CONSULTATION

PHARMAC
Pharmaceutical Management Agency

20 May 2015

Proposal for various pharmaceuticals

PHARMAC is seeking feedback on a proposal for various pharmaceuticals, including a new listing and amendments to funding restrictions, to take effect from 1 August 2015 (unless otherwise specified). The proposed changes are summarised below. Details of the proposed changes and background information can be found on the following pages.

The restrictions applying to the following products would be amended in Section B and/or Part II of Section H of the Pharmaceutical Schedule (as applicable) from 1 August 2015 (unless otherwise specified):

- Aripiprazole: the Special Authority criteria and hospital restrictions would be amended to widen access for patients with severe irritability associated with autism spectrum disorder.
- Benzbromarone: the Special Authority criteria and hospital restrictions would be amended.
- Febuxostat: the Special Authority criteria and hospital restrictions would be amended.
- Diphtheria, tetanus and pertussis vaccine: access would be widened to include vaccination of all pregnant women between gestational weeks 28 and 38 (regardless of whether or not there is an epidemic) from 1 August 2015.
- Somatropin: the Special Authority criteria and hospital restrictions for Prader-Willi syndrome would be widened.
- Tacrolimus: the Special Authority criteria and hospital restrictions would be widened to include patients with treatment-resistant nephrotic syndrome.
- Valaciclovir: the Special Authority criteria and hospital restrictions would be removed from early 2016 (date yet to be determined).

The following product would be listed in Part II of Section H of the Pharmaceutical Schedule from 1 August 2015:

- Nicotine oral spray 1 mg per dose, subject to the same restrictions as nicotine solution for inhalation 15 mg cartridge.

Feedback sought

PHARMAC welcomes feedback on this proposal. **Please specify in your response which product(s) your feedback relates to.** To provide feedback, please submit it in writing by **5 pm** on **Thursday, 4 June 2015** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or its delegate) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request

Details of the proposal

Details of the proposed restriction changes and new listing are provided below. Existing Special Authority criteria and Hospital Medicines List (HML) restrictions for these pharmaceuticals can be found on PHARMAC's website at the links below – for practical reasons these may not be reproduced in their entirety for all pharmaceuticals in this consultation document.

www.pharmac.govt.nz/PharmaceuticalSchedule/Schedule?osq
www.pharmac.health.nz/tools-resources/pharmaceutical-schedule/section-h/

All proposed changes would occur on 1 August 2015 unless otherwise specified.

In relation to aripiprazole

- The Special Authority criteria applying to aripiprazole 10 mg, 15 mg, 20 mg and 30 mg tablets (Abilify) would be widened to include the following new indication in Section B of the Pharmaceutical Schedule:

  Initial application – (Autism spectrum disorder*) only from a psychiatrist or paediatrician.
  Approvals valid for 12 months for applications meeting the following criteria:
  All of the following:
  1 The patient has been diagnosed with an autism spectrum disorder* and has symptoms of severe irritability; and
  2 An effective dose of risperidone has been trialled and has been discontinued because of unacceptable side effects or inadequate response; and
  3 The patient is aged less than 18 years.

  Renewal application – (Autism spectrum disorder*) only from a psychiatrist or paediatrician or medical practitioner on the recommendation of a psychiatrist or paediatrician.
  Approvals valid for 2 years for applications meeting the following criteria:
  Both:
  1 The patient is aged less than 18 years; and
  2 The treatment remains appropriate and the patient is benefiting from treatment.
  Note: Indications marked with * are Unapproved Indications

- The HML restrictions for aripiprazole would be widened in the same way.

