Submission for medicine reclassification for consideration by the Medicines Classification Committee

Introduction

Gout is the most common inflammatory arthritis[1] and it happens when monosodium urate crystals deposit in and around joints and in other tissues. Gout flares are caused by these crystals, presenting as acute inflammatory episodes that are recurrent and self-limiting. Urate lowering therapy is needed so that the crystals can dissolve. In New Zealand the target is < 0.36 mmol/L for most people and < 0.30 mmol/L where there are tophi[2]. Internationally gout is suboptimally treated[1].

Gout has long been under-treated in New Zealand in terms of prophylaxis[3]. Allopurinol, a xanthine oxidase inhibitor, is the main preventor for gout in New Zealand and by far the most commonly used internationally[1], but it needs to be started at a low dose and titrated to the appropriate level for the patient. The person needs to present to a prescriber for an allopurinol prescription every three months. If a person stops taking allopurinol they will need to restart low and titrate again, typically taking months to get to the right level. Stopping allopurinol or being on a suboptimal dose of allopurinol is likely to result in gout flares, with considerable burden for the sufferer, absenteeism from work, negative effects on lifestyle both for the individual and those around them, damage over time and (for some) hospital admissions. Poorly managed gout results in a moderate level of physical disability and a SF-36 physical functioning score similar to people aged 75 years or over in a much younger population[4].

NSAID use rather than urate-lowering therapy (ULT) has been called *"a poor and potentially dangerous stopgap"*. Māori and Pacific patients are more likely than other ethnicities to have repeated NSAIDs for gout attacks[3], despite Māori and Pacific being at increased harm from NSAIDs than other ethnicities, including increased hospital admissions for serious adverse effects[5].

To help people to reach the optimal dose and understand the need for long-term preventative therapy, pharmacy gout programmes are in place in parts of New Zealand, e.g. in Northland, Counties Manukau (primarily South Auckland), Whanganui, Porirua and Hawkes Bay. Some pharmacy gout programmes use standing orders to enable dose titration and continuation supply by the pharmacist. Standing orders have a burden to arrange and oversee, particularly where the GP workforce is stretched, or locums are

primarily used (e.g. areas of Northland). Reclassification will enable safe and appropriate supply without the burden of standing orders and will aid access for patients.

Many people who start allopurinol discontinue them at least temporarily. While reasons for this are multi-factorial, the need to arrange a doctor's prescription, including time off to see the doctor, is an important contributor for therapy gaps. Continuation supply is important to avoid gaps in therapy and therefore avoid gout flares. Avoiding gaps in allopurinol dosing also reduces the need for anti-inflammatories or other acute gout treatments, will reduce emergency department presentations, and will potentially reduce time off work and other activities for the individual.

This application seeks to support specially trained pharmacists to titrate allopurinol as per HealthPathways and to provide continuation supply to aid people with gout to get to the correct dose for them and to reduce barriers to access and reduce the number of therapy gaps and the need to restart titration. This will benefit patients with fewer gout attacks, reduce absenteeism or presenteeism, reduce loss of wages and reduce time missing family, social, sports and church life, and reduce the need for family members to take time off to look after the person with gout. Additionally, it will reduce the burden on pharmacists, GPs and programme managers on arranging and updating standing orders, and for GPs the burden of auditing them. With gout well-managed, the patient and GP can concentrate on other health concerns/prevention of other conditions.

At the 66th Medicines Classification Committee meeting on the 11th of May 2021[6], a reclassification of allopurinol was considered. The committee "agreed that the proposal could support addressing access issues to medical practices and improve continuity of care in remote areas", and that "there are favourable equity outcomes possible from this proposal". The committee had the following concerns:

- The risk of missing and/or undertreating the associated comorbidities of gout
- Duration for pharmacist follow-up with the patient before a follow-up with their doctor
- The absence of an electronic care plan that would allow management between community pharmacies and medical practice
- Processes around training and education for pharmacists.

The meeting minutes further states: "The Committee were supportive of this submission and agreed there is an unmet clinical need however acknowledged that a change in classification alone will have limited impact on improving health outcomes and equity.

The Committee discussed their understanding that reclassification can enable a pathway for policy changes and programmatic development, however holds reservations with the current proposal until the concerns identified are addressed.

The Committee concluded there should be engagement with the Pharmacy Council process for medicines reclassification as outlined in the guidance before a recommendation can be made.

Recommendation

The Committee is deferring the decision and referring this submission to the Pharmacy Council process."

The Pharmacy Council submitted a letter to the following MCC meeting stating[7]:

"The Pharmacy Council (Council) believes that pharmacists possess the base competencies to supply allopurinol as per the proposal in the application. However, we recommend that pharmacists be required to complete a formal training programme that focuses on patient assessment and point of care testing, supply guidelines, and patient advice."

However, the applicant to the original meeting (Dr Natalie Gauld) suggested waiting for evaluation from the redesigned gout programme at Counties Manukau before reconsidering the potential reclassification (personal communication, Dr Natalie Gauld).

Since then, the redesigned Counties Manukau programme was rolled out (2022) with bespoke software from Firecrest (also has INR-Online software) and standing orders for dose titration and continuation supply by the pharmacist for people in the programme. The evaluation was conducted using qualitative interviews, a survey of pharmacists and general practice and a quantitative evaluation. This found the programme was valued and had higher rates of therapy continuation compared with the Atlas of Healthcare Variation. However, it noted: *"Challenges with seeing doctors need to be addressed for long-term continuation on therapy, e.g. pharmacist continuation supply after the programme has been completed, ability to order a repeat prescription or telehealth options."*

The points raised at the 66th MCC meeting are all addressed in this application. There is a greater need than ever before to make allopurinol accessible given the burden of gout, increasing rates of gout, pressure on our health system where gout is a preventable reason for emergency department presentation and inpatient stay, challenges of seeing a GP in NZ, and evidence of pharmacy gout services helping patients.

Part A- Regulatory Context and Proposed Classification

1. International non-proprietary (INN) name of the medicine

Allopurinol

2. Proprietary names (if applicable)

Ipca-allopurinol is the only product currently funded and available in New Zealand. Many allopurinol brands have been registered in NZ over the years, with the earliest being Zyloprim and Z-300, then Progout.

3. Name and contact details of the company/ organisation/ individual requesting a reclassification

Contact details can be removed from the form prior to publication of the Medsafe website if requested.

Arthritis New Zealand Mateponapona Aotearoa
Green Cross Health
Dr Natalie Gauld ONZM DipPharm MPharm PhD FPS
Associate Professor Peter Gow ONZM MBChB FRACP, Rheumatologist

4. Dose form(s) and strength(s) for which a change is sort (if applicable)

Tablets 100 mg and 300 mg

5. Pack size, storage conditions and other qualifications (if applicable)

There is no pack size specified as the quantity will depend on the dose for an individual, and a maximum of three months' supply will be able to be provided. Allopurinol would be dispensed and labelled by the pharmacist with no specific non-prescription pack size as such.
Storage conditions (as per Ipca allopurinol datasheet): store below 25°C. Protect from moisture. Keep container tightly closed.

6. Indications for which change is sought (if applicable)

Prophylaxis of gout.
We have used the indication as per NZ Formulary rather than as per the data sheet.

From the datasheet, this would equate to: For the management of primary gout or secondary hyperuricaemia associated with chronic gout.

7. Present classification of the medicine

Prescription medicine.

8. Classification sought

Prescription medicine except when supplied for prophylaxis of gout to people who meet the clinical and eligibility criteria of an approved training programme, when provided by pharmacists who meet the requirements of the Pharmacy Council.

9. Classification status in other countries (especially Australia, UK, USA and Canada), and any justification for harmonisation

Prescription medicine in other countries.
The 2021 application for reclassification noted there was a Scottish Patient Group Direction for allopurinol. This no longer appears to be available, probably owing to the fact that many community pharmacists can now prescribe in the UK.

