

5 May 2009

## Proposal relating to adalimumab, leuprorelin and levothyroxine and other autoimmune biologic community funding applications

### *Proposal summary*

PHARMAC is seeking feedback on a proposal to widen funded access to adalimumab for treatment of ankylosing spondylitis, Crohn's disease, severe chronic plaque psoriasis and psoriatic arthritis from 1 August 2009, through a provisional agreement with Abbott Laboratories NZ Ltd. The proposal would also result in widening of access to, and reference pricing of, leuprorelin and funding of a new brand of levothyroxine.

In addition, PHARMAC proposes to decline all outstanding community funding applications for etanercept (for rheumatoid arthritis, ankylosing spondylitis, severe chronic plaque psoriasis and psoriatic arthritis), abatacept (for rheumatoid arthritis), infliximab (for rheumatoid arthritis) and rituximab (for rheumatoid arthritis). If the adalimumab proposal is approved, we would undertake further economic assessment on the hospital-administered autoimmune biologic treatments with the aim of issuing advice to DHB hospitals on the cost-effectiveness of these pharmaceuticals in hospitals. Any decision by PHARMAC to decline these funding applications would not prevent PHARMAC from considering future proposals or applications for these medicines; however, it would clearly indicate that no active work on funding these treatments through the Pharmaceutical Schedule would be occurring at this time.

Key aspects of the funding proposal are as follows (all would be implemented 1 August 2009 unless otherwise stated):

#### *Adalimumab (Humira and HumiraPen)*

- Access to adalimumab in Section B of the Pharmaceutical Schedule would be widened to include "last-line" treatment of ankylosing spondylitis, Crohn's disease, psoriasis and psoriatic arthritis. **Proposed Special Authority criteria are attached at the end of this consultation letter.**
- Adalimumab would be subject to a confidential rebate, reducing the net price of this medicine.

#### *Leuprorelin (Lucrin Depot, Lucrin PDS Depot, Eligard)*

- The Special Authority criteria would be removed from leuprorelin.
- A new, prefilled syringe presentation of leuprorelin (Lucrin PDS Depot), including a 6-month (30 mg) preparation, would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule as soon as possible following Medsafe registration.
- A rebate would apply to Lucrin Depot and Lucrin PDS Depot the effect of which would reduce the net price by 25%.
- The subsidy for Eligard would be reduced to the net effective price of Lucrin Depot and Lucrin PDS Depot from 1 October 2009 through the application of reference pricing.

#### *Levothyroxine (Synthroid)*

- A new brand of levothyroxine (Synthroid) tablets 25 µg, 50 µg and 100 µg would be listed in Section B of the Pharmaceutical Schedule.

Further details, including how to provide feedback, 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 29 May 2009** to:

Geraldine MacGibbon                      Email: [geraldine.macgibbon@pharmac.govt.nz](mailto:geraldine.macgibbon@pharmac.govt.nz)  
Therapeutic Group Manager          Fax: (04) 460 4995  
PHARMAC  
PO Box 10-254  
Wellington 6143

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

## **Further details of the Proposal**

### *Adalimumab (Humira and HumiraPen)*

Adalimumab is currently funded, subject to Special Authority criteria, as a "last-line" treatment for rheumatoid arthritis.

The Pharmacology and Therapeutics Advisory Committee (PTAC) has reviewed applications to widen access to adalimumab for use as a last-line treatment for ankylosing spondylitis, Crohn's disease, psoriasis and psoriatic arthritis. The relevant Minutes from the various meetings at which these applications were discussed (November 2006, August 2007, November 2007 and July 2008) can be found on PHARMAC's website at [www.pharmac.govt.nz/PTACminutes](http://www.pharmac.govt.nz/PTACminutes).

We have subsequently reached a provisional agreement with Abbott Laboratories to widen access to adalimumab for all the additional indications. **Proposed Special Authority criteria are attached at the end of this consultation letter.** In addition to the points outlined on the first page of this letter, the agreement would provide adalimumab with protection from delisting and subsidy reduction until 1 August 2012.

If the Board approves this proposal there would be no other funding applications under consideration by PHARMAC with regards to adalimumab; however, we would remain open to receiving future applications for changes to the access criteria.

With this in mind, if your response to this consultation includes a proposal or request to alter the proposed criteria for adalimumab in a way that would, essentially, widen access to additional patient group(s), your response should include at a minimum:

- An estimate of the number of additional patients per year for the next 5 years.
- Epidemiological or similar information in support of the patient number estimates.
- Published clinical trial data in support of the efficacy of adalimumab in the additional patient group.
- Information about alternative treatments and any unmet clinical need in the additional patient group.

If your response includes other suggested changes to the criteria for adalimumab, it should include information (e.g. clinical trial data or other supporting evidence) in support of the change as well as an explanation as to why the proposed change would be unlikely to alter the number of patients, or change the target patient group, who would access adalimumab under the proposed criteria.

