NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

**7 March 2013**

# Decision to fund unapproved medicines for various conditions

PHARMAC is pleased to announce the approval of an agreement with Link Pharmaceuticals Limited to list various unapproved medicines from 1 April 2013. This agreement was the subject of a consultation letter dated 14 January 2013, which can be found on PHARMAC's website at www.pharmac.health.nz/news. Details of the decision are provided on the following pages. In summary:

- The following pharmaceuticals will be listed in Section B and/or Part II of Section H of the Pharmaceutical Schedule from 1 April 2013:

  Benzbromarone for gout

  Diazoxide for hyperinsulinism

  Para-amino salicylic acid and protionamide for tuberculosis infection

  Paromomycin for cryptosporidium infection

  Tetracycline and bismuth for helicobacter pylori infection

  Stiripentol for Dravet syndrome

  Nitazoxanide for protozoan infection

  Pegaspargase (also known as pegylated asparaginase) for acute lymphoblastic leukaemia in combination with chemotherapy

- PHARMAC was made aware during consultation of the possibility of securing supply of an approved brand of rifaximin (a treatment for hepatic encephalopathy). As a consequence, PHARMAC has decided not to fund an unapproved brand of rifaximin at this time. In the meantime, clinicians can continue to make applications for funding of rifaximin via the Named Patient Pharmaceutical Assessment (NPPA) process.

- A number of minor changes to access criteria were made following consideration of consultation responses.

- The brand, strength and pack size of tetracycline to be funded has changed from the proposal consulted on following further consideration of the use of this medicine.

We would like to reiterate that PHARMAC's funding of an unapproved medicine is not an endorsement of the medicine's quality, safety or efficacy. Further, a practitioner prescribing an unapproved medicine is still obligated to comply with relevant legislation and regulations (including the Health and Disability Commissioner's Code of Consumer Rights).

As with any pharmaceutical listed in the Pharmaceutical Schedule, funding will be provided if a prescriber choses to prescribe one of these medicines (providing any funding access criteria are met) but there is no obligation on practitioners to prescribe these medicines if they do not consider them appropriate for their patient.



Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

## Details of the decision

- From 1 April 2013, the following pharmaceuticals will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule (prices and subsidies ex-manufacturer, excluding GST):

| Pharmaceutical | Brand | Form and Strength | Pack Size | Price and Subsidy |
|---|---|---|---|---|
| Benzbromarone | Benzbromaron | Tablet 100 mg | 100 | $45.00 |
| Diazoxide | Proglicem | Capsule 25 mg | 100 | $110.00 |
| Diazoxide | Proglicem | Capsule 100 mg | 100 | $280.00 |
| Para-amino salicylic acid | Paser | Grans for oral liq 4 g sachet | 30 | $280.00 |
| Paromomycin | Humatin | Capsule 250 mg | 16 | $126.00 |
| Pegaspargase* | Oncaspar | Inj 3,750 IU per 5 ml | 1 | $3,005.00 |
| Protionamide | Peteha | Tablet 250 mg | 100 | $305.00 |
| Tetracycline | Tetracyclin Wolff | Capsule 500 mg | 30 | $46.00 |
| Stiripentol | Diacomit | Capsule 250 mg | 60 | $509.29 |
| Stiripentol | Diacomit | Sachet 250 mg | 60 | $509.29 |
| Bismuth trioxide | De-Nol | Tablet 120 mg | 112 | $32.50 |

*Pegaspargase is a hospital-administered Pharmaceutical Cancer Treatment (PCT) and will be listed in Section B for claiming purposes only.

- From 1 April 2013, nitazoxanide will be listed in Part II of Section H of the Pharmaceutical Schedule as follows (price ex-manufacturer, excluding GST):

| Pharmaceutical | Brand | Form and Strength | Pack Size | Price |
|---|---|---|---|---|
| Nitazoxanide | Alinia | Tablet 500 mg | 30 | $1,680.00 |

- The following restrictions will apply to the relevant pharmaceuticals in Section B of the Pharmaceutical Schedule from 1 April 2013:

**Diazoxide (Proglicem)**

**Special Authority for Subsidy**
**Initial application** from any relevant practitioner. Approvals valid for 12 months where used for the treatment of confirmed hypoglycaemia caused by hyperinsulinism.

**Renewal** from any relevant practitioner. Approvals valid without further renewal unless notified where the treatment remains appropriate and the patient is benefiting from treatment.

**Paromomycin (Humatin)**

**Special Authority for Subsidy**
**Initial application** only from an infectious disease specialist or clinical microbiologist. Applications valid for 1 month where the patient has confirmed cryptosporidium infection.

**Renewal** only from an infectious disease specialist or clinical microbiologist. Applications valid for 1 month where the patient has confirmed cryptosporidium infection.

