

Neurological Subcommittee of PTAC

Meeting held 11 November 2015

(minutes for web publishing)

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Note that this document is not necessarily a complete record of the Neurological Subcommittee meeting; only the relevant portions of the minutes relating to Neurological Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Neurological Subcommittee may:

- (a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
- (b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
- (c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 11 & 12 February 2016, the record of which is available on our website.

Record of the Neurological Subcommittee of the Pharmacology and Therapeutics Committee (PTAC) meeting held at PHARMAC on 11 November 2015

1 Correspondence / Matters arising

Lacosamide

- 1.1 The Subcommittee noted correspondence on behalf of the New Zealand committee of the International League Against Epilepsy Committee requesting that the Special Authority (SA) criteria for lacosamide be amended to allow widened access to lacosamide, so that treatment would be a 5th line option, rather than 6th line.
- 1.2 The Subcommittee considered that lacosamide has similar tolerability and efficacy to other new antiepileptic drugs and that the primary reason for its current listing as a 6th-line treatment was fiscal; due to the large cost differential between lacosamide and all other funded new antiepileptic drugs.
- 1.3 The Subcommittee considered that lacosamide is thought to have a unique mode of action via inhibition of slow sodium channels and is useful for patients with refractory epilepsy. The Subcommittee considered that lacosamide would be clinically useful if it was used 5th line for refractory epilepsy as it was generally well tolerated and less time consuming to initiate patients on than some other treatments, for example carbamazepine and phenytoin.
- 1.4 The Subcommittee were supportive of amending the Special Authority criteria to widen access of lacosamide to a 5th line treatment for refractory epilepsy; however, it recognised that this would have the potential to significantly increase patient numbers and would be a financial risk. The Subcommittee considered that patient numbers were difficult to quantify but would likely double at minimum and, at most, quadruple.
- 1.5 The Subcommittee **recommended** widening access to lacosamide as a 5th line treatment for refractory epilepsy with the following changes to the Special Authority criteria below with a medium priority; additions are marked in bold and deletions in strike through:

Special Authority for Subsidy

Initial application from any relevant practitioner. Approvals valid for 15 months for applications meeting the following criteria:

Both:

- 1 Patient has partial-onset epilepsy; and
- 2 Seizures are not adequately controlled by, ~~or patient has experienced unacceptable side effects from~~, optimal treatment, **or patient has experienced unacceptable side effects**, with ~~at~~ **any four** of the following: sodium valproate, topiramate, levetiracetam ~~and any two of~~ carbamazepine, lamotrigine and phenytoin sodium (see Note).

Note: "Optimal treatment" is defined as treatment which is indicated and clinically appropriate for the patient, given in adequate doses for the patient's age, weight and other features affecting the pharmacokinetics of the drug with good evidence of compliance. Women of childbearing age are not required to have a trial of sodium valproate.

- 1.6 The Decision Criteria particularly relevant to this recommendation are: (i) *The health needs of all eligible people within New Zealand;* (iii) *The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;* (iv) *The clinical benefits and risks of pharmaceuticals;* (vi) *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

Infliximab for neurosarcoidosis

- 1.7 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee of PTAC, at its March 2012 meeting had noted that infliximab is sometimes used in patients with neurosarcoidosis which is rare and considered that funding for this should be managed through the NPPA process.
- 1.8 The Subcommittee noted that there had been 7 NPPA applications for infliximab for the treatment of neurosarcoidosis since July 2013, all of which had been approved. The Subcommittee considered that infliximab for neurosarcoidosis would be more appropriate for consideration of listing on the HML as opposed to going through the NPPA process.
- 1.9 The Subcommittee considered that neurosarcoidosis was a rare disease with serious consequences. The Subcommittee considered that patient numbers would be small, approximately 20 patients in total, with approximately half of those patients being unresponsive to steroids.
- 1.10 The Subcommittee considered that corticosteroids should be first line agents for the treatment of neurosarcoidosis and that treatment with IV cyclophosphamide and infliximab should be reserved for steroid-refractory disease. The Subcommittee noted that there have been no randomised-controlled trials published, however; there was weak evidence to support the use of infliximab in this setting, available from published case-series and case-reports.
- 1.11 The Subcommittee noted that there were clinical circumstances where treatment with IV cyclophosphamide would not be clinically appropriate; for example a woman of child bearing age or those at risk of malignancy.
- 1.12 The Subcommittee **recommended** that infliximab be listed on the HML for neurosarcoidosis, subject to the restrictions below with a high priority:

Restricted

Initiation – neurosarcoidosis

Re-assessment required after 18 months

Neurologist

All of the follow:

1. Biopsy consistent with diagnosis of neurosarcoidosis; and

2. Patient has CNS involvement; and
3. Patient has steroid-refractory disease; and
4. Either:
 - 4.1. IV cyclophosphamide has been tried; or
 - 4.2. Treatment with IV cyclophosphamide is clinically inappropriate.

