bpacnz
PRIMARY CARE
UPDATE SERIES

01

GOUT:
WHAT'S IN AND WHAT'S OUT

Welcome to the bpac[nz] primary care update series. Today, we're going to be looking at the management of gout, which has seen a considerable shift in perspective over the years as we've gained greater insight into its causes, and how best to apply the medicines in our toolkit. Therefore, let's find out "what's in and what's out" when it comes to gout. For this, we're fortunate enough to be able to draw on the expertise of **Dr Simon Stebbings**, a consultant Rheumatologist and Associate Professor at the Dunedin School of Medicine, University of Otago.

JUNE 2020
VER 1.3

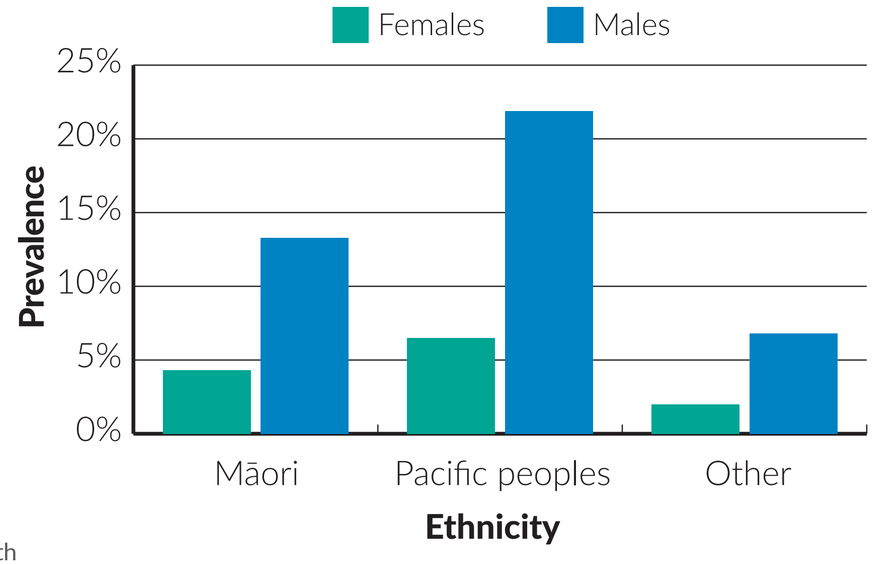
Gout risk is primarily driven by genetic factors and renal function

Urate transporter proteins (e.g. URAT1) are essential for maintaining urate homeostasis as they influence renal clearance of urate – certain alleles are associated with increased urate in the blood

Under-excretion of urate in the kidneys is the primary cause in nine out of ten cases

Gout is more common in Māori and Pacific peoples in New Zealand*

- Rates of hospitalisation with gout as the primary diagnosis are four times higher in Māori and Pacific peoples than in other ethnic groups
- Variants of the *SLC2A9* fructose/urate co-transporter gene have been implicated in the greater prevalence of gout in Māori and Pacific peoples (although environmental factors still play a role)



* In people aged ≥ 20 years.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al.* Arthritis Care Res. 2012;64:1431–46; 2. Richette P, Bardin T. Lacet. 2010;375:318–328; 3. Health Quality & Safety Commission New Zealand. Gout. 2016. Available from: https://www.hqsc.govt.nz/our-programmes/health-quality- evaluation/projects/atlas-of-healthcare-variation/gout (Accessed May, 2020); 4. Dalbeth N, Stamp LK, Merriman. BMC Med. 2017;15:108

Gout risk is primarily driven by genetic factors and renal function

Lifestyle changes are important, but insufficient for managing gout alone

Unless obvious triggers can be determined, dietary modifications must be accompanied by significant weight loss to have any impact on the risk of flares

What should be avoided?	What should be encouraged?	What probably doesn't help?
• Excess purines e.g. beer, shellfish, red meat, marmite • Fructose and sucrose – particularly fruit juice • Tomatoes • A sedentary lifestyle	• Low-fat dairy products e.g. milk, yoghurt • Vegetables • Staying hydrated (≥ 2L water/day) • Maintaining a healthy BMI • Exercise	• Vitamin C

1. Khanna D, Fitzgerald JD, Khanna PP, et al. Arthritis Care Res. 2012;64:1431–46; 2. Flynn T, Cadzow M, Dalbeth N, et al. BMC Musculoskelet Disord. 2015;16:196; 3. Stamp LK, O'Donnell JL, Frampton C, et al. Arthritis Rheum. 2013;65:1636–42; 4. Krishnan E, Lessov-Schlaggar CN, Krasnow RE, et al. Am J Med. 2012;125:499–504.