10. Extent of usage in New Zealand and elsewhere (e.g. sales volume) and dates of the original consent to distribute

The Medsafe product application details show Zyloprim 100 mg tablets were approved 31 December 1969.

Sales data is not available for NZ nor is it available for other countries. However, Atlas of Healthcare readily Variation data for New Zealand identified in 2019 that 209,000 people had gout and 120,000 were prescribed urate-lowering therapy[8]. In most cases this would be allopurinol.

With allopurinol available for over 50 years in NZ, and being first-line as gout prophylaxis, the experience is clearly very extensive in NZ alone. Internationally there have been over 50 years of experience also with allopurinol "by far the most commonly prescribed ULT", e.g. 95% of US NHANES self-reports of ULT therapy being allopurinol, 96% of ULT prescriptions in South Korea in 2011 were for allopurinol[1]. This medicine is extremely well-known.

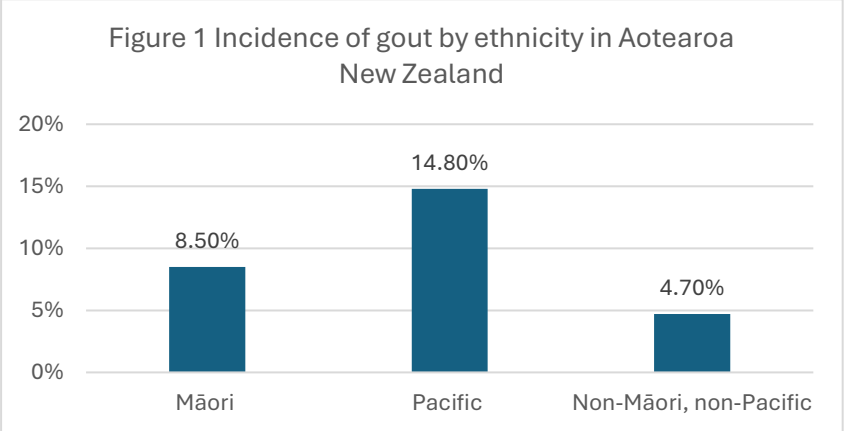
11. Local data or special considerations relating to New Zealand (if applicable)

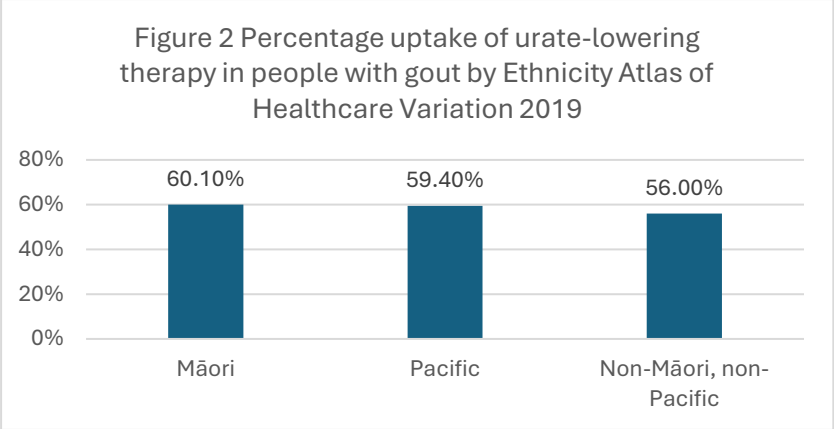
Burden of gout in Aotearoa New Zealand

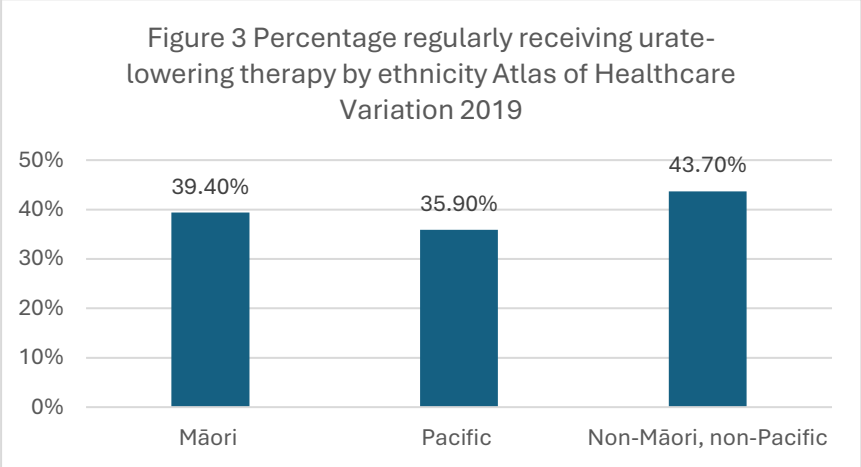
In a global burden of disease study Australasia had a prevalence of 1424 per 100,000, over twice the global prevalence[9]. However, New Zealand has particularly high rates with 5.7% of the adult population suffering from identified gout[10].

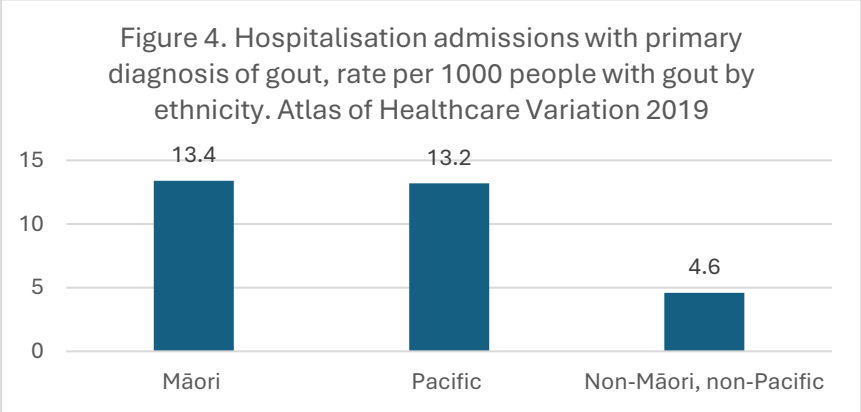
The Atlas of Healthcare Variation 2019[10] data shows that Māori and Pacific peoples are more likely to have gout than Non-Māori, non-Pacific (Figure 1). Of people with gout, Maori and Pacific people are more likely to be prescribed urate lowering therapy than non-Maori, non-Pacific (Figure 2), but less likely to be regularly receiving it (Figure 3, based on dispensing data). Of people with gout, Māori and Pacific are three times more likely to be hospitalised with it than non-Maori, non-Pacific (Figure 4). These numbers from administrative data are likely to be an undercount of perhaps 20% given some people will self-medicate for gout including borrowing others' medicines or buying medicines OTC[11] and some may not realise they have gout for some time[12].

Figure 1 Atlas of Variation Gout Incidence by Ethnicity 2019









The Atlas of Healthcare Variation shows that gout has varying prevalence around NZ, from 3.9-4.4% in Canterbury, Capital and Coast, and Nelson Marlborough to 7.7-9.1% in Counties Manukau, Northland and Tairawhiti.

In NZ, gout has higher prevalence in older age groups, but still affects an important 1.8% of people aged 20-44 years (for Māori 3.2% and Pacific peoples 7.2% in that age group). For those aged 45-64 years it affects 6.3% and for those 65 years and over it affects 13.1%. The rate of gout in males is about threefold higher than females at 9.0% versus 2.7%. In all cases the prevalence is higher in Maori and Pacific peoples than non-Maori, non-Pacific, with the highest prevalence in Pacific peoples aged 65 years or older (38.6% prevalence) and Maori 65 years or older (25.9%).

Serum urate concentrations are higher in Maori and Pacific patients[13, 14], and the impact of gout is higher in terms of pain, activity limitations, health-related quality of life and frequency of gout flares[13].