Continuation – neurosarcoidosis

Re-assessment required after 18 months

Neurologist

Either:

1. A withdrawal period has been tried and the patient has relapsed; or
2. All of the following:
 - 2.1. A withdrawal period has been considered but would not be clinically appropriate; and
 - 2.2. There has been a marked reduction in prednisone dose; and
 - 2.3. Either:
 - 2.3.1. There has been an improvement in MRI appearances; or
 - 2.3.2. Marked improvement in other symptomology.

- 1.13 The Decision Criteria particularly relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals;*

Modafinil

- 1.14 The Subcommittee noted that the Respiratory Subcommittee had recommended that PHARMAC seek the advice of the Neurological Subcommittee on the sensitivity and specificity of electroencephalogram (EEG) testing for diagnosis of narcolepsy and if EEG testing would be an appropriate alternative to criterion 2.1 and 2.2 of the current modafinil SA criteria. The Subcommittee noted the minutes from the Respiratory Subcommittee meeting (September 2015) and considered that an EEG was neither a specific nor a sensitive test for the diagnosis of narcolepsy. The Subcommittee considered that EEGs were a limited resource with an associated cost. The Subcommittee considered that the use of EEG testing was subjective and was not useful for the diagnosis of narcolepsy and that the SA criteria should not be modified to include the option of EEG testing.

2 Methylphenidate for traumatic brain injury (TBI)

- 2.1 The Subcommittee noted that methylphenidate immediate-release 5, 10 and 20 mg tablets and sustained-release 20 mg tablets are currently funded subject to Special Authority and hospital restrictions for patients with attention deficit and hyperactivity disorder (ADHD) and narcolepsy, and methylphenidate extended-release 18 mg, 27 mg, 36 mg and 54 mg tablets and modified-release 10 mg, 20 mg, 30 mg and 40 mg capsules are currently funded subject to Special Authority and hospital restrictions as a second-line treatment for ADHD.

- 2.2 The Subcommittee noted that methylphenidate is only registered for use in New Zealand for the treatment of attention deficit and hyperactivity disorder (ADHD) and narcolepsy. The Subcommittee noted that under regulation 22 of the Misuse of Drugs Regulations 1977, methylphenidate can only be prescribed by a psychiatrist or paediatrician (for ADHD only), an internal medicine specialist (for narcolepsy only) or a palliative care specialist (for use in palliative care only), or by any other medical practitioner on the written recommendation of one of these specialists (only for the relevant condition as specified for each specialty).
- 2.3 The Subcommittee noted that PHARMAC had received funding applications from clinicians for widening access to methylphenidate (all currently funded presentations) for use in treatment-resistant depression, depression in terminally ill patients, and apathy in patients with traumatic brain injury (TBI), all of which are off-label indications.
- 2.4 The Subcommittee noted that the Mental Health Subcommittee had reviewed the funding of methylphenidate in treatment-resistant depression, palliative care and TBI in July 2013. With respect to TBI, the Mental Health Subcommittee deferred making a recommendation pending PHARMAC staff seeking expert advice and advice from the Neurological Subcommittee and PTAC.
- 2.5 The Subcommittee noted that TBI is a highly heterogeneous population and is associated with a wide range of dysfunctions. The Subcommittee noted that a high proportion of patients with TBI have psychosocial and addiction issues. The Subcommittee noted that patients with TBI were often lethargic and had difficulty engaging in physical and cognitive treatment. The Subcommittee noted that most TBI cases were seen by rehabilitation physicians, usually in private practice funded by the Accident Compensation Corporation (ACC).
- 2.6 The Subcommittee noted that methylphenidate enhances synaptic dopamine and noradrenaline levels and, as such, has a stimulant effect.
- 2.7 The Subcommittee reviewed information from PHARMAC staff and submissions from several clinicians regarding the use of methylphenidate for TBI, including the following publications:
- Beaulieu-Bonneau et al. *Sleep Med* 2012;13:598-605.
 - Challman et al. *Mayo Clin Proc* 2000;75:711-721.
 - Chan YP et al. *Paediatrics* 1983;72:56-9.
 - De Marchi et al. *Can.J.Neurol.Sci* 2005;32:4-17.
 - Feeney et al. *Stroke* 1986;17:817-850.
 - Glenn MB. *J Head Trauma Rehabilitation* 1998;13(5)85-90.
 - Grade et al. *Arch Phys Med Rehabil* 1998;79:1047-50.
 - Johansson et al. *Brain Inj* 2014;28:304-10.
 - Johansson et al. *Brain Inj* 2015;29:758-765.
 - Keenan et al. *Br J Neurosurg* 2005;19:46-50.
 - Lombardi F. *Eur J Anaesthesiol Suppl.* 2008;42:131-6.
 - Marin and Wilkosz. *J Head Trauma Rehabil* 2005;20:377-388.
 - McAllister et al. *Neuropsychopharmacol* 2015;Sep 11:doi: 10.1038/npp.2015.282 [Epub ahead of print].

