDs during the initiation of uric acid lowering therapy varies with the clinical setting:
   - Patients with normal renal function can be prescribed colchicine 0.5 mg twice daily for up to 12 months [5]
   - The optimal duration of prophylactic therapy for patients with tophi is uncertain. Colchicine should be continued for a maximum of one year or it is clear that topaceous deposits will not resolve despite persistent normouricemia [6]

10. An NSAID with gastroprotection can be used instead of colchicine or in addition to colchicine for prophylaxis of acute attacks. The evidence base for prophylaxis with colchicine is stronger than that for NSAIDS [4]

11. Aspirin 75-150 mg/day slightly increases plasma urate but should be used where the benefits outweigh the risks

12. Where thiazide or loop diuretics are being used to treat hypertension in patients with gout, alternative therapy should be considered instead. Losartan has a modest uricosuric effect [3]

13. Where statins are contraindicated for lowering cholesterol then fenofibrate should be considered as an alternative lipid lowering agent as it has a modest uricosuric effect.
Table 2.

### Management of Chronic Gout: Key facts

<table>
<thead>
<tr>
<th>First line treatment</th>
<th>Second line treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>Sulphinpyrazone</td>
</tr>
<tr>
<td></td>
<td>Febuxostat</td>
</tr>
<tr>
<td></td>
<td>Benzbromarone</td>
</tr>
<tr>
<td>Increase allopurinol by 100mg every 4 weeks until target reached</td>
<td>Uricosuric agents should be avoided in those with renal stones</td>
</tr>
<tr>
<td>Target uric acid 0.3 mmol/L. Monitor uric acid every 4 weeks until target reached</td>
<td></td>
</tr>
<tr>
<td>Colchicine 0.5 mg twice daily is used for the first 6-12 months after initiating urate lowering therapy</td>
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</table>

### Acute Gout management in patients with Renal Impairment
1. Colchicine is effective but is slower to work than NSAIDs. To minimise risk of diarrhoea doses of 500micrograms two to four times daily should be used. Maximum total dose is 3mg if creatinine clearance <10ml/min and 6mg if creatinine clearance is 10-50ml/min. Do not repeat course within 3 days [9]
2. Opioid analgesics can be used in addition to colchicine.

### Chronic Gout management in patients with Renal Impairment [9]
1. Allopurinol and its metabolites have a long half life. In renal impairment allopurinol 100mg/day can be commenced and the dose titrated up until target urate < 0.3 mmol/L is achieved. In patients with CKD Stage 3-5 lower maintenance doses of allopurinol may be required and occasionally doses of 50mg/day or 100mg alternate days may be sufficient [9]. The incidence of skin rash is increased in patients with CKD.
2. Febuxostat can be used in renal impairment. No dose adjustment is required in mild-to moderate renal impairment (creatinine clearance 30–80 ml/min). The safety and efficacy of febuxostat have not been fully evaluated in patients with creatinine clearance <30 ml/min [6,7].
3. Benzbromarone (50-200 mg/day available on a named patient basis) is an unlicensed uricosuric agent that can be used as an alternative to allopurinol in patients with low creatinine clearance, but is ineffective when the eGFR is less than 15ml/min.
4. During the first 6-12 months of urate-lowering therapy patients are at increased risk of acute gout attacks [5]. Prophylaxis of acute attacks can be achieved using the colchicine doses in table 3.
5. The dosage of colchicine should be adjusted in patients with renal impairment (see Table 3).
6. Duration of colchicine course should be limited to 6 months in patients with renal impairment, at the doses recommended in table 3. Adverse effects such as raised liver function tests are most commonly seen in patients with renal impairment where the duration of colchicine prophylaxis is greater than 6 months [3].

Table 3.

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>Colchicine dose</th>
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<tbody>
<tr>
<td>&lt; 10 mL/min</td>
<td>500 mcg 1-2 days per week under specialist supervision</td>
</tr>
<tr>
<td>10-35 mL/min</td>
<td>500 mcg 3-4 days per week under specialist supervision</td>
</tr>
<tr>
<td>35-50 mL/min</td>
<td>500 mcg daily</td>
</tr>
<tr>
<td>&gt; 50 mL/min</td>
<td>500 mcg twice daily for prophylaxis and up to four times daily during acute attacks</td>
</tr>
</tbody>
</table>

Figure 4. Chronic gouty arthritis and tophi
Drug Monitoring Guidelines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monitoring Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>6 monthly in the first year then stop.</td>
</tr>
<tr>
<td>Sulfinpyrazone</td>
<td>Continue only if patient has CKD 2-4</td>
</tr>
<tr>
<td>Febuxostat</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>Every 4 weeks until urate &lt; 0.3 mmol/L</td>
</tr>
<tr>
<td>Colchicine</td>
<td>3 monthly</td>
</tr>
<tr>
<td>Benzbromarone</td>
<td>monthly for 1st 6 months then every 6 months</td>
</tr>
</tbody>
</table>

Interactions

**Allopurinol**
- Increases toxicity and effects of azathioprine and 6-mercaptopurine. Reduce dose of azathioprine and 6-mercaptopurine to one quarter of usual dose.

