Neurological Subcommittee of PTAC

Meeting held 07 November 2016

(minutes for web publishing)

Neurological Subcommittee minutes are published in accordance with the *Terms* of *Reference* for the *Pharmacology* and *Therapeutics Advisory Committee* (*PTAC*) and *PTAC* Subcommittees 2016.

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 9 & 10 February 2017, the record of which will be available in due course.

Record of the Neurological Subcommittee of the Pharmacology and Therapeutics Committee (PTAC) meeting held at PHARMAC on 7 November 2016

1 Record of the previous Subcommittee meeting

1.1 The Subcommittee noted that PHARMAC staff sought further clarification on paragraph 7.22 regarding the Subcommittee's consideration that a sole supply of lamotrigine would be appropriate. PHARMAC staff noted that potentially there could be a situation where there was one supplier for the paediatric strength tablets (2 mg and 5 mg) and one supplier of the adult strength tablets (25 mg, 50 mg and 100 mg). The Subcommittee considered that it could not perceive a problem with having different suppliers for the adult strength and the paediatric strength preparations of lamotrigine tablets.

2 Monthly dispensing of antiepileptic drugs

- 2.1 The Subcommittee noted a paper by PHARMAC staff regarding the dispensing frequencies of antiepileptic drugs (AEDs) including the background and information considered in the decision making process to remove 'stat' (three months dispensing all at once) dispensing from sodium valproate tablets.
- 2.2 The Subcommittee considered that, anecdotally, some patients may not be adhering to their treatment with sodium valproate due to an inability to pick up new prescriptions every month. Members considered that non-adherence could increase the likelihood of seizures occurring and related adverse effects could include accidents, hospitalisations, inability to drive for 12 months, and in rare cases, sudden, unexpected death of someone with epilepsy (SUDEP).
- 2.3 Members considered that patients with epilepsy unable to visit a pharmacy every month were more likely to have intellectual disabilities, cognitive dysfunction and mobility issues and reside in more socioeconomically deprived areas. The Subcommittee considered that although no published evidence is available to suggest greater adherence with three-monthly dispensing, monthly dispensing could present as a potential barrier to adherence, where good adherence is the greatest modifiable risk factor in preventing seizures.
- 2.4 The Subcommittee noted that epilepsy was a lifelong condition and considered that the monthly dispensing frequency rule for sodium valproate meant that patients would need to visit a pharmacy every single month, for their entire lives. The Subcommittee noted that any medicine, including sodium valproate, may be dispensed 'stat' if the patient meets the 'Access Exemption Criteria', which are that the patient either: a) has limited physical mobility; b) lives and works more than 30 minutes from the nearest pharmacy by their normal form of transport; c) is relocating to another area; or d) is travelling extensively and will be out of town when the repeat prescriptions are due. However, Members considered that this was not always offered by pharmacists and not all prescribers were aware of and/or used the notation. In addition, Members considered that as many patients with epilepsy may also have difficulties with cognitive functioning that they are unlikely to be aware of the 'Access Exemption Criteria' and would be unlikely to ask their pharmacist or doctor to consider it.

- 2.5 The Subcommittee noted that many other AEDs were able to be dispensed 'stat' under the 'Certified Exemption' criteria, which is, where a patient has been stabilised on a medicine and the pharmacist or prescriber has reason to believe the patient will continue on the medicine and is adherent and has endorsed the prescription accordingly. The Subcommittee **recommended** that the 'Certified Exemption' rule be applied to sodium valproate, to allow patients with epilepsy who are stabilised and adherent to access three-monthly dispensings.
- 2.6 The Subcommittee noted that levetiracetam is currently dispensed one-monthly and considered that its considerations regarding sodium valproate (*noted above*) also apply. The Subcommittee **recommended** that the 'Certified Exemption' rule also apply to levetiracetam, to allow patients with epilepsy who are stabilised and adherent to access three-monthly dispensings.