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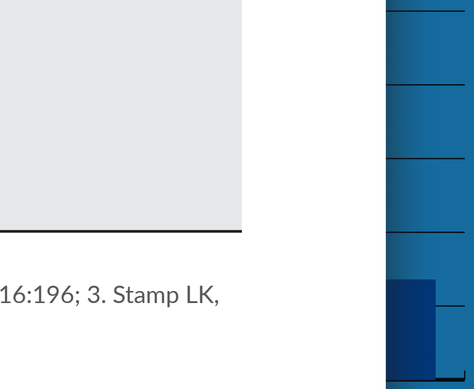

Ethnicity

* In people aged ≥ 20 years.

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Managing gout: consider urate-lowering treatment early and continue long-term

Initial steps

Establish diagnosis and severity
e.g. symptoms, number of joints involved, level of pain, measure serum urate

+

Patient education on cause, lifestyle changes and urate lowering treatment

+

Assess renal function – review/manage co-morbidities and medicine use to preserve this

Acute flare management

- **NSAIDs** (naproxen preferred)
- **Corticosteroids** (prednisone)
- **Low-dose colchicine***

- All acute treatment options are considered equally effective for managing flares
- Choice depends on preference, co-morbidities and other medicine use
- **Combination treatment may be required for severe gout flares**

Initiate urate-lowering medicine if indicated (even during acute treatment of flares) +

Allopurinol is preferred unless contraindicated, ineffective or not tolerated

flare prophylaxis is usually provided for ≥ 6 months (see medicine table at end for options). However, new guidance suggests that 3–6 months might be suitable for some patients.

Up-titrate dose† until serum urate target of < 0.36 mmol/L is reached**

See treatment options table for medicine specific guidance

Once the target is reached, review patient every 6–12 months or after a flare

Symptoms controlled and target achieved → **Continue long-term treatment**

Gout flare or target not achieved → **Acute management for flares; re-review ULT dosing, lifestyle, co-morbidities and medicines**

Long-term management

* Although colchicine is sometimes avoided by New Zealand clinicians, use in low doses has comparable efficacy to NSAIDs and prednisone if given within 36 hours of the flare onset, with an improved safety profile compared to traditional high-dose colchicine regimens; † For allopurinol, up-titration should be performed every four weeks; ** A serum urate target of < 0.30 mmol/L is recommended if tophi are present; NSAIDs, non-steroidal anti-inflammatory drugs.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42. 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. FitzGerald JD, Dalbeth N, Mikuls T *et al*. Arthritis Care & Research. 2020;72:744–60.

Diagnosing gout in primary care

A diagnosis of gout can be made clinically with supporting evidence provided by elevated serum urate levels – scoring systems (e.g. Janssens, 2010) may be useful to help assess the likelihood of gout

See the "practice tool" for more information on diagnosing gout

Repeat serum urate testing may be necessary once the flare has subsided
as up to 40% of patients have levels within a "normal" range during flares

Consider the possibility of alternative diagnoses that present in a similar way to gout, e.g. septic arthritis, CPPD disease

Still unsure?

If there is a high suspicion of another cause, or if infection is suspected, consider joint aspiration:

- A definitive diagnosis of gout can be made by the identification of monosodium urate crystals
- Microbiological analysis of synovial fluid can confirm or exclude the presence of infection

