

27 May 2008

Proposal for levetiracetam

Proposal summary

PHARMAC and Rex Medical Ltd have reached a provisional agreement for funding of a new treatment for epilepsy, levetiracetam.

Under this agreement, Rex Medical's brand of levetiracetam (Levetiracetam-Rex) would be funded without the requirement for Special Authority approval, meaning that it would be subsidised if prescribed by any relevant practitioner for any patient.

The funding of Levetiracetam-Rex is dependent on it gaining Medsafe registration and, due to Medsafe's regulations relating to generic pharmaceuticals, the registration process for Levetiracetam-Rex cannot start until December 2009.

In the meantime, PHARMAC proposes to make funding for levetiracetam available to the small group of patients who have first tried all other funded options and found them to be ineffective. Applications would be considered on a case by case basis via application to a panel.

Until a secured supply of a registered product is available via a funding agreement, obtaining supply would be on an *ad hoc* basis by the patient's doctor and pharmacist. Under such an arrangement there would be no surety of ongoing supply of any particular brand/formulation of levetiracetam, or of any levetiracetam at all.

If the proposal is approved the special access funding would be available from 1 August 2008.

Further details of the proposal can be found on the following pages.

Feedback sought

We welcome your feedback on this proposal. To provide feedback please submit an email, fax or letter by **4 pm, Friday 13 June 2008** to:

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PHARMAC	
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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

The details of the proposal

Levetiracetam-Rex

We have entered into a provisional agreement with Rex Medical Ltd to list Levetiracetam-Rex (levetiracetam) at the following prices and subsidies (ex-manufacturer, excluding GST), as soon as is practical following Medsafe registration:

Pharmaceutical	Brand	Form and Strength	Pack Size	Proposed list price and subsidy
Levetiracetam	Levetiracetam-Rex	Tablet 250 mg	60	\$24.03
Levetiracetam	Levetiracetam-Rex	Tablet 500 mg	60	\$28.71
Levetiracetam	Levetiracetam-Rex	Tablet 750 mg	60	\$45.23

Levetiracetam-Rex would have protection from delisting and subsidy reduction for a period of 3 years after the date of listing or until 1 July 2013, whichever is sooner.

Levetiracetam Special Access

From 1 August 2008 until a fully funded registered version of levetiracetam is listed in the Pharmaceutical Schedule, levetiracetam would be available to selected patients via application to a Levetiracetam Special Access Panel (LSAP) to be established by PHARMAC.

Applications would be considered by the LSAP at regular meetings and approved subject to compliance with the eligibility criteria.

Applications would need to be made on the approved forms which would be available from the coordinator for LSAP (contact details would be listed in the Pharmaceutical Schedule) and on PHARMAC's website.

Completed application forms would need to be sent to the coordinator for LSAP and would be considered by LSAP at the next practical opportunity. Notification of LSAP's decision would then be sent to the applying clinician.

Under this scheme, it is likely that the subsidy that PHARMAC would be paying for levetiracetam would be considerably more than the prices negotiated for Levetiracetam-Rex. For this reason, we would need to ensure that funding of levetiracetam under this scheme is limited to those patients who are most in need. At a minimum, patients would need to meet the following criteria:

- must have been diagnosed with epilepsy; and
- must have been given a reasonable trial or be contraindicated with all currently funded antiepilepsy agents; and
- either seizures are not adequately controlled with optimal treatment with other funded antiepilepsy agents or seizures are controlled adequately but the patient

has experienced unacceptable side effects from optimal treatment with other funded antiepilepsy agents.

Applicants would be required to provide a detailed history of the patient's antiepilepsy treatment.

Initial approvals would be valid for 6 months, with renewals of 12 months where the patient has demonstrated a significant and sustained improvement in seizure rate or severity and/or quality of life from levetiracetam.

Applicants would also be required to provide details of the pharmacy where the patient would collect their medication (the 'nominated pharmacy') and details of the dose of levetiracetam required, the brand of levetiracetam that the pharmacy intends to dispense (if known), and an estimate of the cost of levetiracetam (as quoted by the nominated pharmacy). Funding of levetiracetam under this scheme would be available for any brand of levetiracetam that the pharmacy is able to source, whether it is registered by Medsafe or not, at the pharmacy's purchase price (known as "cost brand source").

If at a later date a fully funded version of levetiracetam is listed in the Pharmaceutical Schedule, approvals under the Special Access scheme would eventually lapse and funding would then be available only for the listed version(s) of levetiracetam (with surety of supply and pricing).

Background to the proposal

PHARMAC received an application to fund levetiracetam (the Keppra brand) for the treatment of epilepsy in May 2005. The application was considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) in August 2005. PTAC recommended listing levetiracetam in the Pharmaceutical Schedule as an adjunctive agent for the treatment of partial seizures, and gave a high priority to this recommendation. PHARMAC subsequently began negotiations with the supplier of the Keppra brand of levetiracetam (UCB Australia). However, despite our best efforts an agreement has not yet been reached, primarily due to the supplier's concerns in connection with PHARMAC's standard requirements around patient safety and continuity of supply.

PHARMAC has now reached a provisional agreement with Rex Medical Ltd to fund its brand of levetiracetam (Levetiracetam-Rex), subject to regulatory consent being issued. As part of Medsafe's consent process, generic pharmaceuticals must demonstrate that they are bioequivalent to the innovator brand, with clinical data from the innovator brand being used to demonstrate that the pharmaceutical itself is safe and effective. However, the innovator brand's clinical data are protected for 5 years from being used in this manner (known as 'data protection' or 'data exclusivity'). The Keppra brand of levetiracetam currently has data protection until December 2009, meaning that Medsafe cannot consider an application to register a generic brand until after this date. This means that the earliest likely listing date under this proposal would be mid 2010.

In the meantime, we propose listing levetiracetam in the Pharmaceutical Schedule cost brand source (indicated in the Pharmaceutical Schedule via the entry "CBS") meaning that there is no set manufacturer's price, and PHARMAC would subsidise the product at the price of whichever brand of levetiracetam the pharmacy is able to source,

regardless of whether or not the brand is registered). Access to subsidies would follow application to a panel to ensure that patients with epilepsy who have no other treatment options available to them can access subsidised levetiracetam.

We highlight that under this arrangement there would be no provisions for surety of ongoing supply of any particular brand/formulation of levetiracetam, or of any levetiracetam at all.