Urate-lowering therapy (ULT) in Aotearoa New Zealand

Most people using ULT in NZ are taking allopurinol. The Atlas of Healthcare Variation reports on ULT usage not allopurinol alone. While 60.7% of people 65 years and over have been prescribed ULT, this is lower in the younger age groups, 56.5% for those 45-64 years and 48.0% in those aged 20-44 years. Importantly, those regularly receiving urate-lowering therapy is far lower for those aged 20-44 years (18.7%) than the older age groups – 38.3% for those aged 45-64 years and 51.3% for those aged 65 years and over. **Many young people with gout are being started on allopurinol but not continuing on it.**

Reasons for not continuing on allopurinol are multi-factorial, including needing a good relationship, perceived stigma, lack of education, communication challenges and an expectation that they see the doctor when unwell/in pain rather than for preventative care[12]. Importantly, they include challenges accessing a doctor[14]. It is important that reasons for intentional non-adherence are addressed by prescribers and pharmacists[15], and the pharmacy gout programmes aim to do this.

BPAC states the following in their audit tool[16]:
"Allopurinol is the first-line urate-lowering medicine and initiation should be discussed with all patients with gout, as soon as a diagnosis has been established. The target for allopurinol treatment is a serum urate level < 0.36 mmol/L. The dose of allopurinol must be titrated to achieve the treatment target and serum urate testing should be performed at each dose adjustment. Once the patient has reached the treatment target, serum urate levels should ideally be checked at least once annually.
When allopurinol is initiated, "start low and go slow". A lower starting dose and lower dose increments are recommended in patients with renal impairment."

BPAC's 2021 two part guide to Managing Gout is available at:
https://bpac.org.nz/2021/docs/gout2021.pdf and is attached.

Pharmacy Gout Programmes in Aotearoa New Zealand

There are pharmacy gout programmes in NZ in Northland, Counties Manukau (South Auckland and rural), Midland, Hawkes Bay, Whanganui and Wellington. These are typically in a small number of pharmacies rather than the whole district. These have been developed to support people with gout including addressing concerns and knowledge gaps, support adherence and to aid appropriate dose titration. They are

varied. Some have standing orders to enable the pharmacists to titrate the allopurinol dose to the optimal level for the patient, and to ensure they do not run out, although this is burdensome to administer for the pharmacists, general practitioners and programme managers and delays or challenges arranging these has impacted on programme delivery. Some programmes have fingerprick point of care serum urate tests typically with the Benecheck meter. Some provide compliance packaging to all. Northland[17, 18], Whanganui[19] and Counties Manukau[14, 18] have had evaluations performed.

The continuation and expansion of these programmes show they are valued, and the evaluations show benefit. Having the reclassification will make it easier for all programmes to add dose titration and continuation supply if they do not already have these. It will reduce workload of standing orders being created for each area, being reviewed and updated locally and being signed and overseen by doctors.

The standing orders at Counties Manukau show the workability of the process and are used as a basis for this reclassification model. These were based on the Auckland HealthPathways for Gout and expert opinion (Associate Professor Peter Gow), and passed through committee review.

Software for the Pharmacy Gout Programmes

Bespoke software was developed by Firecrest (providers of INR-online) for the gout programme for Counties Manukau. It can be used in any pharmacy, at a cost, and has been used also in the Hawkes Bay pharmacy programme. It was developed to address the following needs of the gout programme: easy communication between the pharmacy and the GP, helping the patient to return for fingerprick SU tests and help them take their medicine, and to address challenges of understanding outcomes. This software has the following key features:
- Text or email a welcome to the programme email, motivational emails to back up what the pharmacist says, and reminders to come for the fingerprick SU test, including messages if the person is overdue for this test. These messages are personalised to the patient in name and greeting (e.g. Kia ora/Talofa lava), and have the pharmacy name on them.
- Email the doctor with SU results and change in allopurinol dose for each patient in real time
- A graph of the patient's SU results for them to see
- Reporting to allow evaluation of the service and of individual providers.

This software is useful but not essential, e.g. for continuation supply a pharmacist can email a doctor directly with the patient details.

12. Labelling or draft labelling for the proposed new presentation(s) (if applicable)

Not applicable, the medicine would be dispensed by the pharmacist and labelled specifically for the patient.

13. Proposed warning statements (if applicable)

There are no warning statements to be on packaging, see next section for discussion of contraindications and precautions.

Contraindications and precautions will be covered in the training and tools for supply.

14. Other products containing the same active ingredient(s) which would be affected by the proposed change

Only Ipca-allopurinol is currently funded by Pharmac. Any allopurinol brand that enters the NZ market in the future will be affected.

Part B- Clinical Context and Implications

"The management of gout is sub-optimal in New Zealand, and changes need to be made both in community awareness and in the delivery of healthcare..."[20] BPAC 2021

Gout is a painful debilitating condition with considerable impact on the patient and their whanau. It causes long-term damage and is associated with other health effects, e.g. cardiovascular diseases and stroke[21]. But gout attacks can be prevented. Allopurinol is the first-line agent but needs to start low and be titrated slowly to get to the optimal level. It also needs to be taken continuously. If stopped, it has to be restarted (with flare prophylaxis) and gradually titrated again.

Getting patients to the optimal level, adherence and continuation all need work in NZ. Widening access to allopurinol through specially trained pharmacists will support the gout pharmacy programmes to make them easier to implement and extend. Patients outside of the existing programme will have easy appropriate access to continuation supply to make it easier to keep taking the medication. This reclassification will immediately benefit the patients, their whanau, the health system and communities. It will prevent long-term damage from gout. It will be less work than standing orders for pharmacists, doctors and programme managers. Pharmacists have shown they can do this in other areas such as vaccination, COVID-19 antivirals, oseltamivir, trimethoprim for UTIs, and have recently been trusted to work collaboratively with nurses to treat patients with hepatitis C with antivirals, having shown themselves capable of testing for hepatitis C and working with the patient to help them get treated in another condition with perceived stigma.

Benefits

This reclassification has multiple benefits briefly summarised here and with further details in the sections below.

1. Making it easier for patients to be dose titrated and continued on therapy.
2. More patients will achieve the optimal dose and fewer will have gaps in therapy which will translate to very clear patient benefit – less pain (noting that gout is typically excruciating and very debilitating), less time off work and loss of income, less burden on family members (who may otherwise need to take time off work or school), less isolation, more participation in family, church, social and sporting life. Benefits are much wider than simply the individual with gout.
3. With gout managed, the general practice can concentrate on other health needs and preventative therapy.
4. Reducing the burden of standing orders which need to be developed in each location, reviewed and signed off by Health NZ, then signed and audited by either local GPs or a

person for the area. Pharmacists can use a national system and take responsibility for working within it as they do in so many other therapeutic areas.
5. Logically improved management will reduce presentations with gout to emergency departments, need for urgent appointments with the GP and hospitalisations. With a burdened primary and secondary care, this is an important benefit.
6. Good gout control will reduce long-term sequelae including tophi, joint damage and renal damage.

Risks will be managed as follows:

1. Pharmacists will undergo appropriate training which will be endorsed by the Pharmacy Council.
2. All gout patients where allopurinol is being provided or dose titrated by the pharmacist must have a consultation with their general practice at least once a year.
3. Only for gout management, no other indications.
4. Maximum 600 mg/day of allopurinol.
5. The patient will be initiated on allopurinol by a prescriber, not the community pharmacist.
6. The general practice is informed of any serum urate fingerprick test results and allopurinol dose changes.
7. The pharmacist and person with gout will share information to help understanding and motivation.
8. Pregnancy, breastfeeding and key interactions (e.g. azathioprine, mercaptopurine, didanosine, theophylline) will be excluded from pharmacist-supply. Training will cover these.