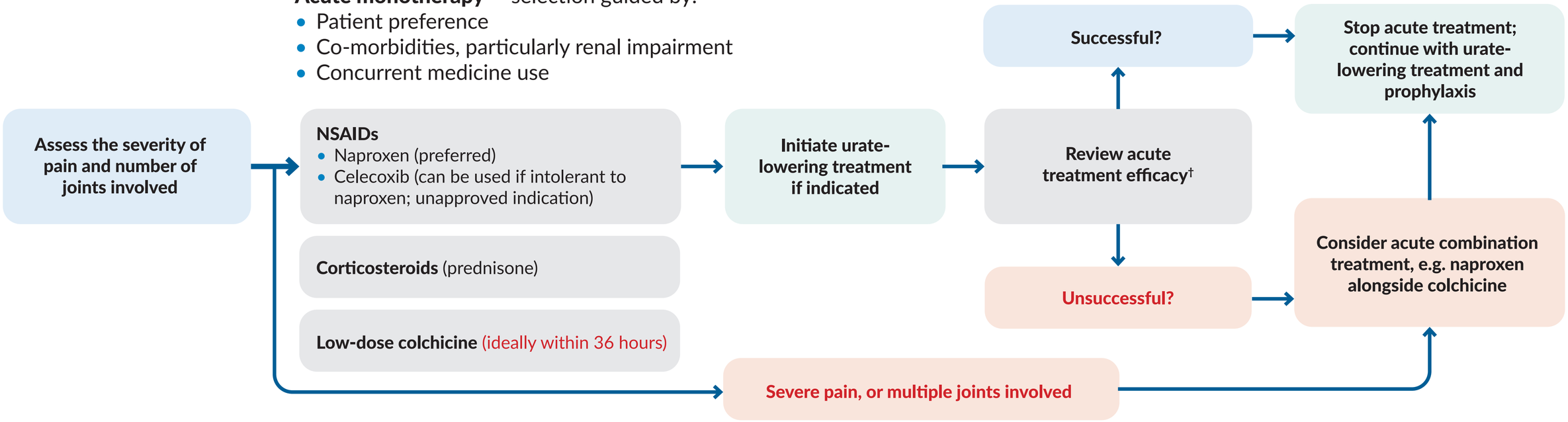
CPPD, calcium pyrophosphate deposition.

1. Schlesinger N. Postgrad Med. 2010;122:157–61; 2. Janssens HJEM, Fransen J, van de Lisdonk EH, *et al*. Arch Intern Med. 2010;170:1120–6; 3. Dalbeth N, Winnard D, Gow PJ, *et al*. N Z Med J. 2015;128:65–8.

Acute and prophylactic management of gout

Acute monotherapy*– selection guided by:

- Patient preference
- Co-morbidities, particularly renal impairment
- Concurrent medicine use



Consider urate-lowering treatment** and investigate serum urate levels immediately; this includes during a flare

Prophylaxis involving lower doses of acute gout medicines should be routinely administered when initiating urate-lowering treatment for ≥6 months and continued if there are ongoing symptoms. However, new guidance suggests that 3–6 months might suitable for some patients.

For further information on the acute and prophylactic management of gout, see **https://bpac.org.nz/2018/gout- part1.aspx** and **https://bpac.org.nz/2018/gout- part2.aspx**

* Dosing regimens for acute flare management and flare prophylaxis can be found later in this presentation and at the NZ formulary (NZF); † The timing of this review is patient- and medicine- specific; in general, a scheduled review should take place within a couple of days, but the patient should also be advised to initiate contact if symptoms are unmanageable or increase in intensity; ** Indications for ULT in the next slide. Abrreviations: NSAIDs, non-steroidal anti-inflammatory drugs.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. NZ Formulary. NZF v95. 2019. Available from: www.nzf.org.nz (Accessed May, 2020).

Acute and prophylactic management of gout

Acute monotherapy*– selection guided by:

- Patient preference
- Co-morbidities, particularly renal impairment
- Concurrent medicine use

Successful? → **Stop acute treatment; continue with urate-lowering treatment and prophylaxis**

Community pharmacists: be alert for persistent OTC NSAID use

Some patients self-manage gout flares by purchasing OTC NSAIDs, e.g. diclofenac, and do not consider long-term prevention

If you establish that a patient is persistently using OTC NSAIDs for this purpose, suggest they see their doctor regarding urate-lowering treatments

NSAID, non-steroidal anti-inflammatory drugs; OTC, over the counter

Prophylaxis involving lower doses of acute gout medicines should be routinely administered when initiating urate-lowering treatment for ≥6 months and continued if there are ongoing symptoms. However, new guidance suggests that 3–6 months might suitable for some patients.