In relation to benzbromarone

- The Special Authority criteria applying to benzbromarone 100 mg tablets (Benzbromaron AL 100) would be amended as follows in Section B of the Pharmaceutical Schedule (additions in bold, deletions in strikethrough):

Initial application from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:
All of the following: ~~Both:~~
1 Patient has been diagnosed with gout; and
2 Any of the following:
2.1 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~~ **addition of** probenecid **at doses of up to 2 g per day or maximum tolerated dose**; or
2.2 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~~ **use of** probenecid **at doses of up to 2 g per day or maximum tolerated dose**; or
2.3 Both:
2.3.1 The patient has renal impairment **such that probenecid is contraindicated or likely to be ineffective** and serum urate remains greater than 0.36 mmol/l despite optimal treatment with allopurinol (see Notes); and
2.3.2 The patient has a rate of creatinine clearance greater than or equal to 20 ml/min.
2.4 All of the following:
2.4.1 The patient is taking azathioprine and requires urate-lowering therapy; and
2.4.2 Allopurinol is contraindicated; and
2.4.3 Appropriate doses of probenecid are ineffective or probenecid cannot be used due to reduced renal function; and
3 The patient is receiving monthly liver function tests.

Renewal from any relevant practitioner. Approvals valid for 2 years for applications meeting the following criteria:
Both:
1 The treatment remains appropriate and the patient is benefitting from the 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.
In chronic renal insufficiency, particularly when the glomerular filtration rate is 30 ml/minute or less, probenecid may not be effective. 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.
The New Zealand Rheumatology Association has developed information for prescribers which can be accessed from its website at www.rheumatology.org.nz/downloads/Benzbromarone-prescriber-information-NZRA-V2.pdf

- The HML restrictions for benzbromarone would be amended in the same way.

In relation to febuxostat

- The Special Authority criteria applying to febuxostat 80 mg and 120 mg tablets (Adenuric) would be amended as follows in Section B of the Pharmaceutical Schedule (additions in bold, deletions in strikethrough):

Initial application from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:
Both:
1 Patient has been diagnosed with gout; and
2 Any of the following:
2.1 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~~ **addition of** probenecid **at doses of up to 2 g per day or maximum tolerated dose**; or
2.2 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~~ **use of** probenecid **at doses of up to 2 g per day or maximum tolerated dose**; or
2.3 ~~Both:3.1~~ The patient has renal impairment **such that probenecid is contraindicated or likely to be ineffective** and serum urate remains greater than 0.36 mmol/l despite optimal treatment with allopurinol (see Notes)~~; and~~
~~3.2 The patient has a rate of creatinine clearance greater than or equal to 30 ml/min.~~

Renewal from any relevant practitioner. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefitting from the treatment.

Notes: **In chronic renal insufficiency, particularly when the glomerular filtration rate is 30 ml/minute or less, probenecid may not be effective. The efficacy and safety of febuxostat have not been fully evaluated in patients with severe renal impairment (creatinine clearance less than 30 ml/minute). No dosage adjustment of febuxostat is necessary in patients with mild or moderate renal impairment.** 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.

- The HML restrictions for febuxostat would be amended in the same way.

In relation to diphtheria, tetanus and pertussis vaccine

- The listing of diphtheria toxoid 2IU with tetanus toxoid 20 IU, pertussis toxoid 8 mcg, pertussis filamentous haemagluttinin 8 mcg and pertactin 2.5 mcg in 0.5 ml syringe (Boostrix) on the National Immunisation Schedule (Section I of the Pharmaceutical Schedule) would be amended as follows (deletions in strikethrough):

Funded for any of the following criteria:
1) A single vaccine for pregnant woman between gestational weeks 28 and 38 ~~during epidemics~~; or
2) A course of up to four vaccines is funded for children from age 7 to 17 years inclusive to complete full primary immunisation; or
3) A course of up to four vaccines is funded for children from age 7 to 17 years inclusive for reimmunisation following immunosuppression.

Notes: Tdap is not registered for patients aged less than 10 years. Please refer to the Immunisation Handbook for appropriate schedule for catch up programmes.

- The HML restrictions for diphtheria, tetanus and pertussis vaccine would be amended in the same way.