**Benzbromarone (Benzbromaron)**

**Special Authority for Subsidy**
**Initial application** from any relevant practitioner. Applications valid for 6 months for applications meeting the following criteria:
Both:

1 Any of:
   1.1 The patient has a serum urate level greater than 0.36 mmol/l despite treatment with allopurinol at doses of at least 600 mg/day and appropriate doses of probenecid; or
   1.2 The patient has experienced intolerable side effects from allopurinol such that treatment discontinuation is required and serum urate remains greater than 0.36 mmol/l despite appropriate doses of probenecid; or
   1.3 Both:
      1.3.1 The patient has renal impairment and serum urate remains greater than 0.36 mmol/l despite optimal treatment with allopurinol (see Note); and
      1.3.2 The patient has a rate of creatinine clearance greater than or equal to 20 ml/min; or
   1.4 All of the following:
      1.4.1 The patient is taking azathioprine and requires urate-lowering therapy; and
      1.4.2 Allopurinol is contraindicated; and
      1.4.3 Appropriate doses of probenecid are ineffective or probenecid cannot be used due to reduced renal function; and
2 The patient is receiving monthly liver function tests.

**Renewal** from any relevant practitioner. Applications valid for 2 years for applications meeting the following criteria:
Both:

1 The treatment remains appropriate and the patient is benefitting from treatment; and
2 There is no evidence of liver toxicity and patient is continuing to receive regular (at least every three months) liver function tests.

Notes: Benzbromarone has been associated with potentially fatal hepatotoxicity.
Optimal treatment with allopurinol in patients with renal impairment is defined as treatment to the creatinine clearance-adjusted dose of allopurinol then, if serum urate remains greater than 0.36 mmol/l, a gradual increase of the dose of allopurinol to 600 mg or the maximum tolerated dose.

**Para-amino Salicylic Acid (Paser)**

Retail Pharmacy – Specialist. Specialist must be an infectious disease specialist, clinical microbiologist or respiratory physician.

**Protionamide (Peteha)**

Retail Pharmacy – Specialist. Specialist must be an infectious disease specialist, clinical microbiologist or respiratory physician.

**Tetracycline (Tetracyclin Wolff)**

**Special Authority for Subsidy**
**Initial application** from any relevant practitioner. Approvals valid for 3 months for applications meeting the following criteria:
Both:

1 For the eradication of helicobacter pylori following unsuccessful treatment with appropriate first-line therapy; and
2 For use only in combination with bismuth as part of a quadruple therapy regimen.

**Stiripentol (Diacomit)**

**Special Authority for Subsidy**
**Initial application** only from a paediatric neurologist or Practitioner on the recommendation of a paediatric neurologist. Approvals valid for 6 months for applications meeting the following criteria:
Both:

1 Patient has confirmed diagnosis of Dravet syndrome; and
2 Seizures have been inadequately controlled by appropriate courses of sodium valproate, clobazam and at least two of the following: topiramate, levetiracetam, ketogenic diet.

**Renewal** from any relevant practitioner. Approvals valid without further renewal unless notified where the patient continues to benefit from treatment as measured by reduced seizure frequency from baseline.

**Pegaspargase (Oncaspar)**

PCT only – Specialist - **Special Authority for Subsidy**
**Initial application** only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1 The patient has newly diagnosed acute lymphoblastic leukaemia; and
2 Pegaspargase to be used with a contemporary intensive multi-agent chemotherapy treatment protocol; and
3 Treatment is with curative intent.

**Renewal** only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1 The patient has relapsed acute lymphoblastic leukaemia; and
2 Pegaspargase to be used with a contemporary intensive multi-agent chemotherapy treatment protocol; and
3 Treatment is with curative intent.

- Decisions on restrictions that may apply in DHB hospitals from 1 July 2013 have not yet been made for all these pharmaceuticals; however it is likely that any such restrictions would be similar to those outlined above.

## Feedback received

We appreciate all the feedback that we received and acknowledge the time people took to respond. All consultation responses received were considered in their entirety in making the decisions on the proposed changes. Most responses were supportive of the proposal, and the following common issues were raised in relation to specific aspects of the proposal:

| Response/Issue | PHARMAC comments |
|---|---|
| ***General issues/responses*** | |
| A responder requested clarification of the proposed changes to the wastage rules – specifically, could a pharmacist dispense the remainder of partly-used packs and only claim for what they are unable to dispense, or do they have to claim for the full pack on the first dispensing even if only part of the pack was dispensed? | The wastage rule is designed to allow pharmacy to claim for the remainder of a product when they are unable to use it. The procedures manual notes the following with respect to the wastage rule: "Remainder can be claimed as wastage if unused. At the time of dispensing the Pharmacist must keep a record of the quantity discarded". PHARMAC anticipates that pharmacy would be able to claim wastage for what they are unable to dispense. For example, if a patient has repeats the wastage should only be claimed once the prescription is completed. If a patient returns with a new prescription and the pharmacist has not |