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Urate-lowering treatment for long-term gout control

Indications for initiating urate lowering treatment

Symptomatic hyperuricaemia, with at least one of:

- ≥ 2 gout flares in a year
- Presence of tophi (or tophus)
- Renal impairment (eGFR < 60 mL/min/1.73 m^2)
- Past urolithiasis
- Serum urate level ≥0.54 mmol/L

For further information on the use of allopurinol and other urate-lowering medicines, see "Managing gout in primary care part 2 – controlling gout with long-term urate-lowering treatment", **https://bpac.org.nz/2018/gout-part2.aspx**

Treat to target

A serum urate level of < 0.36 mmol/L* should be the target during treatment;

once this has been achieved through monthly reviews and corresponding dose adjustments, levels should be reassessed every 6–12 months or following a gout flare

Ensure consistent follow-up is scheduled

Two-thirds of patients dispensed urate-lowering medicines in New Zealand do not receive a follow-up serum urate test within six months

Stress the importance of adherence

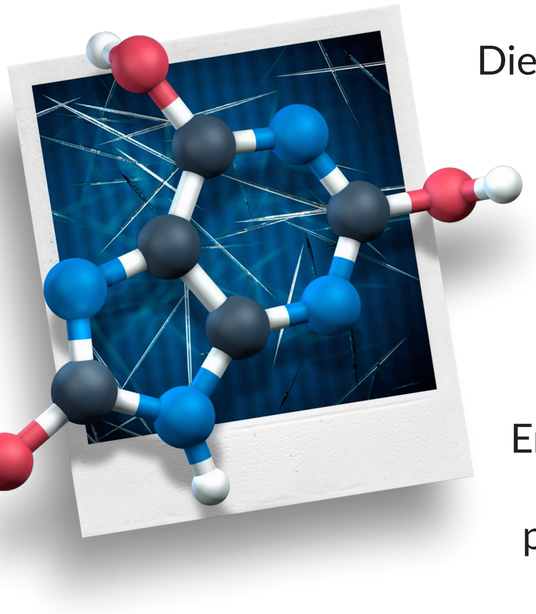
Gout is not "curable" but effective long-term management can stop flares occurring

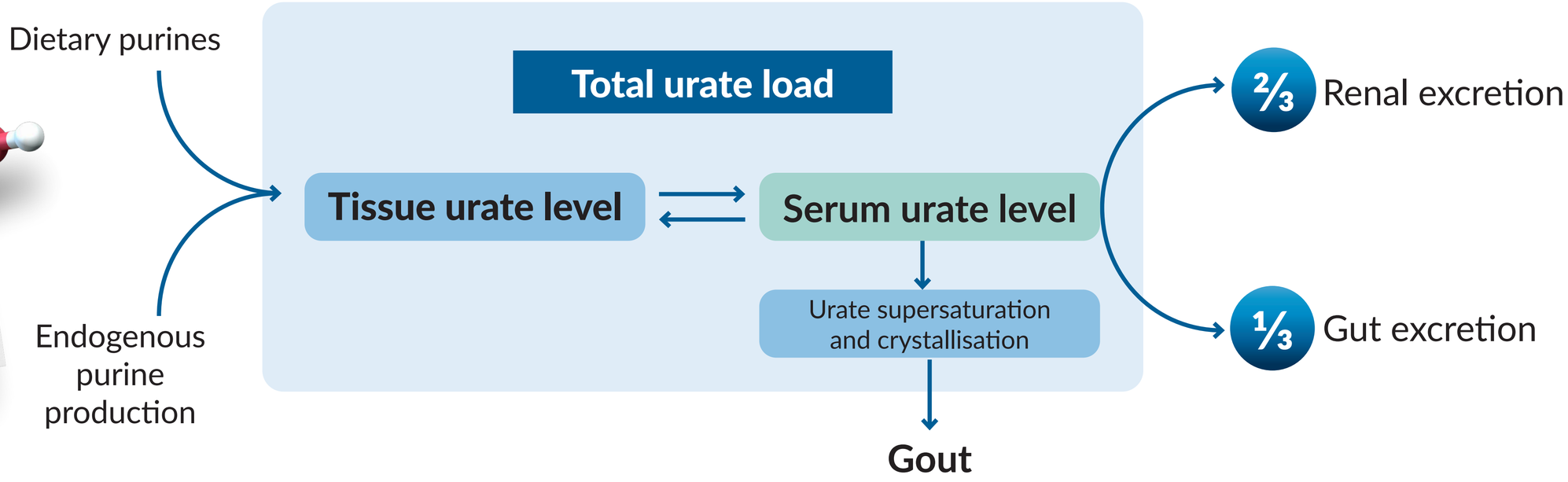
* A serum urate target of < 0.30 mmol/L is recommended if tophi are present.

eGFR, estimated glomerular filtration rate.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. Health Quality & Safety Commission New Zealand. Gout. 2016. Available from: https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/gout (Accessed May, 2020).