In relation to somatropin

- The initial Special Authority criteria for Prader-Willi syndrome applying to somatropin 5 mg, 10 mg and 15 mg injection (Omnitrope) would be amended as follows in Section B of the Pharmaceutical Schedule (deletions in strikethrough):

  Initial application — (Prader-Willi syndrome) only from a paediatric endocrinologist or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:
  All of the following:
  1 The patient has a diagnosis of Prader-Willi syndrome that has been confirmed by genetic testing ~~or clinical scoring criteria~~; and
  ~~2 The patient's height velocity is < 25th percentile (adjusted for bone age/pubertal status if appropriate) as calculated over 6 to 12 months using the standards of Tanner and Davies (1985); and~~
  ~~3 Either:~~
  ~~3.1 The patient is under two years of age and height velocity has been assessed over a minimum six month period from the age of 12 months, with at least three supine length measurements over this period demonstrating clear and consistent evidence of linear growth failure (with height velocity < 25th percentile); or~~
  ~~3.2 The patient is aged two years or older; and~~
  4 A current bone age is < 14 years (female patients) or < 16 years (male patients); and
  5 Sleep studies or overnight oximetry have been performed and there is no obstructive sleep disorder requiring treatment, or if an obstructive sleep disorder is found, it has been adequately treated under the care of a paediatric respiratory physician and/or ENT surgeon; and
  6 There is no evidence of type II diabetes or uncontrolled obesity defined by BMI that has increased by ≥ 0.5 standard deviations in the preceding 12 months.

- The HML restrictions for somatropin would be amended in the same way.

In relation to tacrolimus

- The Special Authority criteria applying to tacrolimus 0.5 mg, 1 mg and 5 mg capsules (Tacrolimus Sandoz) would be widened to include the following new indication in Section B of the Pharmaceutical Schedule:

  Initial application – (steroid resistant nephrotic syndrome) only from a relevant specialist. Approvals valid without further renewal unless notified for applications meeting the following criteria:
  Either
  1 The patient is a child with steroid resistant nephrotic syndrome (SRNS) where ciclosporin has been trialled in combination with prednisone and discontinued because of unacceptable side effects or inadequate clinical response; or
  2 The patient is an adult with SRNS: and
  2.1 Both
  2.1.1 Ciclosporin has been trialled in combination with prednisone and discontinued because of unacceptable side effects or inadequate clinical response; and
  2.1.2 Cyclophosphamide or mycophenolate have been trialled and discontinued because of unacceptable side effects or inadequate clinical response, or these treatments are contraindicated.

- The HML restrictions for tacrolimus would be amended in the same way.

In relation to valaciclovir

- The Special Authority criteria and HML restrictions applying to valaciclovir 500 mg tablets would be removed from early 2016 (date yet to be determined).

In relation to nicotine

- Nicotine oral spray 1 mg per dose (example brand name Nicorette QuickMist Mouth Spray) would be listed under the Treatments for Substance Dependence (Nervous System) subheading of Part II of Section H of the Pharmaceutical Schedule (the HML) subject to the following restrictions:

  Restricted
  Any of the following:
  1 For perioperative use in patients who have a 'nil by mouth' instruction; or
  2 For use within mental health inpatient units; or
  3 For acute use in agitated patients who are unable to leave the hospital facilities.

Background

Aripiprazole

Aripiprazole is an antipsychotic that is currently funded subject to Special Authority and HML restrictions as a second-line treatment for schizophrenia and related psychoses. PHARMAC has received a funding application to widen access to aripiprazole for patients with severe irritability associated with autism spectrum disorder. The proposed changes are in line with those recommended by the Pharmacology and Therapeutics Advisory Committee (PTAC) when it reviewed the application. A link to the relevant PTAC minutes can be found in the Application Tracker record on PHARMAC's website at:
www.pharmac.govt.nz/ApplicationTracker?ProposalId=1272

Benzbromarone and febuxostat

Benzbromarone and febuxostat are both funded subject to Special Authority and HML restrictions for patients with treatment-resistant gout. The Special Authority criteria for both treatments have recently been reviewed by the Rheumatology Subcommittee of PTAC and by PTAC. The proposed changes are in line with recommendations from PTAC, with the exception that PTAC recommended amending the dose of allopurinol required to be tried under criterion 2.1 from "at least 600 mg/day" to "at least 600 mg/day and up to 900 mg/day". While we are not currently proposing to make this change, we would be interested to receive feedback on PTAC's recommendation. Links to the PTAC and Subcommittee minutes can be found on the relevant Application Tracker record at:
www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1312