- Moein et al. Clin Neurol Neurosurg 2006;108:539-42.
- Ponsford et al. J Head Trauma Rehabil 2014;29:321-37.
- Ramasubbu and Goodyear. Neuropsychiatr Dis Treat 2008;4:1251-66
- Sami and Faruqi. Acta Neuropsychiatrica 2015;Apr 8:1-11 [Epub ahead of print].
- Scher et al. Curr Psychiatry 2011;10:21-37.
- Siva et al. Clin Rehabil 2010;24:110-121.
- Talsky et al. BC Medl JI 2010;53:26-31.
- Tardy et al. Neuroimage 2006;33:913-22.
- Walker et al. PM R 2012;4:778-82.
- Wheaton et al. J Clin Psychopharmacol 2011;31:745-57.
- Willmott et al. J Rehab Med 2009;41:585-587.
- Willmott and Ponsford. J Neurol Neurosurg.Psychiatry 2009;80:552-557.
- Whyte et al. Am J Phys Med Rehabil 2004;83:401-20
- Wroblewski et al. J Head Trauma Rehabilitation 1994;9:19-42.

- 2.8 The Subcommittee noted that there was very little good data in support of the use of methylphenidate in TBI, with limited randomised controlled trial (RCT) data. The Subcommittee noted that even in the published RCTs, patient numbers were very low, with less than 50 participants.
- 2.9 The Subcommittee noted that the assessment tools and outcome measures in the studies were heterogeneous; most use neuropsychological modalities, which members considered was appropriate but makes it difficult to compare outcomes between studies.
- 2.10 The Subcommittee noted that most studies were of short duration and the dose of methylphenidate was variable.
- 2.11 The Subcommittee noted that many of the published studies had high dropout rates. In addition, the Subcommittee noted that the inclusion criteria in some studies appeared to exclude a large proportion of patients with TBI, for example in the study by Whyte et al (2004), more than 1500 patients were screened but only 34 patients entered the study. Because of this, the Subcommittee considered that the trial populations in most studies were unlikely to be representative of 'real world' patients in New Zealand.
- 2.12 The Subcommittee noted that one of the publications (Moein et al. 2006) found that methylphenidate was associated with a reduction in length of intensive care unit (ICU) stay but not in overall hospital stay in patients with moderate TBI and a reduction in length of hospital stay in patients with severe TBI. The Subcommittee noted that there was a range of factors that contribute to determining length of hospital stay, and members considered that the patient numbers in this trial were too low to make definitive conclusions about the likely impact of methylphenidate on the length of ICU and hospital stay for New Zealand patients with TBI.
- 2.13 The Subcommittee considered that the best available evidence was from three RCTs: Whyte et al (2004) (n=34), Willmott et al (2009) (n=40) and McAllister et al (2015) (n=32). The Subcommittee noted that these studies were of relatively short duration (6, 2 and 12 weeks, respectively).