Serum urate measurements are just one snapshot of the bodies' total urate load





Urate from crystals within tissues and joints is released progressively during urate lowering treatment; the time taken to reach a serum urate target depends on the total urate load – which can be significant if a number of tophi are present – as well as the patients renal and gut function

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42.

Urate-lowering treatment: start low and gradually up-titrate the dose

Allopurinol is the first-line treatment:

Usually start with allopurinol 100 mg once daily*

Up-titrate
dose every four weeks, usually in 100 mg increments

Continue until serum urate target is reached
up to a maximum of 900 mg

*Is the patient's renal function impaired?

Level of renal impairment (eGFR; mL/min/1.73m^2)	**Initial dose of allopurinol**	**Up-titration protocol**
30–60	50 mg once daily	Increase by 50 mg, every four weeks if tolerated
< 30	50 mg every second day	Increase to 50 mg once daily, then increase by 50 mg, every four weeks if tolerated

- The maximum tolerated dose of allopurinol may be lower in patients with renal impairment; discussing this limit with a rheumatologist should be considered
- Usually apply prophylaxis for ≥ 6 months during initial treatment to prevent acute flares of gout†
- Allopurinol is not indicated for the treatment of asymptomatic hyperuricaemia

† In some cases, stopping prophylaxis may be considered within three to six months of starting ULT, e.g. if the patient has not experienced any subsequent flares and urate levels have reduced significantly

eGFR, estimated glomerular filtration rate.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020).

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Continue until serum urate target is reached
up to a maximum of 900 mg

Once the serum urate target is reached, review patient every 6–12 months *or* after a flare

- **Check:** serum urate, renal function, blood pressure, and HbA_{1C}, in addition to ongoing monitoring and treatment of co-morbidities
- **Emphasise:** the importance of medicine adherence and lifestyle (especially weight loss)

eGFR, estimated glomerular filtration rate.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020).

Urate-lowering treatment: start low and gradually up-titrate the dose

Gout is often associated with co-morbidities

- Cardiovascular disease
- Diabetes
- Renal impairment
- Alcoholic and non-alcoholic fatty liver disease
- Obesity

Avoid high-dose thiazide diuretics in patients with gout and hypertension; consider losartan if there are no contraindications

40% of people with gout in New Zealand also have **diabetes and/or CVD**

1. Jackson R, Shiozawa A, Buysman EK, *et al*. BMJ Open 2015;5:e007214; 2. Edwards NL, Sundy JS, Forsythe A, *et al*. J Med Econ. 2011;14:10–5; 3. Winnard D, Wright C, Jackson G, *et al*. N Z Med J. 2012;126:53–64.

eGFR, estimated glomerular filtration rate.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020).

Other urate-lowering options if allopurinol is contraindicated, not tolerated or ineffective

Medicine	Hierarchy	Initial dose	Up-titration protocol	Notes
Probenecid* (either as an add-on to allopurinol or as a monotherapy)	**Second-line**	250 mg BD for one week, then 500 mg BD	Increase dose in 500 mg increments up to 1 g BD if required (2 g total)	• Avoid if the patient's eGFR is < 30 mL/min/1.73m^2 or they have urolithiasis • Patients must consume at least 2 L of fluid per day • There is insufficient evidence to support alkalising urine with potassium citrate (as previously recommended in guidelines) • No need to check urinary uric acid excretion
Febuxostat† ** See next slide for more info	**Third-line**	80 mg once daily	Increase dose up to 120 mg once daily after 2–4 weeks if required	• Use with caution if eGFR is < 30 mL/min/1.73m^2 • More rapid effect than allopurinol which can trigger gout flares • Liver function test required prior to initiating • **Associated with an increased risk of cardiovascular and all-cause mortality compared with allopurinol**; If a patient experiences a cardiovascular event while taking febuxostat, ideally they should be switched to another ULT; if the patient has already trialled the other available options, discuss with a rheumatologist
Benzbromarone** See next slide for more info	**Third-line**	100 mg once daily	–	• Avoid if the patient's eGFR is < 30 mL/min/1.73m^2 • **Associated with a high risk of hepatotoxicity in all patients and variable INR measurements if the patient is taking warfarin and being monitored** • Liver function tests required monthly for at least the first six months and three-monthly thereafter • Patients must consume at least 2 L of fluid per day • Not an approved medicine in New Zealand; patient consent is needed