Diphtheria, tetanus and pertussis vaccine

Diptheria, tetanus and pertussis vaccine is currently funded for pregnant women between gestational weeks 28 and 38 during epidemics, as well as for patients aged 7-17 years. Following a request from a DHB, the Immunisation Subcommittee of PTAC recommended that pertussis vaccination of pregnant women between gestational weeks 28 and 38 should

be extended beyond epidemics with a high priority. This recommendation has been accepted by PTAC. A link to the relevant Subcommittee minutes can be found at:
www.pharmac.health.nz/assets/ptac-immunisation-subcommittee-minutes-2014-02.pdf

Somatropin

Somatropin is a form of human growth hormone. It is funded subject to Special Authority and HML restrictions for a range of patients with growth deficiencies, including Prader-Willi syndrome. During consultation on changes to somatropin funding in 2014, we received feedback in relation to the Prader-Willi syndrome criteria. The proposed changes are a result of consideration of this feedback.

Tacrolimus

Tacrolimus is an immunosuppressive agent used to reduce the risk of organ rejection following organ transplant. It is currently funded subject to Special Authority and HML restrictions for organ transplant recipients. Following receipt of a clinician funding application, PTAC recommended widening access to tacrolimus for patients with ciclosporin and steroid-resistant nephrotic syndrome essentially as proposed. The minutes of PTAC's discussion can be found in the Application Tracker record at:
www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1177

Valaciclovir

Valaciclovir is an antiviral agent used in the management of herpes. It is currently funded subject to Special Authority and HML restrictions for recurrent genital herpes, ophthalmic zoster, cytomegalovirus prophylaxis in patients who have undergone organ transplantation, and immunocompromised patients with herpes zoster. The Anti-Infective Subcommittee of PTAC recommended removal of the Special Authority provided that the costs to the health sector are acceptable, with a medium priority; this recommendation has been accepted by PTAC. The proposal is in line with this recommendation. If the proposal was approved, the date of Special Authority removal would be notified later in the year. Minutes of the Anti-Infective Subcommittee's discussion can be found in the Application Tracker record at:
www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1198

Nicotine oral spray

PHARMAC has assessed funding applications for nicotine inhaler and oral spray, for both community and hospital use. Currently nicotine inhaler is funded subject to restrictions on the HML only, following a recommendation by PTAC to list the inhaler and oral spray for urge control in patients in psychiatric wards, perioperative patients, and other agitated patients while in hospital. The Committee noted that the price of the inhaler was significantly less than the oral spray and that it may, therefore, be preferable to fund only the inhaler. As the oral spray is more expensive, only the inhaler was listed at the HML's inception in 2013. We have received a request from a DHB hospital to list the oral spray as well, as per this proposal. However, we note that it remains more expensive than the inhaler.

For the avoidance of doubt, we are not proposing to fund either the inhaler or oral spray for use in the community. These presentations have been reviewed by PTAC on several occasions, most recently in August 2014. The Committee noted that there was a lack of robust evidence of benefit beyond 6 months. Given this, and the potential for a large proportion of smokers to use the new formulations if funded, the Committee considered that there would be no clinical or financial justification to fund the new presentations if they were

more expensive than the average weighted daily cost of the existing funded treatments. Therefore, the Committee recommended that nicotine inhalers and/or nicotine oral spray be funded only if the average daily cost of each treatment was no more expensive than the weighted combined average daily cost of the currently funded nicotine presentations (gum, lozenges and patches). Given the current relative pricing, our assessment is that funding the new presentations would require new spending, which would be difficult to justify given the advice from PTAC and in the context of a large number of potential alternative funding options for treatments in other therapeutic areas and the range of smoking cessation treatments already funded (nicotine gum, patch and lozenge, bupropion, nortriptyline and varenicline).

More details about the applications can be found in the Application Tracker records at:
www.pharmac.govt.nz/ApplicationTracker?ProposalId=780
www.pharmac.govt.nz/ApplicationTracker?ProposalId=904