3 EDSS reviews for MS treatments

- 3.1 The Subcommittee noted that following the funding decision in November 2014 to list new MS treatments and to amend the access criteria for all MS treatments, there had been a significant increase in workload for neurologists and their clinics to conduct the necessary Expanded Disability Status Scale (EDSS) reviews as required by the renewal criteria. Some Members considered this increase had significantly affected time available for other activities; however, they also considered that due to more effective treatments being available, the changes may have lessened the amount of time required to be spent managing MS relapses.
- 3.2 The Subcommittee noted that each EDSS review and consultation took between 20 and 45 minutes depending on the neurologist and the patient, and required additional time to fill out the MS Panel application form for treatment.
- 3.3 The Subcommittee noted the technical knowledge and abilities required to assess EDSS, and considered that anyone undertaking such EDSS assessments for MS treatment funding should be 'Neurostatus' accredited. The Subcommittee considered that the EDSS assessment could be completed by a specialist nurse or an advanced trainee/registrar provided it was countersigned by the supervising consultant neurologist. Members considered that this was not well known and suggested that a member of MSTAC raise it at the next Neurology Association of New Zealand meeting (NANZ).

4 PTAC Reviews

4.1 The Subcommittee noted the funding applications in the Neurology therapeutic area that PTAC had reviewed since the Subcommittee last met; deflazacort for Duchenne muscular dystrophy (DMD), and rituximab for myasthenia gravis (reviewed at PTAC's August 2016 meeting). The Subcommittee **recommended** that PTAC review its recommendations for both deflazacort for DMD and rituximab for myasthenia gravis based on the Subcommittee's review of PTAC's minutes.

Deflazacort for Duchenne muscular dystrophy (DMD)

- 4.2 The Subcommittee noted that PTAC recommended that the application for the funding of deflazacort for treatment of patients with DMD who are unable to tolerate prednisone be declined.
- 4.3 The Subcommittee noted that PTAC had noted that there was an ongoing RCT (the FOR-DMD study) comparing prednisone with deflazacort in boys with confirmed DMD, with planned follow-up of between 3 to 6 years and that PTAC had requested that this trial be brought back for review once it was published.
- 4.4 The Subcommittee noted that since PTAC's review of the application a randomised controlled trial (Griggs et al. Neurology 2016; DOI 10.1212/WNL.00000000003217) investigating the efficacy and safety of deflazacort versus prednisone and placebo for DMD over a 52-week period had been published. The Subcommittee considered that, in light of this new evidence, PTAC should review its recommendation.

Rituximab for myasthenia gravis

- 4.5 The Subcommittee noted that PTAC had recommended that the funding of rituximab be widened to include patients with severe, rapidly progressive myasthenia gravis (MG), as a third-line treatment, with a high priority. Members noted that PTAC further recommended that the funding of rituximab be widened to include patients with myasthenia gravis that is considered for disease that follows the usual time course but is refractory to alternative treatments, as a third-line treatment, with a low priority.
- 4.6 The Subcommittee considered that the definition of severe, rapidly progressive MG did not reflect clinical practice as the condition is more like asthma, in that some patients have mild, moderate or severe disease exacerbations and then enter remission. The Subcommittee noted the mild, moderate, severe classifications defined by the Myasthenia Gravis Foundation of America (MGFA) (Jaretszki et al Ann Thorac Surg 2000;70:327-34). The Subcommittee considered that the terminology of severe refractory was more suited to MG, and that this terminology 'severe refractory' represented the group recommended by PTAC for funding with a low priority.
- 4.7 The Subcommittee considered that rituximab would not be used in an acute setting to control an exacerbation but should instead be considered as an alternative medium to long term preventative therapy if a patient was admitted to an Intensive Care Unit (ICU) as result of poor control with existing therapy.
- 4.8 The Subcommittee noted that PTAC had assumed that rituximab was required for an exacerbation to prevent the patient requiring ICU admission for ventilator support, which is why the Committee gave the recommendation a high priority. The Subcommittee clarified that during a crisis, a patient would be managed with intravenous immunoglobulin (IVIG) or plasma exchange until the patient was reestablished with regular immunosuppressants (for example azathioprine, mycophenolate mofetil and high dose prednisone). At this time the patient's standard treatments would be reassessed with the aim of preventing future exacerbations.