**Colchicine**
- Toxicity of colchicine increased if co-prescribed with clarithromycin or erythromycin.
- Increases plasma concentrations of ciclosporin. Possible increased risk of nephrotoxicity and myotoxicity.
- Possible increased risk of myopathy if co-prescribed a statin.

**Sulfinpyrazone**
- Increases the anti-coagulant effect of warfarin.
- Enhances the hypoglycaemic effect of sulphonylureas.
- Increases plasma concentrations of phenytoin.
- Reduces plasma concentrations of ciclosporin.

**Febuxostat**
- Increases toxicity of azathioprine, 6-mercaptopurine and theophylline. Co-prescription of azathioprine, 6-mercaptopurine or theophylline with febuxostat is not recommended [6].

**Benzbromarone**
- Avoid co-prescription of hepatotoxins e.g. isoniazid.

For a complete list of potential drug interactions refer to the BNF or Summary of Product Characteristics.


Education

Optimal treatment of gout requires both non pharmacologic and pharmacologic treatment.

- Patient education (ARC leaflet)
- Lifestyle advice: where indicated weight loss, diet and reduced alcohol intake (especially beer including non-alcoholic beer) are essential
- Co-morbidities such as hypertension, hyperlipidaemia hyperglycaemia and smoking should be addressed.

Lifestyle Advice [1]

1. In overweight patients dietary modification to achieve ideal body weight should be attempted but crash dieting and high protein Atkins-type diets should be avoided
2. Skimmed milk, low fat yoghurt, soy beans, cherries and vegetable sources of protein should be encouraged in the diet
3. Liver, kidneys, shellfish and yeast extracts should be avoided. Intake of high purine foods and red meat and overall protein intake should be restricted
4. Patients with gout and urolithiasis should drink > 2 litres of water per day. In recurrent stone formers alkalisation of the urine with potassium citrate (6.5mg/ day) should be considered
5. Beer, stout, port and fortified wines should be avoided. Alcohol consumption should be restricted to < 21 units/week (men) and 14 units/week (women). Patients should have at least 3 alcohol free days per week. Moderate wine consumption does not appear to increase frequency of gout attacks
6. Patients wishing to try herbal remedies for gout should first discuss them with their doctor
7. Moderate physical exercise should be encouraged but intense exercise or trauma to joints should be avoided.
8. Vitamin C intake up to 1400mg / day is recommended. A combination of supplements and dietary intake is recommended. See table below. [10-12]
9. Fructose is used as a sweetener especially in the USA where a high intake of fructose in soft drinks (but not diet drinks) doubled the incidence of gout [3].
### Risk factors for Gout

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raised serum urate</td>
<td>The higher the urate level, the greater the risk of gout.</td>
</tr>
<tr>
<td>Genetics</td>
<td>Mutations in genes for urate transporter URAT1 and fructose transporter GLUT9 are associated with gout.</td>
</tr>
<tr>
<td>Age</td>
<td>2% of 45-64 year old men and 6% men &gt;75 years old have gout.</td>
</tr>
<tr>
<td>Gender</td>
<td>Male :Female ratio 3:1 in those &gt; 65 years</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Gout attacks more likely in joints affected by OA while Rheumatoid Arthritis is protective</td>
</tr>
<tr>
<td>Diet and alcohol</td>
<td>Wine in moderation appears safe</td>
</tr>
</tbody>
</table>
Indications for GP referral of Gout Patients to Rheumatology

1. Acute gout attack that fails to resolve within 14 days when treated as above.
2. Uncontrolled recurrent gout attacks despite use of Allopurinol 900mg daily or Sulphinpyrazone and guideline advice.
3. Uncontrolled recurrent attacks when serum urate < 0.3 mmol/L and use of guideline advice.
4. Intolerance of Allopurinol and Sulphinpyrazone

Patients with urolithiasis should be assessed by a Urologist.

Indications for X-Ray in Gout Patients
An X-Ray of the affected joint should be undertaken in all patients that have had one or more gout attacks. The presence of an erosion is an indication for urate lowering therapy. The diagnosis of gout is clinical and X-Rays are often not useful in making a gout diagnosis.

When Can Urate Lowering Therapy be Reduced?

If serum urate is < 0.3 mmol/L and there have been no gout attacks for 1 year Allopurinol can safely be reduced by 100 mg. Serum urate should be re-checked 6 monthly and Allopurinol dose lowered further if urate remains < 0.3 mmol/L. The risk of a gout attack rises as serum urate levels rise. Patients that have tophi are most likely to require lifelong urate lowering therapy.

Gout Management: Key Facts Summary

| An NSAID +/- PPI is first line therapy in acute gout | Colchicine 0.5 mg twice daily is used for the first 6-12 months after initiating urate lowering therapy. |
| 2 or more gout attacks, tophi or renal stones are indications for indefinite urate lowering therapy | Gout therapy should be adjusted in renal impairment |
| Allopurinol dose should be escalated until uric acid is < 0.3 mmol/L | Education and lifestyle advice should be given to all patients |

References


5. Lowering Serum Uric Acid levels: What is the optimal Target for Improving Clinical Outcomes in Gout? Perez-Ruiz Fernando and Liote F Arthritis and Rheum 57; 7 1324-1328.


11. A little citrus might go a long way Gelber AC J. Rheum. 2008 35(9) 1692-4