- 2.14 The Subcommittee considered that the findings of Whyte et al (2004) and Willmott et al (2009) provided moderate quality evidence to support an increase in processing speed from the short-term use of methylphenidate in patients with moderate to severe TBI, which members considered could potentially enhance the ability of patients to engage in short-term tasks. The optimal dose for this effect appears to be 0.3 mg/kg.
- 2.15 The Subcommittee noted that other examples of ‘waking agents’ potentially useful in TBI are amantadine, bromocriptine, selegiline, rivastigmine, donepezil and levodopa with carbidopa or benserazide.
- 2.16 The Subcommittee noted that McAllister et al (2015) reported that 12 weeks’ treatment with methylphenidate or galantamine was associated with improvements on measures of cognitive complaints in patients with a history of post-traumatic stress disorder or TBI or both conditions, compared with placebo. However, the Subcommittee noted that the study had been terminated early due to slow enrolment and only nine patients received methylphenidate. The Subcommittee considered that it was not possible to generalise the results of this pilot study to the New Zealand population.
- 2.17 The Subcommittee noted that there is little published research on longer-term treatment with methylphenidate in this patient group. The Subcommittee noted that attention deficit is a long-term issue and that if methylphenidate was effective for this symptom after short-term treatment in patients with TBI, clinicians would want to prescribe it long-term. The Subcommittee considered that this would be associated with a significant financial risk, with no good evidence to support its use and no information about likely dose or duration of treatment. Members noted that some patients may meet the current funding criteria for methylphenidate for ADHD. The Subcommittee noted that the doses of methylphenidate for adults with ADHD (30–60 mg per day) were generally higher than those used in the published trials.
- 2.18 The Subcommittee noted that “TBI” encompasses a large population, of which approximately 80% are mild TBI, 10% moderate TBI and 10% severe TBI. The Subcommittee noted that incidence of TBI in New Zealand based on information from guidelines and local data is approximately 600–750 patients with mild TBI per 100,000 people and 40–60 patients with moderate-to-severe TBI per 100,000 people. Taking into account information in the clinician submissions, the Subcommittee considered that approximately one-third of patients with moderate-to-severe TBI might try methylphenidate if it was funded.
- 2.19 The Subcommittee noted that clinician submissions proposed that the patient group be expanded to include acquired brain injury (ABI); however, the Subcommittee noted that this encompassed a very large group of heterogeneous patients (eg patients with stroke or subarachnoid haemorrhage) and considered that it had not seen evidence for methylphenidate in this patient group. The Subcommittee considered that the patient pool for methylphenidate treatment would be approximately two-to-three times the size of the TBI only population.

- 2.20 The Subcommittee noted that there is a high risk of abuse and diversion with methylphenidate, which is a significant concern for patients with TBI given the relatively high proportion of patients with drug and alcohol addiction issues.
- 2.21 The Subcommittee considered that it would be difficult to place a restriction on the use of methylphenidate for TBI on the basis of TBI severity, for example limiting funding to patients with moderate-to-severe TBI, as this would be difficult to enforce given the heterogeneity of the patient population. The Subcommittee considered that restricting applications to rehabilitation physicians would be an effective way of preventing more widespread use.
- 2.22 The Subcommittee noted that restricting access to use in patients in a rehabilitation facility would disadvantage rural patients who do not have ready access to brain rehabilitation facilities. Similarly, restricting access to use in DHB hospitals would result in inequitable access as many patients are treated through private facilities funded by ACC.
- 2.23 Based on the available evidence, the Subcommittee considered that there could be some benefit of short-term methylphenidate use in patients with moderate to severe TBI; however, the magnitude of the benefit appears small and of uncertain clinical relevance, there is no evidence that important clinical endpoints such as memory are improved, there is no evidence that the benefit of short-term treatment is sustained or leads to longer-term improved outcomes.
- 2.24 Overall, taking into account the difficulties in defining the patient group, dose and duration of treatment, the lack of evidence of longer-term benefit, the risk of abuse and diversion, the financial risk and the legal issues, the Subcommittee **recommended** that the funding application for methylphenidate for TBI and ABI be declined.

3 Antiepileptic Switching

- 3.1 The Subcommittee noted that PHARMAC staff sought clinical advice on Antiepileptic brand switching. The Subcommittee noted that the following antiepileptic drugs (AEDs) currently have two or more brands listed on the Pharmaceutical Schedule: lamotrigine, gabapentin and topiramate.
- 3.2 The Subcommittee noted that where there are multiple brands listed switching can occur at a pharmacy level unless the prescription has been annotated with the brand and it is specified no brand substitution allowed. Members considered, anecdotally, that despite annotation, brand switching can still occur.
- 3.3 The Subcommittee noted that the New Zealand Transport Association (NZTA) guidance considers epilepsy is uncontrolled when treatment has changed and the new treatment has to be monitored for a period of time to assess its impact. The Subcommittee considered that a change in brand of a medication would not constitute a change in treatment.