Titration

9. The patient must be on flare prophylaxis before the pharmacist titrates them, and the patient's GP/prescriber and patient in agreement that the pharmacist titrates them before they start titration – this will typically run under a pharmacy gout programme (as available in pockets around the country to provide funding for the pharmacist to perform this service). Further prophylaxis will need a doctor prescription.
10. Titration has a minimum age of 18 years and no maximum age.
11. eGFR must be at least 30 mL/min to start titration, measured no more than three months prior to dose titration starting.
12. Fingerprick serum urate point of care testing is advisable monthly if possible (noting the different programmes). Or serum urate at the lab is a less preferred option.

Continuation supply

13. Continuation supply is provided to any patient on allopurinol for gout who is on a stable dose and has not had a break of more than 5 consecutive days. If the break is

longer the person needs to be referred to the general practice as they are likely to need to start low and titrate again.

14. eGFR is required annually and needs to be at least 60 mL/min.
15. An annual Serum Urate is recommended.
16. Age 18-65 years.
17. Referral back to the GP for titration is required where the dose may be suboptimal – i.e. gout flares despite good adherence to dosing. This may be guided by serum urate. However, allopurinol can still be provided in this case.
18. Up to three months' supply is provided. This will be dispensed and labelled as usual and the information will be added to the patient's electronic record as for other dispensings.
19. Patients can get continuation supply without being in a pharmacy gout programme.
20. The same dose is provided as the dose the patient was originally on.
21. If having two or more gout flares per year despite good adherence, refer back to the doctor (can supply in the meantime).

Addressing previous MCC minuted points

In 2021 the MCC saw benefit in the reclassification but outlined several points to address[6]:

- The risk of missing and/or undertreating the associated comorbidities of gout.
- Duration for pharmacist follow-up with the patient before a follow-up with their doctor.
- The absence of an electronic care plan that would allow management between community pharmacies and medical practice.
- Processes around training and education for pharmacists.

The response to this is as follows:

1. *The risk of missing and/or undertreating the associated comorbidities of gout*

- People with gout are at risk of other medical conditions and this is well known to pharmacists. The pharmacist will ensure that they have seen their GP at least once a year when supplying the allopurinol, and the pharmacists' training will discuss risk for other health priority conditions such as diabetes and heart disease.
- Importantly, by getting the gout under control through appropriate dose titration and information sharing, and then keeping it under control through continuation supply between doctor visits, the doctor's discussion with the patient can move beyond gout to preventative health.
- If the patient uses allopurinol appropriately and gets into the habit of taking allopurinol daily long-term, they will also get confidence in the medical system and medicines for helping with other conditions.

2. *Duration for pharmacist follow-up with the patient before a follow-up with their doctor*

- In all cases the patient needs to have a consultation at their general practice at least once a year.
- When a patient starts on allopurinol through the general practice, then works with the pharmacist on titration this will be a collaborative exercise. The prescriber will be prescribing allopurinol for the patient to start on, and flare prophylaxis to cover the titration. It is likely that people will need a second prescription for flare prophylaxis at 3 months so will see the doctor then. If the pharmacist is titrating the patient's dose, the pharmacist will inform the doctor of allopurinol dose changes and finger prick serum urate tests (if done). This communication can be done through software, automated, or manually by the pharmacist sending the GP an email.

3. *The absence of an electronic care plan that would allow management between community pharmacies and medical practice*

- Pharmacists can only do the titration if the patient's prescriber of allopurinol is in agreement. Based on the experience of Dr Natalie Gauld at Counties Manukau, GPs were happy for pharmacists to help titrate given the workload and challenges for patients to reach the optimal dose. This may be done in multiple ways: the GP writes on the prescription that the pharmacist is to do the dose titration; the pharmacist checks with the general practice for permission for a specific patient, or the general practice or individual prescriber has a blanket written agreement with the pharmacy to do dose titration for anyone new starting allopurinol for gout and the pharmacy simply advises the doctor by email when a patient starts this. The pharmacist advises the doctor of any allopurinol dose changes and fingerprick SU test results (if done, not all models require this but most are using it).
- This system has worked very well at Counties Manukau as a useful collaborative exercise. At Counties Manukau and Hawkes Bay there is a software system from Firecrest which provides automation of communication to the GP. However, an email can be sent instead if desired.

4. *Processes around training and education for pharmacy*

- This is straightforward. The Pharmacy Council has confirmed that training would be needed, and this was intended in the original application.
- A pharmacy gout training is available from the Pharmaceutical Society of NZ. Gout training is also available specific to different programmes around the country. The Pharmacy Council can endorse appropriate training for the pharmacist to undertake. These would all need to include an understanding of gout, cultural competency related to gout management, perceived stigma of gout, relationship building, working with patients on gout, adherence, the usual information about the drug ie indications, dosing, contraindications, precautions, interactions and adverse effects, point of care serum urate testing, HealthPathways for gout, as well as the requirements specific to

the reclassification such as what is required to undertake titration versus continuation supply.

- It is recommended that any provider of the training has input from a rheumatologist, a rheumatology nurse, a pharmacist experienced in running the programme and providing education and Arthritis New Zealand, as happened at Counties Manukau, for example.
- The reclassification of the hepatitis C treatment is an excellent example of how training had input from a liver specialist, hepatology nurses, a programme manager and a pharmacist experienced in managing the programme and others, and was well-aligned to national HealthPathways to ensure high quality including optimising the patient experience and helping overcome perceived stigma, and using the learnings from earlier hepatitis C pharmacy and outreach test and treat programmes.

Evidence for pharmacy's role.

The Northland model published paper[17] found: "Collaboration between prescribers, community pharmacists and support workers reduced barriers to initiating prevention and long-term urate-lowering treatment and urate testing in this high-needs gout population."

The Counties Manukau gout programme redesign evaluation[14] found: *"Early data from the Gout Busters programme found high Maaori and Pasifika participation in the programme and better long-term adherence to allopurinol than in the Atlas of Variation, including for these groups, albeit limited by small numbers…. Challenges with seeing doctors need to be addressed for long-term continuation on therapy, e.g. pharmacist continuation supply after the programme has been completed, ability to order a repeat prescription or telehealth options."*

The Synergia report of the Counties Manukau earlier Own My Gout Programme and the Northland programme[18] found: *"The value chain created by the programmes enables the assumption that the programmes have contributed to the identified benefits for patients and communities. The programmes have also contributed to the broader health system by promoting integrated teamwork, contributing to health equity, reducing the burden of gout on the sector through a management focus, and providing good value for the resource required locally. Both programmes have continued to develop iteratively and have identified improvements to enhance or sustain programme benefits."* It also noted the need for easy access to medicines.

The Whanganui Stop Gout Programme[19] found: "*The early adopters of this programme demonstrated that the GSP is effective in improving the quality of life of Māori with gout. The challenge for future collaborative LTC programmes is being able to roll-out a programme with buy-in from all providers. Getting the implementation right is the key to programme reach and success. This could be supported by sustainable funding for implementation, national activities to build awareness, and integrated IT systems that better enable information sharing and collaboration."*

There is no need for further evaluations. We now need a national mechanism to enable pharmacists to support people with gout to access allopurinol appropriately – within the gout pharmacy programmes with titration and continuation supply, or outside of the programmes with continuation supply.

15. Indications and dose

- *What is the medicine indicated for, and for which indication(s) is the reclassification application for?*
- *What is the evidence that the proposed indication is an OTC indication ie, that the diagnosis and treatment can be understood by the consumer; that the risks of inappropriate treatment can be minimised?*
- *What is the treatment population for the indication (age, gender etc.)?*
- *What is the dose and dose frequency of the medicine for this indication?*

What is the medicine indicated for, and for which indication(s) is the reclassification application for?

The only indication for the reclassification is prophylaxis of gout. This is the main use of allopurinol. It has other uses which will not be treated without prescription. The data sheet lists these as:

• uric acid nephropathy.

• recurrent uric acid stone formation.