| | |
|---|---|
| | discarded the stock then the pharmacy should unclaim the wastage and continue to use stock.<br>The wastage rule is different from the Original Pack rule where the entirety of the pack must be claimed at each dispensing. We note that it is considered fraud to claim wastage and then use the remaining product. |
| Responders noted that there are costs to pharmacies associated with the supply of unapproved medicines that are likely to exceed the current level of stockholding and dispensing reimbursement from DHBs. | We acknowledge that in some cases the costs associated with unapproved medicines may not be covered by the DHB stock and dispensing reimbursement in the current Community Pharmacy Services Agreement (CPSA). We consider that this is a distribution issue, not a pharmaceutical funding issue; therefore, we encourage pharmacies to discuss with DHBs the possibility of addressing the issue via an amendment to the existing CPSA. |
| One responder was concerned about the risks to patients associated with the prescribing and use of unapproved medicines and suggested that there should be a requirement for written, informed consent for funded unapproved medicines, including a requirement for clinicians to clearly state the risks and benefits to the patient. | Consumer protection – particularly with respect to matters such as informed consent – is managed by the obligations on practitioners set out in the Health & Disability Commissioner's (HDC) Code of Consumer Rights, including the obligation to obtain informed consent. The Pharmaceutical Schedule clearly states (in the glossary) with respect to unapproved medicines that practitioners should be aware with and comply with their obligations under the Medicines Act 1981 & its regulations, the HDC Code of Consumer rights, as well as "exercise their own skill, judgement, expertise and discretions, and make their own prescribing decisions with respect to the use of an unapproved pharmaceutical". |
| *Benzbromarone-specific responses* | |
| There were a number of responses in relation to the safety of benzbromarone and the importance of liver function monitoring to reduce the risk of harm. | Regular liver function monitoring is a requirement of both the initial and the renewal criteria. We consider that it is the responsibility of the prescriber to ensure that the testing is performed if they are continuing to prescribe benzbromarone.<br><br>Updated information about gout treatment, including the safe and appropriate use of benzbromarone, will be included in the March 2013 issue of Best Practice Journal. |
| A number responders requested changes to the proposed Special Authority criteria for benzbromarone. | Some of these changes have been made and/or will be addressed in the abovementioned Best Practice Journal article. Some requested changes were not implemented at this time either because they were inconsistent with clinical advice we had received from our advisory committee or because we need to take further advice. We intend to monitor the use of benzbromarone with a view to making further changes to the access criteria in the future if necessary. |
| *Diazoxide-specific responses* | |
| Several responders requested funding of an | We acknowledge that compounding preparations |

| | |
|---|---|
| oral liquid preparation of diazoxide, particularly for paediatric patients. One responder considered that an extemporaneously compounded product made from the capsules would not be appropriate, mainly because it is only stable for 7 days and must be refrigerated. | such as diazoxide suspension is time consuming for pharmacy particularly given that this product has a short expiry date. We would be willing to consider funding a proprietary oral liquid formulation if it is similar to the cost of extemporaneously compounding the product; however, at this time we are not aware of an oral liquid product in this price range. |
| *Nitazoxanide-specific responses* | |
| One responder requested funding of an oral liquid preparation of nitazoxanide for paediatric patients. | We are not aware of any significant unmet clinical need for an oral liquid presentation. If a patient required the oral suspension a Named Patient Pharmaceutical Assessment (NPPA) application could be made. We will monitor NPPA applications with a view to re-visiting this issue if necessary. |
| *Pegaspargase-specific responses* | |
| Several responders commented on the proposed age restrictions. | After consideration of the responses, and the clinical advice we had previously received, the age-related restrictions have been removed. |
| *Tetracycline-specific responses* | |
| One responder noted that a renewal application for tetracycline is not necessary as the treatment should only be given once and having a renewal option would encourage inappropriate prescribing. The same responder considered that the full details of the quadruple treatment should be included in the Special Authority (omeprazole 20 mg bd, tetracycline 500 mg qid, bismuth one tabled qid and metronidazole 400 mg tds). | After reviewing this response the renewal was removed from the Special Authority and the wording of criterion 2 was altered to refer to quadruple therapy. We encourage prescribers to review prescribing guidelines, such as those on the New Zealand Society of Gastroenterology website, for full details of the appropriate quadruple therapy regimen. |
| *Rifaximin-specific responses* | |
| Among other responses relating to rifaximin, a supplier of rifaximin notified PHARMAC that it is in the process of seeking registration of its brand of rifaximin in New Zealand. | It is PHARMAC's preference to fund approved pharmaceuticals where possible. Therefore, rifaximin was removed from the agreement with Link and we intend to progress a proposal to fund an approved version at a later date. The other rifaximin-related responses to the Link consultation will be taken into account when any decision is made on rifaximin in the future. |

## More information

If you have any questions about these decisions, you can call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.