- 3.4 The Subcommittee noted that formulation changes can occur for AEDs and that in general batch to batch variability may exist.
- 3.5 The Subcommittee considered information provided by Te Arai Biofarma (supplier of Valopin) regarding three formulation changes of the Epilim brand of sodium valproate since it has been registered. The Subcommittee considered that this was of interest and that there had been no obvious clinical impact from these formulation changes that it was aware of.
- 3.6 The Subcommittee considered published evidence regarding AED brand switching that included systematic reviews (Kesselheim et al. *Drugs* 2010;70:605-21, Yamada et al. *Ann Pharmacother* 2011;45:1406-15, Talati et al. *Pharmacotherapy* 2012;32:314-22); prospective studies (Ting et al. *Epilepsia* 2015;56:1415-24, Vari et al. 2015: Pubmed PMID:26507620); and retrospective studies (Kinikar et al. *Ann Pharmacother* 2012;46:650-8, Shin et al. *Int J Clin Pharmacol Ther* 2014;52:1017-22, Chaluvadi et al. *Epilepsia* 2011;52:810-5, Hartung et al. *CNS Drugs* 2012;26:707-16, Lessing et al. *Appl Health Econ Health Policy* 2014;12:537-46, Gagne et al. *Clin Pharmacol Ther* 2010;88:347-53, Erickson et al. *Epilepsia* 2011;52:1365-71, Hansen et al. *Epilepsy Res* 2013;106:237-43, Polard et al. *Pharmacoepidemiol Drug Saf* 2015;24:1161-9).
- 3.7 The Subcommittee considered that, in general, evidence from the randomised controlled trials did not appear to suggest that switching brands of AEDs has an effect on seizure frequency; however, some of the small non-experimental cohort studies reported high switch back rates and increase in health resources in patients who switched.
- 3.8 The Subcommittee noted that one of the publications (Kinikar et al. 2012), involving 222 patients switching from Dilantin to a single generic phenytoin over a 10 month period found that there was no change in seizure events in the pre switch period compared with the post switch period. In contrast, in another publication (Shin et al. 2014) authors analysed charts of 80 patients switching from one generic phenytoin to another during an 18 month period, where 33 out of 80 patients were reported to have increased seizure frequency, an increase in medical visits and a decrease in serum phenytoin concentrations.
- 3.9 The Subcommittee noted that Hartung et al (2011) reported, in a retrospective cohort study involving 616 patients, there was no statistically significant increase in emergency department visits, hospitalisations or condition specific encounters for patients with epilepsy, bipolar or migraine who switched brands of lamotrigine. The Subcommittee noted that Lessing et al (2014) had investigated the impact of lamotrigine switching in New Zealand on health outcomes and healthcare utilisation. This study also reported no differences in health outcomes measures (hospital admissions, use of specialist service, death, use of other AEDs, adverse reports) were associated with switching from originator lamotrigine to a generic equivalent for patients switching brands compared with those who did not switch brands.
- 3.10 The Subcommittee noted that in July 2013 the Medicines & Healthcare products Regulatory Agency (MHRA) in the UK issued advice regarding brand switching of AEDs. The Subcommittee noted that the MHRA categorised AEDs to help

healthcare professionals decide whether it is necessary to maintain a patient on a specific manufacturer's product; as follows:

- Category 1: phenytoin, carbamazepine, phenobarbital, primidone:
 - Doctors are advised to ensure their patient is maintained on a specific manufacturer's product
- Category 2: sodium valproate, lamotrigine, perampanel, retigabine, rufinamide, clobazam, clonazepam, oxcarbazepine, eslicarbazepine, zonisamide, topiramate.
 - Need for continued supply of a particular manufacturer's product should be based on clinical judgement and consultation with patient and/or carer taking into account factors such as seizure frequency and treatment history
- Category 3: levetiracetam, lacosamide, tiagabine, gabapentin, pregabalin, ethosuximide, vigabatrin.
 - It is usually unnecessary to ensure that patients are maintained on specific manufacturer's product unless there are specific concerns such as patient anxiety and risk of confusion or doing errors.