• certain enzyme disorders or blood disorders which lead to overproduction of urate (e.g. Lesch-Nyhan syndrome; haemolytic anaemia).

• hyperuricaemia associated with malignancy and cytotoxic therapy which result in a high cell turnover rate.

• The prevention and treatment of calcium oxalate/phosphate renal stones in the presence of high uric acid levels of the blood and/or urine.

What is the evidence that the proposed indication is an OTC indication, ie that the diagnosis and treatment can be understood by the consumer; that the risks of inappropriate treatment can be minimised?

This reclassification is for pharmacists who have successfully completed additional training. They have already proven themselves able to manage allopurinol under standing orders, e.g. in Counties Manukau. This is not an OTC reliant on the health care consumer self-diagnosing, self-selecting and self-managing. The patient has already been diagnosed by the doctor who has assessed the patient and initiated allopurinol. The pharmacist is dose titrating effectively as per HealthPathways and will refer anyone with red flags. The pharmacist does not diagnose in this case. The pharmacist will help ensure the consumer has good understanding of gout and the treatment. Risks of inappropriate treatment are aided by clear guidelines, pharmacist

training and the collaborative general practice-pharmacist arrangement. The pharmacist will ensure flare prophylaxis has been prescribed before titrating the dose.

What is the treatment population for the indication (age, gender, etc)?
There is a minimum age of 18 years and no maximum age for titration and a maximum age of 65 years for continuation supply outside of the pharmacy gout programme.
All patients must have an eGFR > 30mL/min for dose titration and > 60 mL/min for continuation supply. The eGFR must be taken no more than three months before starting dose titration and be within 12 months for continuation supply.
About three times as many males as females will likely need this service given current prevalence of gout.
We expect dose titration will be in all ages but most commonly in those who are young who have initiated on allopurinol, or been restarted on allopurinol by the doctor or other prescriber.
We expect continuation supply to be used almost exclusively in people under 65 years, and most often in people who are not taking other long-term medication. Those who are older people and/or on multiple medicines with multiple comorbidities will be regularly seeing their doctor and regularly getting prescriptions. We do not see these people will have a need for continuation supply of allopurinol in that environment. The young working age people with allopurinol as their only long-term medication will be the ones who will find it hardest to get to the doctor every three months for a condition that is not a bother at that time. They will still need an annual visit to the doctor.
All of the population the pharmacy will help will have already been prescribed allopurinol before.

What is the dose and dose frequency of the medicine for this indication?
This dosing information is drawn from the NZ Formulary and is in line with HealthPathways:
Indication for the reclassification: Prophylaxis of gout
Dosage: Adult initially 100 mg once daily (but see Renal impairment above), increasing by 100 mg every four weeks, if tolerated, until target serum urate is reached (<0.36 mmol/L); usual maintenance dose 100–600 mg daily; maintenance dose of 700–900 mg daily may be required in severe conditions.

The datasheet has differing dosage information*:
The average daily dose is 2-10 mg/kg bodyweight, or 100mg to 200mg for mild conditions, 300mg to 600mg daily for moderately severe conditions and 700mg to 900mg for severe conditions.
Allopurinol may increase the frequency of acute attacks during the first few months of therapy; it is therefore recommended that low doses be given initially and slowly increased, and that anti-inflammatory agents or colchicine should be given

concomitantly during this period as prophylactic cover. In patients with good renal function, doses of 100mg should be given and increased by 50mg to 100mg at weekly intervals until serum urate levels of 0.6 mg per ml are achieved.

*The NZ Formulary and HealthPathways information will be used for the training and other information, NOT the datasheet. This is in line with currently used Standing Orders and appropriate for New Zealand.

16. Presentation

- *What is the proposed dose form and strength of the medicine to be reclassified? Is this the same for all indications?*
- *What disposal considerations need to be made for the medicine?*
- *How practical and easy to use is the proposed presentation?*

Tablets 100 mg and 300 mg
The disposal considerations are no different from if the medicine was dispensed pursuant to a prescription. It is hoped that the tablets will be taken and not needing to be disposed of.
The tablets are very easy to take. They may be provided loose in bottles or in blister packs also known as compliance packs. People use these packs all the time.

17. Consumer benefits

- *What is the history of this medicine's use for the proposed indication(s) ie, number of users; number of countries used in?*
- *To what extent is this medicine used for the proposed indication(s) ie, duration of use; frequency of use?*
- *What is the evidence that improved access is beneficial for the individual?*
- *What is the evidence of improved consumer involvement in their health?*
- *What are the benefits from a consumer viewpoint?*

NZ data shows that gout causes significant disability, pain, inability to work, shame and embarrassment (or "*whakama*"), isolation from social and family activities, not playing sport or doing physical activities with their children, inability to drive, and dependence on family members who may have to miss work or school to help the person. This dependence can include toileting, washing and providing food and drink. Loss of income can be significant. In some cases people can be bedridden for some time[12, 14, 22, 23], or hospitalised[3].

Additional to this, a paper published in JAMA in 2022 found that a gout flare was associated with statistically significant increased risk of a cardiovascular event in the following 60 days (adjusted odds radio 1.93) in a nested case-control study of patients[21]. A causal link was considered *"eminently reasonable"* based on human and animal studies[24]. Similarly, venous thromboembolism incidence is significantly higher following a gout flare with a 2.31 adjusted incidence rate ratio in the first 30 days after gout flare versus the baseline period[25].

Urate lowering therapy (ULT) is recommended to prevent gout flares.
Access barriers to ULT and its continuation include: not realising they have gout, stigma of gout, communication difficulties, time off work, difficulty seeing a doctor (e.g. service opening hours, affordability, geographic location, unavailability of doctors) and insufficient knowledge about the need for ULT and gout itself[12, 14, 19, 22]. Intentional non-adherence is common with many reasons[15] which will be addressed with education by the specially trained pharmacists as per the current pharmacy programmes.

What are the benefits from a consumer viewpoint?

Reducing access barriers to ULT through continuation supply will mean more people will stay on allopurinol without a break. The benefits of this logically include:

- Reduced frequency of gout flares.
- Reduced absenteeism and presenteeism at work, and reduced loss of wages.
- Being able to continue to participate in sports, including the cardiovascular benefits of this.
- Being able to continue to participate in family events, community work, social events, church events.
- Avoiding feeling shame or embarrassment from having a gout attack.
- Less need for NSAIDs and therefore less risk of adverse effects (note: Māori and Pacific at higher risk of adverse events with NSAIDs[5]).
- Less need for urgent after hours care to address gout issues (and therefore less cost).
- Less need for long waits to treat a gout flare at urgent after hours care or the emergency department.
- With gout under control, less likelihood of needing hospitalisation for gout.
- With gout under control, less likelihood of long-term damage to joints or kidneys.
- Less need for family to care for the person with an acute gout flare, taking time off work or school to do this.
- Able to participate fully in family life, running around with Tamariki and mokopuna.
- Saving time from having to arrange an appointment with the doctor every three months.

- Convenience of getting allopurinol at a time that suits with no appointment needed.
- Getting additional education and understanding.

Supporting pharmacies to do dose titration has the following benefits for patients:
- Getting to the optimal dose of allopurinol.
- Reducing gout flares – and all the attendant concerns listed above.
- Getting gout under control means other health issues can come to the fore when seeing the doctor.
- Getting gout under control will give patients confidence in how medicine works and is likely to help them understand the importance of adherence and belief in medicine if other conditions develop.

What is the history of this medicine's use for the proposed indications ie number of users, number of countries used in?
Allopurinol will have been used by many tens of millions of people all over the world given that an estimated 55.8 million people globally had gout in 2020[9] and this medicine has been first line prophylaxis of gout for decades, and should be available in every country in the world.

To what extent is this medicine used for the proposed indication, ie duration of use; frequency of use?
The medicine is used daily long-term as prophylaxis for gout. Most people will take it until the end of their lifetime.