- 4.9 The Subcommittee considered that most patients were well managed with corticosteroids and immunosuppressants and would not require additional treatment with rituximab. The Subcommittee considered that the severe refractory group were those patients who did not remain stable on high-dose steroids and other immunosuppressants or were unable to satisfactorily reduce corticosteroid daily doses despite treatment with other immunosuppressants. The Subcommittee considered that rituximab would be appropriate for this severe refractory group, the group that PTAC gave a low priority recommendation to.
- 4.10 The Subcommittee considered that immunosuppressants could take 9 months before a clinical effect is seen, and that for a patient to be classed as having severe refractory MG, corticosteroids and at least one immunosuppressant should be trialled for at least 12 months.
- 4.11 Members considered that there are three different dosage regimens that have been used in clinical trials for rituximab for MG (375mg/m weekly for four weeks, 500 mg weekly for four weeks and two 1000 mg doses given two weeks apart) and that restrictions for rituximab for this indication should permit usage of any of these regimens. The Subcommittee considered that it would be reasonable to review the dosage regimens in the proposed restrictions once the results from BeatMG trial become available (NN103 BeatMG randomised controlled trial. Nowak, unpublished). The Subcommittee considered that an approval should last for 12 months and that a patient would need to demonstrate relapse, despite 12 months' treatment with corticosteroids and an immunosuppressant for continuation of funding. The Subcommittee considered the restrictions could be drafted as follows:

Initiation – Severe refractory Myasthenia Gravis

Re-assessment required after 24 months Both:

- 1. One of the following dose regimens is to be used: 375 mg/m² of body surface area per week for a total of four weeks, or 500 mg once weekly for four weeks, or two 1000 mg doses given two weeks apart; and
- 2. Either:
 - 2.1. Treatment with corticosteroids and at least one other immunosuppressant for at least a period of 12 months has been ineffective; or
 - 2.2. Both:
 - 2.2.1. Treatment with at least one other immunosuppressant for a period of at least 12 months; and
 - 2.2.2. Corticosteroids have been trialled for at least 12 months and have been discontinued due to unacceptable side effects.

Continuation – Severe refractory Myasthenia Gravis

Re-assessment required after 24 months

All of the following:

- One of the following dose regimens is to be used: 375 mg/m² of body surface area per week for a total of four weeks; or 500 mg once weekly for four weeks; or two 1000 mg doses given two weeks apart; and
- 2. An initial response lasting at least 12 months was demonstrated; and
- 3. Either:
 - 3.1. The patient has relapsed despite treatment with corticosteroids and at least one other immunosuppressant for a period of at least 12 months; or
 - 3.2. Both:
 - 3.2.1. The patient's myasthenia gravis has relapsed despite treatment with at least one immunosuppressant for a period of at least 12 months; and
 - 3.2.2. Corticosteroids have been trialled for a least 12 months and have been discontinued due to unacceptable side effects.

5 Agents for Parkinsonism and Related Disorders

- 5.1 The Subcommittee noted that PHARMAC was seeking clinical advice around appropriate implementation activities that could be used to support transition periods for any brand changes of the levodopa/carbidopa formulations, should they occur.
- 5.2 The Subcommittee considered that it did not have any clinical concerns regarding a brand change for any of the levodopa/carbidopa formulations. The Subcommittee considered that a brand change was likely to have less of an impact than when the formulation for levodopa/carbidopa tablets (Sinemet brand) was changed. The Subcommittee considered that there are currently difficulties with splitting both of the currently funded brands of levodopa/carbidopa tablets, even if a score mark is present. Members considered that levodopa/benserazide (Madopar) is available in a low strength and may be a more appropriate funded alternative when small dose increments are needed, rather than halving the tablets.
- 5.3 The Subcommittee considered that a brand change would necessitate communication going out to primary, secondary, and tertiary care clinicians and nurses as well as pharmacists and patients. The Subcommittee considered that General Practitioners (GPs) and pharmacists working in primary care would be the health care professionals most likely to manage a brand switch. The Subcommittee considered that 3-6 months would be an appropriate timeframe to allow patients to transition to an alternative brand.
- 5.4 Members noted that patients with Parkinson's Disease were particularly susceptible to anxiety as part of the disease process. Members considered that due to this disease feature, patients may be particularly anxious around any changes to their medication and therefore pharmacists may need extra counselling time, as they may be required to reassure patients of any change in the appearance of their medication. The Subcommittee considered that a leaflet, similar to the one provided to primary care around a brand switch for carvedilol, would be helpful for implementation, especially if there were any changes to the appearance of the packaging and the tablets.