* Probenecid can be added even if the patient is taking a relatively high dose of allopurinol (e.g. 600 mg once daily); † Febuxostat can also be used in combination with probenecid; ** Fully subsidised with Special Authority approval.

Abbreviations: BD, twice daily; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; INR, international standardised ratio; ULT, urate-lowering treatment.

1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61;
3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020).

Other urate-lowering options if allopurinol is contraindicated, not tolerated or ineffective

Update – febuxostat

New ACR 2020 guidelines have re-evaluated the place of febuxostat in the ULT hierarchy.

Based on these, the second-line choice would be:

- **Probenecid** if patients have a history of CVD and an eGFR ≥30 mL/min/1.73m^2
- **Febuxostat** if patients do not have a history of CVD and/or they have a history of urolithiasis, and/or an eGFR <30 mL/min/1.73m^2

However, these new ACR 2020 guidelines have not yet been integrated into New Zealand guidelines. In addition, Special Authority criteria for funded access to febuxostat requires that both allopurinol and probenecid have first been trialled (or probenecid is contraindicated due to renal impairment)

Update – benzbromarone

As of May 2020, benzbromarone is out of stock at a wholesaler level in New Zealand, and PHARMAC has advised that it will likely delist it from the Pharmaceutical Schedule (no date is currently set). **Therefore:**

- Do not start any patients on this medicine
- Begin switching patients currently taking it to an alternative ULT

ACR, American College of Rheumatology; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ULT, urate-lowering treatment.

1. FitzGerald JD, Dalbeth N, Mikuls T *et al*. Arthritis Care & Research. 2020;72:744–60; 2. Benzbromarone out of stock. PHARMAC. Available from: https://www.pharmac.govt.nz/informationfor/enquiries/benzbromarone-supply-issue/ (Accessed May, 2020)

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3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020).

Severe adverse effects associated with allopurinol e.g. DRESS, Stevens-Johnson syndrome

DRESS is rare but serious

- Occurs in approximately 0.1% of patients that receive allopurinol
- Mortality is estimated at 20–25%

Individuals at risk of having a DRESS reaction often have a genetic predisposition (*HLA B5801*)

Consider checking anyone of Han Chinese, Korean or Thai ancestry for the *HLA B5801* allele before prescribing allopurinol

For further information on genetic testing, see: **www.genetichealthservice.org.nz**

If a patient has allopurinol hypersensitivity, yet no other oral ULT agent can be used, discuss appropriate management with a rheumatologist

Factors increasing the risk of severe adverse effects	Factors reducing the risk of severe adverse effects
Genetics (*HLA B5801*)	**Low allopurinol starting dose**
Time (recent commencement of allopurinol)	**Patient education to identify symptoms**
Drug concentration (dose, renal function, diuretics)	**Alternative treatment** for patients at high risk

DRESS, drug rash with eosinophilia and systemic symptoms.

1. Stamp LK, Barclay, ML. Rheumatology. 2018;57(suppl_1):i35–41; 2. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46.

What are the treatment options for gout?