What is the evidence that improved access is beneficial for the individual?
We have evidence of harm from the current situation with many people in NZ not taking this medicine long-term, particularly in the younger age groups. The poorly managed gout causes many problems as listed in the first paragraph in this section. Gout programmes in NZ in pharmacies have been associated with positive outcomes in terms of achieving target serum urate in individuals[14, 17, 19] and higher than expected rates of continuation of allopurinol therapy one year on[14]. As an example of the benefit for an individual, in the Counties Manukau gout programme, one male of Pacific heritage in his 20s had never worked, having had gout since he was in his teens. After doing the gout programme with the pharmacy, he was able to get a job for the first time. These programmes vary, in some the pharmacies have been paid to do finger prick serum urate testing, provide education and help titrate doses of allopurinol and provide continuation supply.

This reclassification will support the pharmacy programmes or enable allopurinol continuation making getting allopurinol much easier. This will help overcome the barrier of having to arrange a prescription from the doctor, typically having to go in person and take half a day off work. Most pharmacies are open extended hours, they

do not need an appointment, and you do not need to be enrolled so can attend one handy to where you are at the time.

The additional education pharmacists will do to prepare for this work will ensure they are well-equipped to provide advice to people with gout collecting allopurinol about the need for long-term treatment and how it works, to encourage them to get to the right dose for them and to stay on it.

What is the evidence of improved consumer involvement in their health?
The whole point of this is to make it easier for consumers to access this medicine so they do not have therapy gaps. If they resolve their gout they may be more interested in sorting other health areas. We are not aware of evidence collected to specifically answer this question for a reclassification.

18. Contraindications and precautions

- *What are the contraindications for the medicine and how easy are they to identify and prevent?*
- *What are the precautions for this medicine and how easy are these to understand?*
- *Does the medicine have a low therapeutic index?*
- *What class effects need to be considered and what are the risks?*
- *What are the risks of the medicine being used in an OTC environment?*
- *What other drug interactions need to be considered?*
- *What food and/ or drink interactions need to be considered?*
- *Are there any other restrictions when taking the medicine ie, driving restrictions or operating machinery?*
- *Are there any special populations where exposure to the medicine needs to be restricted?*

Warning statements from the NZ formulary include:
Contraindication: not for treatment of acute gout or asymptomatic hyperuricaemia.
Cautions: initiation can precipitate gout flare—flare prophylaxis with an NSAID or colchicine should be used and continued for at least one month after hyperuricaemia has been corrected (usually for the first 3-6 months); consider testing for HLA-B*58:01 allele in individuals of Han Chinese or Thai origin (avoid unless no alternative—risk of severe and potentially life threatening cutaneous adverse reactions in presence of HLA-B*58:01 allele); ensure adequate fluid intake (2–3 litres/day) .
Renal impairment: caution in impairment, risk of accumulation and increased risk of hypersensitivity reactions.
eGFR 30–60 mL/min/1.73m^2, initially 50 mg once daily; increase dose by 50 mg every 4 weeks, if tolerated, until target serum urate is reached (<0.36 mmol/L).

eGFR less than 30 mL/min/1.73m^2, initially 50 mg every second day; increase dose by 50 mg every 4 weeks, if tolerated, until target serum urate is reached (<0.36 mmol/L).
Pregnancy – limited human data.
Breast-feeding – limited human data, potential toxicity.

These contraindications and precautions will be covered in the training and tools for supply. Pharmacists will not be initiating any patients so the doctor will already have considered contraindications and precautions. The key consideration will be renal impairment, which can change over time. An eGFR will need to be available within 3 months before a pharmacist does dose titration. An annual eGFR will be needed after this. Pharmacists have already been working with eGFR in pharmacy programmes in which they titrate the dose, e.g. the Counties Manukau Gout Busters, and with the supply of COVID antivirals. This will be available from the electronic health record the pharmacist has access to in Auckland and Northland (Testsafe) and in the South Island (HealthOne).

As with the standing orders used in Counties Manukau, the eGFR will need to be >30 mL/min for pharmacist supply to take place.

These standing orders, Auckland Health Pathway and NZ Formulary have the following dose titration: start with 100 mg/day and increase by 100 mg approximately monthly for those with an eGFR>60 mL/min; and start with 50 mg/day and increase by 50 mg approximately monthly for those with an eGFR 30-60 mL/min.
Flare prophylaxis must be prescribed by the GP during initiation and dose titration
Anyone who is pregnant or breastfeeding cannot be treated with allopurinol by the pharmacist.
Known allopurinol allergy eg anaphylaxis or previous rash with allopurinol cannot be managed with standing orders.
Maximum daily dose of 600 mg for pharmacist provision
Minimum age 18 years old
Taking febuxostat and allopurinol cannot be managed by the pharmacist but managed through the doctor.

Note: it is important that allopurinol is continued for all patients. Where continuation supply is not possible because of above criteria, emergency supply provision could be used for up to 72 hours and the person referred back to the GP. Emergency supply is not ideal because 3 days' supply does not give much time to get into the doctor and will be relatively expensive for a small number of tablets when paying for the pharmacist's time.

19. Undesirable effects

- *What are the known undesirable effects and the frequencies of these? Do these vary for special populations?*
- *What are the risks and consequences of known undesirable effects?*
- *Are there any significant safety concerns for the medicine under review?*
- *Have there ever been any withdrawals of the medicine or other regulatory actions taken for safety reasons (during a time period or in a specific jurisdiction)?*
- *Are there any withdrawal effects following cessation of use of the medicine?*

BPAC states that "Adverse effects of allopurinol are relatively uncommon"[26]
BPAC further notes as follows:
Adverse effects include gastrointestinal symptoms. Hypersensitivity reactions can occur e.g. drug rash with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome. DRESS most often occurs in the first few weeks to months of starting therapy and has a lower risk with starting at a low dose and gradually titrating as the pharmacist can support to happen. The pharmacist will be trained on adverse events and can advise to seek prompt advice if a rash is seen. Risk factors for DRESS include renal impairment, elevated starting dose relative to renal function, use of diuretics and having the HLA-B*5801 allele – often present in those of Korean, Thai or Han Chinese descent. Genetic testing for this allele is available. The doctor will be initiating therapy not the pharmacist.

The datasheet (attached) has the full list of adverse effects. There are no frequencies for this, apart from noting rash in 10% of patients, and as mentioned, this may be a significant adverse reaction.

Allopurinol has been on the market for decades, used by many people. It is well-known and generally well-tolerated.

SMARS (Suspected Medicine Adverse Reaction Search Results) data is provided from 1/1/2000 t0 31/5/2024. This included 42 cases of DRESS and 12 of Stevens Johnson syndrome.

The adverse effects section of the NZ Formulary is as follows:
Rash (see Hypersensitivity syndrome below); less commonly nausea, vomiting, abdominal pain; rarely malaise, headache, vertigo, drowsiness, visual and taste disturbances, hypertension, alopecia, hepatotoxicity, paraesthesia, neuropathy, gynaecomastia, blood disorders (including leucopenia, thrombocytopenia, haemolytic anaemia, aplastic anaemia), severe cutaneous adverse reactions (SCARs, such as Drug

Reactions with Eosinophilia and Systemic Symptoms (DRESS)), hypersensitivity reactions (including fever, arthralgia, leucopenia, and also skin reactions—see Hypersensitivity syndrome below)

Hypersensitivity syndrome

Hypersensitivity syndrome occurs rarely, but may be fatal, and includes skin reactions, exfoliation, fever, lymphadenopathy, arthralgia, eosinophilia, vasculitis, hepatitis, renal impairment, and very rarely seizures. If hypersensitivity occurs, allopurinol should be withdrawn immediately and permanently; when it is being used for gout consider consultation with a rheumatologist.