- 3.11 The Subcommittee noted that the following AEDs were not funded in New Zealand: perampanel, retigabine, rufinamide, oxcarbazepine, eslicarbazepine, zonisamide, tiagabine and pregabalin.
- 3.12 The Subcommittee considered the MHRA categorisation to be pragmatic and were broadly supportive of the majority of the categorisation, with two exceptions. The Subcommittee considered that lacosamide should be in category two. The Subcommittee was unable to come to a consensus in relation to lamotrigine; whether it should be in category one or two, or in category two or three.
- 3.13 The Subcommittee considered that AEDs in category one have a narrow therapeutic index and should only have one brand listed to avoid inadvertent brand switching. The Subcommittee noted that there is currently only one brand of carbamazepine, phenytoin, phenobarbital (phenobarbitone) and primidone (category one of the MHRA guidance) listed in the Pharmaceutical Schedule.
- 3.14 With regards to category two of the MHRA categorisation (including lacosamide), the Subcommittee expressed a preference for a managed brand switch if, as a result of a competitive process, a sole supply arrangement was entered into which resulted in one brand of AED being funded. The Subcommittee considered that a managed brand switch would require a transition period of 3 to 6 months.
- 3.15 The Subcommittee considered that switching between brands for AEDs in category three (not including lacosamide) was unlikely to be clinically problematic. The Subcommittee noted that levetiracetam tablets (category three of the MHRA guidance) had previously changed brands and that the transition of this had been acceptable.

Levetiracetam

- 3.16 The Subcommittee noted that levetiracetam tablets, injection and liquid had been included in PHARMACs Annual Invitation to Tender 2015/16.
- 3.17 The Subcommittee considered that should the tender result in a managed brand switch, for any of the oral formulations, general practitioners (GPs) and pharmacists would be the most likely health care professionals (HCP) to directly support patients. The Subcommittee considered that additional clinic visits and blood tests would be unlikely to be required, should there be a change in brand.
- 3.18 The Subcommittee considered that there would not be any specific requirements for implementation of a switch in IV levetiracetam and noted that the Tender Medical Subcommittee would be involved in assessing suitability of any products (IV or oral) that are submitted for consideration.
- 3.19 The Subcommittee considered a transition period of 3 to 6 months would be required to assist with any patients needing to switch brands of oral formulations of levetiracetam.

Lamotrigine

- 3.20 The Subcommittee noted that there were currently several brands of lamotrigine listed.
- 3.21 The Subcommittee was unable to come to a consensus whether lamotrigine should be in category one, two or three. Members expressed a preference for one brand to be listed. The Subcommittee considered that a managed switch to one brand of lamotrigine would be preferable to having multiple brands listed.
- 3.22 The Subcommittee considered a competitive process for one brand (sole supply) of lamotrigine would be appropriate, provided that a suitable transition period was available. The Subcommittee considered that a transition period of 3 to 6 months would be required to support any possible brand switches. Members considered that patients could be considered through the NPPA pathway if they were unable to transition for exceptional clinical reasons.
- 3.23 The Subcommittee considered that patients are generally averse to change and there is a risk that, should PHARMAC run a competitive process for lamotrigine that resulted in a managed brand switch, any change in seizure frequency could be perceived to have been caused by a change in brand.
- 3.24 The Subcommittee considered that there were no blood tests that would be useful to assist with monitoring a brand switch for lamotrigine. The Subcommittee considered that serum level monitoring of AEDs was only useful for those AEDs with a narrow therapeutic index, for example phenytoin, and that in practice epilepsy control is monitored by assessing seizure frequency.
- 3.25 The Subcommittee expressed the importance of HCPs providing support and reassurance around brand changes and considered that the most important factor for maintaining epilepsy control was medication adherence.

- 3.26 The Subcommittee considered that GPs and pharmacists would be the HCPs most likely to be involved in supporting a brand change for lamotrigine, should this occur.
- 3.27 The Subcommittee noted that the NZTA guidance details that driving should cease if an individual is having seizures or has had a seizure in the last 12 months and that driving may resume after 12 months, or 6 months, if the likelihood of further seizures is minimal or if there are favourable modifiers such as medication changes.
- 3.28 The Subcommittee considered that if a patient were to have a seizure after a brand switch, their physician may be likely to report to the NZTA that they had had a change in brand of treatment by way of explanation. The Subcommittee **recommended** that PHARMAC consult with the Chief Medical Officer of the NZTA, should PHARMAC run a competitive process that could result in a managed brand switch for lamotrigine.