6 Antiepilepsy Drugs

Vigabatrin

- 6.1 The Subcommittee noted that PHARMAC sought advice on the appropriate use of vigabatrin following a number of Named Patient Pharmaceutical Assessment (NPPA) applications for various AEDs for treatment refractory epilepsy whereby applicants considered that vigabatrin was not a clinically suitable funded treatment due to possible visual field defects.
- 6.2 The Subcommittee noted that vigabatrin was funded via Special Authority criteria for patients with infantile spasms or refractory epilepsy; in conjunction with regular

visual field testing or where regular visual field testing was impractical or impossible. The Subcommittee noted that just over half of all patients taking vigabatrin regularly were aged 19 years or younger. The Subcommittee considered that there was an ongoing clinical need for vigabatrin to be listed in both the community and hospital schedule and considered that the current Special Authority criteria remained appropriate.

- 6.3 The Subcommittee noted that vigabatrin has been associated with vision loss which is permanent and irreversible if it occurs. The Subcommittee considered that the groups most likely to benefit from vigabatrin would be paediatric epilepsy patients with infantile spasms or hypsarrhythmia, and that for these indications vigabatrin would be a clinically appropriate treatment. The Subcommittee considered that in adult patients, with refractory epilepsy, the risk of permanent vision loss, in most cases, is likely to outweigh the potential benefits. The Subcommittee considered that in the majority of adult patients with treatment refractory epilepsy that vigabatrin would not be a clinically appropriate treatment.
- 6.4 The Subcommittee noted that there may be other types of paediatric epilepsies, in addition to infantile spasms and hypsarrhythmia, where vigabatrin is a clinically appropriate treatment, and **recommended** that PHARMAC seek further advice from a paediatric epilepsy expert on this.

Midazolam

- 6.5 The Subcommittee noted that PHARMAC had received two requests from general practices to make midazolam injection for use in the treatment of status epilepticus available on a Practitioners Supply Order (PSO), and that PHARMAC was seeking advice regarding these requests.
- 6.6 The Subcommittee considered that the plastic 5 mg per ml (3 ml) ampoules were used to administer midazolam buccally for the treatment of status epilepticus in the hospital setting. Members noted that the plastic ampoules are used for this indication as they are able to be squeezed.
- 6.7 The Subcommittee considered that midazolam administered buccally has the same or similar therapeutic effect to rectal diazepam. The Subcommittee noted diazepam was a longer acting benzodiazepine. However, Members considered that midazolam may be a more suitable alternative as it is easier to administer, allows dose titration (via dripping the solution buccally) and was not able to be expelled, as is the case with rectal diazepam.
- 6.8 The Subcommittee considered that the patient group that would most likely benefit from plastic midazolam ampoules being available on a PSO would be any patients in community at risk of status epilepticus.
- 6.9 The Subcommittee considered that if buccal midazolam was made available on a PSO for epilepsy that this would be utilised by children in supportive care, children or adults with severe developmental delay and elderly patients in care homes. The Subcommittee considered that if buccal midazolam was made available by PSO, over 80% of practitioners would switch from using rectal diazepam.

- 6.10 The Subcommittee considered that there may be a higher prevalence of epilepsy among Maori compared with the overall population.
- 6.11 The Subcommittee considered that the use of buccal midazolam would be unlikely to create any significant changes in health sector expenditure.
- 6.12 The Subcommittee noted that the midazolam 1 mg per ml (5ml) glass ampoule did not need to be available on a PSO for use in epilepsy. However, Members noted that this, and the plastic midazolam 5 mg per ml (3ml) ampoule, would likely be of interest to palliative care, dentists and any practitioner providing minor paediatric procedures or emergency care.
- 6.13 The Subcommittee **recommended** that two ampoules of midazolam (5 mg per ml, 3ml plastic ampoules) for the treatment of status epilepticus be available on a PSO with a **high** priority.
- 6.14 The Subcommittee considered that if, buccal midazolam was available on a PSO for the treatment of status epilepticus, that 2 ampoules would be required as the maximum quantity to allow for a spare ampoule at all times.