Rash is a common adverse reaction with allopurinol; it may occur at any time during treatment but risk is greatest in the first 2 months. Skin reactions (including rash) may occur as part of a generalised hypersensitivity reaction and in more severe cases can progress to Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms)—see Severe Cutaneous Adverse Reactions (SCARs).

Patients should inform their doctor if a rash occurs, and therapy should be immediately withdrawn. If the rash is mild, allopurinol may be re-introduced cautiously at a low dose and gradually increased but discontinue promptly if the rash recurs.

Higher starting doses, rapid titration, and renal impairment increase risk of hypersensitivity reactions; ACE inhibitors and thiazide diuretics may also increase risk. See Readdressing the risk of DRESS with cautious titration Prescriber Update, September 2022 and SafeRx bulletin: Allopurinol—Safe Prescribing for more information.

It is the doctor's decision to initiate therapy. The pharmacist will be informed about adverse effects during the training and will look out for any and manage as appropriate if they occur. The doctor and pharmacist need to warn the patient of rare but important effects and to advise of any rash promptly.

There are no significant safety concerns with the medicine under review. It has not been withdrawn from markets that we are aware of, and remains first-line for gout prophylaxis.

Allopurinol does not cause withdrawal effects when discontinued. The serum urate is

20. Overdose

- *Is there a potential for overdose of the medicine?*
- *What are the consequences of overdose of the medicine?*
- *Are there any reports of overdose of the medicine?*

The datasheet states the following under the heading overdose:
Symptoms: Nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20g of allopurinol. Ingestion of larger doses have been reported without adverse effects. Treatment: The patient should be monitored and receive normal supportive measures and should be adequately hydrated to maintain urinary excretion of allopurinol and its metabolites. Concomitant medication may affect the effects noted. Haemodialysis may be used if necessary.

SMARS data reports 1 episode of intentional overdose since 2000.

There is no greater risk of overdose than the current risk with allopurinol prescribed.

21. Medication errors and abuse/ misuse potential

- *Would reclassification affect the risk of unnecessary use?*
- *Should the medicine be provided with necessary tools to allow correct dosing eg, liquids supplied with a measuring device?*
- *What are the reported medication errors post-market?*
- *What are the reported cases of abuse/misuse/accidental overdose?*
- *How would reclassification affect import considerations?*
- *What is the addiction potential of the medicine?*

Errors are no more likely than with use on prescription.

SMARS data reports 12 medication errors since 2000. This is minimal for a prescription medicine so widely used. No accidental overdose is reported in this data.

There will not be unnecessary use, the person has been diagnosed with gout and a prescriber has considered allopurinol is needed. People with gout need this medication long-term. The problem is always underuse not overuse.

The tablets are taken once a day, the directions will be clear on the label.

The medication will remain a prescription medicine for the purposes of importation so there is no risk.

This medicine is not addictive nor abused or misused.

22. Communal harm and/or benefit

- *What are the possibilities of community harm resulting from wider use of the medicine in question (e.g., the development of antibiotic resistance in bacteria or increased immunisation rates)?*
- *What are the possibilities of community benefit resulting from wider use of the medicine in question (e.g., greater herd immunity as a result of improved access to a communicable disease vaccine)?*

There is no community harm from this provision of allopurinol.

The community benefits include:

- reduced hospitalisation from gout is a benefit to all given hospitals are so often under pressure.

- having less need for urgent doctors' visits for acute gout flares is a benefit to all who may need to see the doctor given how difficult it is to get to see them.

- having more participation in sports, community life, church, social events is important to the cohesion of a community.

- not requiring time off work every three months to see the doctor for a prescription or not requiring extensive time off for repeated gout attacks is a benefit to the workplace, other workers and the family income.

- avoiding the agony of gout makes for a happier family and community.

23. Integrated benefit-risk statement

- *A summary of the reclassification benefits*
- *A summary of the reclassification risk of harm*
- *A summary of the need for the medicine at the classification proposed*
- *Precedent – how are other medicines in the same class classified?*

Benefits in short

- Making it easier for patients to be dose titrated and continued on therapy.
- More patients will achieve the optimal dose and fewer will have gaps in therapy which will translate to very clear patient benefit – less pain (noting that gout is typically excruciating and very debilitating), less time off work and loss of income, less burden on family members (who may otherwise need to take time off work or school), less isolation, more participation in family, church, social and sporting life. Benefits are much wider than simply the individual with gout.
- With gout managed, the general practice can concentrate on other health needs and preventative therapy.

- Reducing the burden of standing orders which need to be developed in each location, reviewed and signed off by Health NZ, then signed and audited by either local GPs or a person for the area. Pharmacists can use a national system and take responsibility for working within it as they do in so many other therapeutic areas.
- Logically improved management will reduce presentations with gout to emergency departments, need for urgent appointments with the GP and hospitalisations. With a burdened primary and secondary care, this is an important benefit.
- Good gout control will reduce long-term sequelae including tophi, joint damage and renal damage.

Risks of harm key points

- Patient needs to see the doctor regularly because at risk of comorbidities – the pharmacist is required to ensure annual visits
- Adverse effects listed above – these will be no more likely under this model in which the doctor starts the medicine, and sees the patient at least annually. The pharmacist has training.
- Patients with many comorbidities and polypharmacy could get allopurinol from the pharmacy and the doctor not know – these people will be regularly attending the doctor and getting prescriptions and will not need continuation supply outside of a pharmacy programme of titration (which the doctor agrees to). Almost all users of the continuation supply will be only using allopurinol long term and seeing the general practice annually.
- Interactions – no more likely than with prescribing. Pharmacists will have training.
- The general practice is not informed – this risk is managed by the requirement for the pharmacist to share allopurinol dose titration information and continuation supply. Software could enable this but communication does not need it to happen when it is a requirement as in this instance.
- Pharmacist won't know eGFR or Serum Urate results – the pharmacist needs to know this for allopurinol supply. The majority of NZ – Auckland, Northland, South Island have Testsafe or HealthOne. In other areas there can be other arrangements, e.g. Hawkes Bay where pharmacists already do this and access information through the Clinical Portal. If they don't have access, they cannot supply.
- Risk mitigation with a screening/documentation tool and mandatory training plus safeguards mentioned above, eg ages, eGFR frequency and minimum levels, ensures that this model has good safety. It has been used already with standing orders and has worked well.

Need for the medicine reclassification

This is clear – patients are having poorly managed gout when they have not got to an optimised dose or have breaks in therapy. We urgently need to solve this problem through supporting patients to get to the right dose, know what they need to about their medicine, discuss concerns about their medicine and be able to access it safely and conveniently to help them stay on it. Please do not delay.

Precedent

Patients can repeatedly use OTC NSAIDs for their gout (a very poor practice with risk) or borrow medicines, a very unsafe practice. Allopurinol reclassification in the model proposed is beneficial with mitigated risk. We also have the current precedent of management as per standing orders as in Counties Manukau Health.

24. Risk mitigating strategies

- *Are there any risk mitigation strategies required? If so, what risk mitigation strategies are required e.g., healthcare professional education; integration of care; consumer information to be provided etc?*
- *What is the evidence that these proposed risk mitigation strategies would be effective?*
- *What post-market surveillance activities would be carried out?*
- *Is the proposed reclassification supported by professional bodies?*

Risks will be managed as follows:

1. Pharmacists will undergo appropriate training which will be endorsed by the Pharmacy Council.
2. All gout patients where allopurinol is being provided or dose titrated by the pharmacist must have a consultation with their general practice at least once a year.
3. Only for gout management, no other indications.
4. Maximum 600 mg/day of allopurinol.
5. The patient will be initiated on allopurinol by a prescriber, not the community pharmacist.
6. The general practice is informed of any serum urate fingerprick test results and allopurinol dose changes.
7. The pharmacist and person with gout will share information to help understanding and motivation.
8. Pregnancy, breastfeeding and key interactions (e.g. azathioprine, mercaptopurine, didanosine, theophylline) will be excluded from pharmacist-supply. Training will cover these.