Treatment	Medicine/option		Dose range	Notes
Lifestyle modifications	Healthy overall diet (reduce purines and fructose), exercise, maintenance of normal BMI, adequate hydration			Lifestyle changes are important but are insufficient to control gout alone
Acute treatment (usually monotherapy, but combination treatment may be required for severe flares)	**NSAIDs**	**Naproxen** (preferred)	750 mg initially, 500 mg eight hours later, then 250 mg every eight hours until the flare settles	All options are equally effective for manging flares Naproxen is the preferred NSAID but celecoxib* can be used in patients intolerant to this Stop colchicine prophylaxis before initiating acute colchicine treatment. In elderly patients or in those with renal impairment, initial colchicine dose should not exceed 1 mg in first 24 hours; total max 3 mg over four days; do not repeat course within three days
		Celecoxib*	Up to 800 mg once, followed by 400 mg on day 1, then 400 mg BD for one week	
	Corticosteroids	**Prednisone**	Oral: 20–40 mg once daily for five days; tapering the dose over ten days can reduce the likelihood of a rebound flare, but is not always necessary	
	Low-dose colchicine (most effective if within 36 hours of flare onset)		1 mg immediately, followed by 500 µg after one hour on day 1, and then BD dosing of 500 µg until the flare settles (this is an alternative dose now recommended by many experts; see NZF for traditional regimen)	
Flare prophylaxis (prescribed alongside urate-lowering treatment)	**NSAIDs with PPI**	**Naproxen**	250 mg BD (with PPI if indicated)	Usually provide prophylactic medicines for six months alongside urate-lowering treatment; continue if symptoms do not resolve. However, new guidance suggests that 3-6 months might be suitable for some patients Only use prednisone for prophylaxis if NSAIDs and colchicine are contraindicated
	Very low-dose colchicine*		500 µg BD; reduce to 500 µg once daily or every other day if needed	
	Corticosteroids	**Prednisone**	5 mg once daily; tapered slowly on withdrawal	
Long-term	**Urate-lowering medicine‡**	**Allopurinol** (First-line)	100 mg once daily (**adapt to renal function**);† increase dose every 4 weeks if required (up to 900 mg max usually; lower if renal function is impaired)	Probenecid can be used as either an add-on to allopurinol (or febuxostat), or as a second-line monotherapy if serum urate target is not met Febuxostat (and benzbromarone)‡ are typically third-line for patients where allopurinol and/or probenecid are ineffective, contraindicated or not tolerated; for more information on the risks associated with these medicines and guidance about use, see: **https://bpac.org.nz/2018/gout-part2.aspx** New ACR 2020 guidelines prioritise feboxustat as the second-line ULT (over probenecid) in patients without a history of CVD that have previously taken allopurinol. However, this is not yet reflected in New Zealand guidance and the Special Authority criteria for funding requires that probenecid is trialled first unless contraindicated
		Probenecid (Second-line)	250 mg BD for one week, then 500 mg BD; increase dose up to 1 g BD (2 g total) if required; avoid if eGFR is < 30 mL/min/1.73m^2	
		Febuxostat** (Third-line)	80 mg once daily; increase dose up to 120 mg once daily after 2–4 weeks if required; use with caution if eGFR is < 30 mL/min/1.73m^2	

* Unapproved indication; † If the patient's eGFR is 30–60 mL/min/1.73m^2, then use an initial dose of 50 mg once daily; if their eGFR is < 30 mL/min/1.73m^2, use 50 mg every other day; ** Special Authority required. There is an increased risk of cardiovascular and all-cause mortality with febuxostat compared with allopurinol; ‡ Benzbromarone is an additional urate-lowering treatment that is an unapproved medicine in New Zealand but can be obtained fully subsidised with Special Authority. However, as of May 2020, benzbromarone is out of stock at a wholesaler level in New Zealand, and PHARMAC has advised that it will likely delist this ULT from the Pharmaceutical schedule (no date is currently set). No new patients should be started on benzbromarone and those currently taking it should be switched to another ULT. Benzbromarone is associated with an increased risk of hepatotoxicity, so liver function monitoring is recommended.

BD, twice daily; BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; NSAIDs, non-steroidal anti-inflammatory drugs; NZF, New Zealand Formulary; PPI, proton pump inhibitor. 1. Khanna D, Fitzgerald JD, Khanna PP, *et al*. Arthritis Care Res. 2012;64:1431–46; 2. Khanna D, Khanna PP, Fitzgerald JD, *et al*. Arthritis Care Res. 2012;64:1447–61; 3. Graf SW, Whittle SL, Wechalekar MD, *et al*. Int J Rheum Dis. 2015;18:341–51; 4. Richette P, Doherty M, Pascual E, *et al*. Ann Rheum Dis. 2017;76:29–42; 5. NZ Formulary. NZF v95. Available from: www.nzf.org.nz (Accessed May, 2020). 6. FitzGerald JD, Dalbeth N, Mikuls T *et al*. Arthritis Care & Research. 2020;72:744–60.