Gabapentin/pregabalin commercial process

- 6.15 The Subcommittee noted that PHARMAC was considering running a commercial process that could result in sole supply of both gabapentin and pregabalin and sought advice from the Subcommittee regarding assumptions for patient numbers and the rate that patients would be expected to move to treatment with pregabalin, if it was available.
- 6.16 The Subcommittee noted that neuropathic pain was a difficult condition to treat and gabapentin was usually used when other treatments had failed. Members considered that neither gabapentin nor pregabalin are particularly clinically effective for treating neuropathic pain. Members considered that improved access to non-pharmacological treatments that are routinely used in the management of chronic pain, including physical and psychological therapies and educating patients about their treatments was needed.
- 6.17 The Subcommittee considered that if a cost neutral pricing for pregabalin was achieved, it would be clinically appropriate to apply the same Special Authority (SA) and hospital restrictions as for gabapentin.
- 6.18 The Subcommittee considered that that approximately 30% of patients on gabapentin would gradually switch to pregabalin. Members were uncertain how quickly switching to pregabalin would occur. Members did consider however that funding pregabalin would result in market growth of approximately 30-50%. The Subcommittee considered that this increase in volume would likely be due to patients who still have refractory neuropathic pain but have ceased treatment with gabapentin due to lack of efficacy or tolerability.
- 6.19 The Subcommittee noted that gabapentin and pregabalin have recently been reported in an editorial as drugs of misuse (Stannard. Addiction 2016;111:1699-1700).

6.20 The Subcommittee noted that it has not reviewed evidence to support the use of pregabalin and gabapentin in combination, and therefore it considered that it would seem clinically reasonable to limit the use of gabapentin and pregabalin in combination, to minimise fiscal risk.

7 Apomorphine

- 7.1 The Subcommittee noted that PHARMAC was planning on running a commercial process for one supplier of apomorphine and apomorphine infusion pumps and sought clinical advice from the Subcommittee on the appropriateness of the varying presentations of apomorphine and any implementation activities which would be required should a brand change result.
- 7.2 The Subcommittee noted that apomorphine was used for motor response in late stage Parkinson's where conventional oral therapy was no longer providing the desired effect and for patients with early onset Parkinson's Disease where Deep Brain Stimulation would not be suitable or had failed. Members noted there were a small number of patients not receiving apomorphine but who were currently receiving compassionate supply of an intestinal infusion of levodopa/carbidopa (Duodopa) following on from a clinical trial.
- 7.3 The Subcommittee considered that that the following presentations of apomorphine would have the same or similar therapeutic effect: 5 mg per ml (20 ml vial), 5 mg per ml (10 ml prefilled syringe) and 10 mg per ml (1 ml, 2ml and 5 ml ampoules). The Subcommittee considered that there was no clinical reason that any of the apomorphine presentations would not be suitable for sole supply. However, the Subcommittee considered that the smaller presentation of apomorphine would be likely to reduce wastage.
- 7.4 The Subcommittee considered that approximately 90% of patients were administering apomorphine via a pump with the remaining 10% administering by intermittent injection. The Subcommittee considered that any of the presentations (described above) would be suitable for intermittent dosing; however, if only larger volumes of apomorphine were available ie a 10 mg per ml (20 ml vial), or a 10 mg per ml (10 ml prefilled syringe) there would be increased wastage. Members noted that patients using intermittent dosing typically use 2–5 injections of 4–6 mg per day, ie 8-30mg per day. The Subcommittee noted that patients, typically, would draw up the contents of one 10 mg per ml (10 mg vial) undiluted into 2 x 1 ml syringes and that very few patients require doses of >5 mg per injection. One member advised that there are no patients using >50 mg per day. Members considered the use of a pump was more practical for patients who require \geq 50 mg per day.
- 7.5 The Subcommittee considered that approximately 30-40% of patients in New Zealand who are using the pump use a syringe spacer. This allows them to load 10 ml rather than 20 ml to administer doses of ≤50 mg per day. At present they use 3 x 2 ml ampoules (60 mg) and make this up to 12 ml via a 1:1 dilution with saline, then discard 2 ml.