Titration

9. The patient must be on flare prophylaxis before the pharmacist titrates them, and the patient's GP/prescriber and patient in agreement that the pharmacist titrates them before they start titration – this will typically run under a pharmacy gout programme (as available in pockets around the country to provide funding for the pharmacist to perform this service). Further prophylaxis will need a doctor prescription.
10. Titration has a minimum age of 18 years and no maximum age.

11. eGFR must be at least 30 mL/min to start titration, measured no more than three months prior to dose titration starting.
12. Fingerprick serum urate point of care testing is advisable monthly if possible (noting the different programmes). Or serum urate at the lab is a less preferred option.

Continuation supply

13. Continuation supply is provided to any patient on allopurinol for gout who is on a stable dose and has not had a break of more than 5 consecutive days. If the break is longer the person needs to be referred to the general practice as they are likely to need to start low and titrate again.
14. eGFR is required annually and needs to be at least 60 mL/min.
15. An annual Serum Urate is recommended.
16. Age 18-65 years.
17. Referral back to the GP for titration is required where the dose may be suboptimal – i.e. gout flares despite good adherence to dosing. This may be guided by serum urate. However, allopurinol can still be provided in this case.
18. Up to three months' supply is provided. This will be dispensed and labelled as usual and the information will be added to the patient's electronic record as for other dispensings.
19. Patients can get continuation supply without being in a pharmacy gout programme.
20. The same dose is provided as the dose the patient was originally on.
21. If having two or more gout flares per year despite good adherence, refer back to the doctor (can supply in the meantime).

No post-market surveillance activities will be carried out.

Professional bodies and many individuals including GPs, pharmacists, gout programme managers and rheumatologists have been consulted and are encouraged to write in themselves.

Conclusion

A brief summary of the purpose of the submission and any concluding remarks

This reclassification application has been submitted by Arthritis New Zealand Mateponapona Aotearoa, Green Cross Health, Dr Natalie Gauld (pharmacist specialising in access to medicines) and Associate Professor Peter Gow (rheumatologist). It has been developing over several years, and has been well-informed by an understanding of the

challenges of people with gout in New Zealand, and pharmacy programmes here. The input of many people and organisations involved in gout has been greatly appreciated.

The model is for the doctor or other prescriber to initiate allopurinol and specially trained pharmacists to titrate (in collaboration with the general practice) allopurinol. It also allows for continuation supply for anyone on allopurinol that meets set criteria. This will help people get to the appropriate dose and then stay on medication. We expect this to benefit patients, their whanau, the community and the health system. There is a potential to reduce long-term harm and hospitalisations.

Allopurinol is generally well-tolerated and the model provides considerable safety. Communication with general practice is an important part of the model and so is a visit at least annually to general practice for anyone getting continuation supply.

The immediate benefit of this is to reduce the burden of standing orders, help the existing pharmacy gout programmes work as well as possible for patient benefit and help reduce people running out of tablets and stopping even temporarily then having to restart.

The Pharmacy Council would endorse training as is appropriate.

References

1. Dehlin, M., et al., *Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors*. Nature Reviews Rheumatology, 2020.**16**(7):380-390.
2. *Gout*. Auckland Region HealthPathways 2020 14 Jan 2021]; Available from: https://aucklandregion.communityhealthpathways.org/18727.htm.
3. Dalbeth, N., et al., *Gout in Aotearoa New Zealand: The equity crisis continues in plain sight*. NZ Med J, 2018.**131**(1485):8-12.
4. Kim, S.Y. and H.K. Choi, *Gout and quality of life*. J Rheumatol, 2009.**36**(5):865-8.
5. Tomlin, A., et al., *Ethnic inequality in non-steroidal anti-inflammatory drug-associated harm in New Zealand: A national population-based cohort study*. Pharmacoepidemiol Drug Saf, 2020.**29**(8):881-889.
6. Medsafe, *Minutes of the 66th meeting of the Medicines Classification Committee held in Wellington on 11 May 2021 at 9:39 am*. 2021, Medsafe:Wellington.
7. Pead, M.A. *Pharmacy Council submission on the Reclassification of Allopurinol 66th meeting on 11 May 2021*. 2021 14 Aug 2024]; Available from: https://medsafe.govt.nz/profs/class/Agendas/Agen67/Allopurinol.pdf.
8. Health Safety and Quality Commission. *Gout*. 2019 1220 Nov 2022 25 July 2024]; Available from: https://public.tableau.com/app/profile/hqi2803/viz/PHOanalysis/Gout2019.

9. Cross, M., et al., *Global, regional, and national burden of gout, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021*. The Lancet Rheumatology, 2024.**6**(8):e507-e517.
10. Health Quality and Safety Commission New Zealand Kuru Taurangi Hauora o Aotearoa. *Atlas of Healthcare Variation Gout*. 2019 20 Nov 2022 25 July 2024]; Available from: https://public.tableau.com/app/profile/hqi2803/viz/Goutsinglemap/AtlasofHealthcareVariationGout/viz/Goutsinglemapdraft2021/AtlasofHealthcareVariationGout.
11. Jackson, G., et al., *Potential unmet need for gout diagnosis and treatment: Capture-recapture analysis of a national administrative dataset*. Rheumatology (United Kingdom), 2012.**51**(10):1820-1824.
12. Fatafehi-Finau, T., *Experiences and Perceptions of Tongan people diagnosed with gout living in South Auckland*. 2019, Whitireia Community Polytechnic.
13. Dalbeth, N., et al., *The experience and impact of gout in Māori and Pacific people: A prospective observational study*. Clinical Rheumatology, 2013.**32**(2):247-251.
14. Gauld, N., et al., *Gout Busters: Evaluation of the redesigned pharmacy gout management programme in Te Whatu Ora Counties Manukau* 2023, Te Whatu Ora Counties Manukau:Auckland.
15. Emad, Y., et al., *Why Do Patients With Gout Not Take Allopurinol?* J Rheumatol, 2022.**49**(6):622-626.
16. *Clinical Audit - Lowering serum urate levels in patients with gout*. 2023 July 2023 13 Aug 2024]; Available from: https://bpac.org.nz/audits/gout.aspx.
17. Lawrence, A., et al., *Facilitating equitable prevention and management of gout for Māori in Northland, New Zealand, through a collaborative primary care approach*. J Prim Health Care, 2019.**11**(2):117-127.
18. Andrews, S., et al., *Evaluation of Gout Stop and Owning My Gout management programmes*. 2020, Synergia.
19. Whanganui Regional Health Network, *Whanganui Gout Stop Programme Evaluation*. 2022, Whanganui Regional Health Network.
20. *Managing gout in primary care. Part 1 - Talking about gout: time for a re-think*. BPAC, 2021.**July**:1-8.
21. Cipolletta, E., et al., *Association between Gout Flare and Subsequent Cardiovascular Events among Patients with Gout*. JAMA, 2022.**328**(5):440-450.
22. Lindsay, K., et al., *The experience and impact of living with gout: A study of men with chronic gout using a qualitative grounded theory approach*. Journal of Clinical Rheumatology, 2011.**17**(1):1-6.
23. Stewart, S., et al., *The experience of a gout flare: a meta-synthesis of qualitative studies*. Seminars in Arthritis and Rheumatism, 2020.**50**(4):805-811.
24. Anderson, J.L. and K.U. Knowlton, *Cardiovascular Events and Gout Flares*. JAMA, 2022.**328**(5):425-426.
25. Cipolletta, E., et al., *Risk of Venous Thromboembolism With Gout Flares*. Arthritis and Rheumatology, 2023.**75**(9):1638-1647.
26. *Managing gout in prinary care. Part 2 - controlling gout with long-term urate-lowering treatment*. BPAC, 2021(July):1-6.