Brand change

Phenobarbitone tablets

The funded brand of phenobarbitone tablets is changing, and all patients will need to change brands to continue taking phenobarbitone tablets. To ensure patients with epilepsy transition safely, prescribers are encouraged to discuss changing brands with their patients as soon as practicable. This will need to be done in a timely manner, so the required pre-switch phenobarbital serum level measurements are not missed.

Key points

- Patients taking phenobarbitone tablets for epilepsy require alerting to the impending brand change and required actions.
- Two appointments with a healthcare provider are needed: at one month before and one month after the brand change.
- Serum phenobarbital testing is required to check that concentrations remain at the same level before and after the brand change. Testing is recommended:
    - three weeks prior to the change
    - within the week prior to the change
    - within the first week of the change
    - one month after the change.
- The brand change necessity may provide health professionals with an opportunity to review patient clinical management.
- Funding is available from Pharmac to avoid extra patient cost associated with this change.
- Waka Kotahi recommends that patients consider a voluntary driving stand-down period of eight weeks following an antiepileptic medication brand change.

Background

Phenobarbitone (PSM) 15mg and 30mg tablets, supplied by API Consumer Brands, will soon be replaced with another brand of phenobarbitone 15mg and 30mg tablets. The new brand will be funded and available from 1 June 2023, ahead of expected depletion of PSM 30mg and 15mg tablets in July and October, respectively.

The closure of the API manufacturing facility has necessitated this brand change for phenobarbitone *tablets*. Note that the supply of phenobarbitone injection and powder formulations will *not* be impacted.

Phenobarbitone tablets are sometimes used "off-label" for premedication and sedation, and for conditions other than epilepsy, including anxiety, sleeping disorders and cyclic vomiting syndrome. Phenobarbitone tablets can also be used to manage palliative care, assisted dying, and drug withdrawal/neonatal abstinence.

The advice concerning serum phenobarbital monitoring in this article relates only to people with epilepsy.

Patient group

Around 400 people are dispensed phenobarbitone tablets each year in Aotearoa New Zealand (see table), with most of the dispensing occurring in the community and prescribed by GPs.

Number of people dispensed phenobarbitone since 1 July 2022 to January 2023[1]

Phenobarbitone	Total	Māori	Pacific peoples
15 mg	60	7	2
30 mg	374	30	10

It is estimated that around 80 per cent of people currently taking phenobarbitone tablets have epilepsy. Many of these patients (most aged ≥65y) have been on phenobarbitone for a substantial amount of time.[1]

Recognise vulnerable people

Vigilance is required to ensure people in disability care facilities and aged residential care who are prescribed phenobarbitone are considered.

Monitor for change in therapeutic effect

Phenobarbitone is a UK-classified Category One epilepsy medicine. Hence, clinically relevant differences between different brands of phenobarbitone may occur, despite bioequivalence having been demonstrated and pharmaceutical formulations being the same between brands.[2]

Although not usual practice, during this brand change it is important for health professionals to monitor serum phenobarbital concentrations in patients with epilepsy, to check that these remain at the same level before and after the medication change.

Testing timeline

Testing for serum phenobarbital concentration should be performed on samples collected at trough (pre-dose) periods and by the same laboratory, to maintain consistency.

Four occasions are recommended for testing relative to the time of the patient changing phenobarbitone brands.[3]

1. Three weeks prior to the change (baseline 1).
2. Within the week prior to the change (baseline 2).
3. Within the first week of the change – ideally four to 10 days after the first dose of the new brand.
4. One month after the change.

Prescribers will need to monitor the results of these blood tests.

Testing outcomes

The formal therapeutic range for serum phenobarbital concentration is derived from group average data, and can differ between laboratories.

Some clinicians may find their patient's serum phenobarbital concentration is less than the lower limit of this range and therefore considered sub-therapeutic. However, if the patient's phenobarbitone dose is providing a clinically therapeutic effect and the patient is well-managed, there is no need to increase the dose in order to meet the lower limits of the serum phenobarbital formal therapeutic range.[3]

A variation of ±10 per cent between the two baseline measurements is considered stable. However, appreciable variation indicates instability and, in this case, a patient will require closer monitoring of their serum phenobarbital concentrations after the brand change, especially early on.[3]

What to expect if phenobarbital levels are too low or high

Effects of reduced phenobarbital levels include:[3]

- sleep difficulties
- insufficient clinical effects, including seizure activity.

Effects of increased phenobarbital levels may include:[3]

- headache
- mood changes
- drowsiness
- sedation.

Once phenobarbital serum levels increase above the therapeutic range, the patient is at substantial risk of adverse effects. Symptoms of barbiturate toxicity vary between individuals but commonly include:[4]

- difficulty thinking
- decreased level of consciousness
- bradycardia or rapid and weak pulse
- poor coordination
- vertigo
- nausea
- muscle weakness
- thirst
- oliguria
- decreased temperature
- dilated or contracted pupils.

Deaths have resulted from marked respiratory depression, hypotension and coma.

Extra funding provided to help cover costs

Patients will require two appointments with their healthcare provider, one before and one after the brand change, in addition to the testing required to assess serum phenobarbital levels. To reduce barriers and so that patients pay no extra costs associated with this brand change, Pharmac will fund GP copayments for the two recommended appointments.

Pharmac will also implement an early brand switch fee (BSF) as support for pharmacists to discuss the brand change with patients, as well as proactively identify those who haven't yet discussed the change with their prescriber.

Driving after a brand change

Waka Kotahi New Zealand Transport Agency recognises that health professionals, by consideration of their knowledge of their patient's medical history and other relevant factors, are best placed to determine patient ability to drive.[5]

To help with this determination, Waka Kotahi has developed a guide for health professionals on the medical aspects of fitness to drive[6] (tinyurl.com/43vcscy5), and a fact sheet on epilepsy/seizures and driving for patients who drive privately and for work (tinyurl.com/msnxmryy).[7]

During medication changes or withdrawal of antiepileptic drugs, and for six months afterwards, Waka Kotahi has previously recommended advising patients not to drive.

When changing brands of medication, Waka Kotahi advises caution and recommends that patients consider a voluntary driving stand-down period of eight weeks following the change.[5,8]

Other guidance available

The necessity of a brand change may provide health professionals with an opportunity to review a patient's clinical management prior to the change if the patient's epilepsy is not currently well controlled on phenobarbitone tablets. Switching to an alternative epilepsy medicine may be a consideration.

Although not a requirement when managing the phenobarbitone brand change, health professionals treating patients with epilepsy may like to discuss the change and seek guidance on switching epilepsy medicines with a neurologist.

Talking with a neurologist may help clinicians, practice nurses and pharmacists to understand potential issues with a brand change and the need for serum phenobarbital monitoring. This information will also aid in discussions with patients, so they feel appropriately and accurately informed.

Consumer information about anti-seizure medicines and a variety of epilepsy topics is available on Health Navigator.

The Māori Pharmacists' Association Ngā Kaitiaki o te Puna Rongoā also has a non-urgent, free phone line, 0800 664 488, to answer questions whānau have about their medicines.

References available at akohiringa.co.nz/education/phenobarbitone-tablets