- 7.6 The Subcommittee considered that literature values suggest mean daily doses, when administered via an infusion pump, of 66 mg per day (Borgemeester et al Parkinsonism Relat Disord 2016;23:17-22) and 75 mg per day (Walter and Odin J Med Econ 2015;18:155-165). The Subcommittee noted that typical pump infusion rates in NZ are 3-6 mg/hr for 12-16 hours per day for the majority of patients. However, Members noted that there are a small number of patients (~6) who receive, in addition to this, 1.5-3 mg per hour overnight. The typical pump infusion dose range would be 36-120 mg per day, (with a mean daily dose likely to be 60 70 mg per day), with additional bolus doses of 6-36 mg per day thus making the typical daily pump dose 36-156 mg per day. Members considered that there was therefore potential for wastage especially for patients receiving just over 100 mg per day and just over 50 mg per day, if only large volumes of apomorphine were available ie a 10 mg per ml (20 ml vial), or a 10 mg per ml (10 ml prefilled syringe).
- 7.7 The Subcommittee considered that very few patients using an infusion pump would also be using intermittent dosing (2-5 injections of 4-6 mg per day); however, most patients using a pump use pump boluses of 2 -6 boluses at 50% of the hourly rate i.e. 6-36 mg per day. Members considered that for bolus dosing, the effect would be to bring people closer to, or above the total mg in one unit and would not be likely to increase wastage.
- 7.8 The Subcommittee noted that apomorphine was investigated as a treatment for erectile dysfunction. However, due to the side-effects of sudden vomiting was not suitable for this indication. The Subcommittee were not aware of any other apomorphine treatment indications apart from Parkinson's Disease.
- 7.9 The Subcommittee was not aware of any clinical circumstances whether apomorphine may be mixed with other injectables, other than saline.
- 7.10 The Subcommittee noted that no patients or DHBs are buying pumps and that these, along with the pump syringes, are provided 'free of charge' by the supplier. Members considered that there appeared to be some national inconsistency with regards to provision of consumables for the pump with some DHBs providing these to patients and some patients being required to privately purchase them. Members expressed a concern with regards to equity of access and considered that ideally all patients should receive the consumables without having to pay for them.
- 7.11 The Subcommittee noted that as part of a competitive process PHARMAC may consider proposals which include all associated consumables. Members considered that PHARMAC should consider that there may be a patient preference for Neria needles, which are inserted at 90 degrees to the skin surface, as opposed to the commonly used butterfly needles as they can be difficult to insert. However, Members noted that Neria needles were significantly more expensive compared to butterfly needles.
- 7.12 The Subcommittee considered essential features of an infusion pump would be to have rate modifier components, and more than one rate programmable rate (preferably 3 rates) to allow variations between night time and day time use. The size of the pump is a key component to patient comfort, the smaller the better. Long battery life and easy to use functionality.

- 7.13 The Subcommittee noted most patients, ~60% had apomorphine administered by their partner, relative or carer, 30% self-administered and a small portion (~5%) had it administered by a district nurse/care home staff. Members noted that this could vary by region.
- 7.14 The Subcommittee noted that although there had not been a change in brand, the recent change in distributor had felt like a brand change and Members felt that there had been a lack of communication from the distributors about the change. Members noted that to support transition during the change in distributor, a company nurse had been provided, and considered that this provision of resource had greatly reduced the time needed from neurologists and DHB nurses to help with the management (initiation and maintenance) of patients on pumps. The Subcommittee considered that if there was to be a change in brand of apomorphine that the provision of this nursing service would need to be contemplated. Members considered that if there was to be a change in brand that it may be useful to discuss any implementation materials/communications with a neurology nurse that assists with the management of apomorphine.
- 7.15 The Subcommittee considered that neurology nurses would most likely manage a brand switch; however, it noted that there are other Health Care Professionals (HCPs) involved in the management of PD such as GPs and geriatricians. The Subcommittee considered that 3 to 6 months would be an appropriate time frame to allow patients to transition to an alternative brand.
- 7.16 The Subcommittee noted that the use of apomorphine has rapidly increased since 2014. The Subcommittee considered that this had resulted from a change in clinical practice due to a leading clinician in PD management gaining experience with use of apomorphine and subsequent education of other centres was likely to account for the rapid increase in use. The Subcommittee considered that this increase in use reflected response to an unmet health need, as many patients had previously had limited access often due to their location and access to a Neurology service