*Leuprorelin (Lucrin Depot, Lucrin PDS Depot, Eligard)*

A new prefilled syringe presentation of leuprorelin (Lucrin PDS Depot), including a 6-monthly preparation (30 mg), would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule as soon as possible following Medsafe registration at the following prices and subsidies (ex-manufacturer, excluding GST):

Pharmaceutical	Brand	Form and Strength	Strength	Pack Size	Proposed price and subsidy
Leuprorelin	Lucrin PDS Depot	Solution for injection (prefilled syringe)	3.75 mg	1	\$221.60
Leuprorelin	Lucrin PDS Depot	Solution for injection (prefilled syringe)	11.25 mg	1	\$591.68
Leuprorelin	Lucrin PDS Depot	Solution for injection (prefilled syringe)	30 mg	1	\$1,109.40

A rebate would apply to all Lucrin Depot and (when listed) Lucrin PDS Depot community subsidies and hospital dispensings, the effect of which would reduce the net subsidy and price of Lucrin Depot and Lucrin PDS Depot by 25%.

Lucrin Depot and Lucrin PDS Depot would have protection from delisting and subsidy reduction until 1 August 2012.

The subsidy for Eligard (supplied by Hospira NZ Limited) would be reduced to the net effective price of Lucrin Depot and Lucrin PDS Depot through the application of reference pricing as outlined in the following table (prices/subsidies expressed ex-manufacturer, excluding GST) from 1 October 2009 (or, in the case of Eligard inj 45 mg, at the time of listing Lucrin PDS Depot 30 mg, whichever is the later):

Pharmaceutical	Brand	Form and Strength	Pack Size	Current list price	Proposed price and subsidy
Leuprorelin	Eligard	Inj 7.5 mg	1	\$184.90	\$166.20
Leuprorelin	Eligard	Inj 22.5 mg	1	\$554.70	\$443.76
Leuprorelin	Eligard	Inj 30 mg	1	\$739.60	\$591.68
Leuprorelin	Eligard	Inj 45 mg	1	\$1,109.40	\$832.05

This would mean that if the supplier of Eligard does not decrease the price to match the new subsidy, a manufacturer's surcharge would apply to Eligard and patients would need to take the Lucrin Depot or Lucrin PDS Depot brands to remain on a fully funded medicine.

### *Levothyroxine (Synthroid)*

Levothyroxine (Synthroid) tablets would be listed in Section B of the Pharmaceutical Schedule from 1 August 2009 as follows (prices/subsidies expressed ex-manufacturer, excluding GST):

<b>Pharmaceutical</b>	<b>Brand</b>	<b>Form and Strength</b>	<b>Pack Size</b>	<b>Proposed price and subsidy</b>
Levothyroxine	Synthroid	Tablet 25 µg	1,000	\$43.24
Levothyroxine	Synthroid	Tablet 50 µg	1,000	\$45.00
Levothyroxine	Synthroid	Tablet 100 µg	1,000	\$46.75

### *Decline of outstanding community funding applications*

If this Abbott proposal is approved, we intend to recommend that the PHARMAC Board declines all outstanding community funding applications for other autoimmune biologics, i.e. etanercept (for rheumatoid arthritis, ankylosing spondylitis, severe chronic plaque psoriasis and psoriatic arthritis), abatacept (for rheumatoid arthritis), infliximab (for rheumatoid arthritis) and rituximab (for rheumatoid arthritis).

We have been unable to reach a commercially acceptable agreement for the funding of etanercept in the abovementioned indications. We consider that funding of just one TNF inhibitor for these indications (i.e. adalimumab, as per the current proposal) would be sufficient for “first-line” autoimmune biologic use. We remain open to considering new funding applications or proposals for etanercept (or any other community use autoimmune biologic) should we receive any in the future.

Our current view is that abatacept, infliximab and rituximab are hospital-use (not community) pharmaceuticals. PHARMAC is not currently accountable for the funding of hospital treatments (with the exception of Pharmaceutical Cancer Treatments delivered within hospitals), which is why we are proposing that applications for community funding of these treatments are declined. However, if the current proposal for adalimumab is approved it would be our intention to undertake further economic assessment on the hospital-administered autoimmune biologic treatments with the aim of issuing advice to DHB hospitals on the cost-effectiveness of these pharmaceuticals in hospitals.

Any decision by PHARMAC to decline these funding applications does not mean that future proposals or applications for these medicines could not be considered. Rather, it indicates that we would no longer be actively working on the proposals that we currently have.

## Proposed Special Authority Criteria for Adalimumab (Humira and HumiraPen)

**Initial application – (rheumatoid arthritis)** only from a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following

- 1 Patient has had severe and active erosive rheumatoid arthritis for six months duration or longer; and
- 2 Treatment is to be used as an adjunct to methotrexate therapy or monotherapy where use of methotrexate is limited by toxicity or intolerance; and
- 3 Patient has tried and not responded to at least three months of oral or parenteral methotrexate at a dose of at least 20 mg weekly or a maximum tolerated dose; and
- 4 Patient has tried and not responded to at least three months of oral or parenteral methotrexate in combination with at least two of the following (triple therapy): sulphasalazine, prednisone at a dose of at least 7.5 mg per day, azathioprine, intramuscular gold, or hydroxychloroquine sulphate (at maximum tolerated doses); and
- 5 Either:
  - 5.1 Patient has tried and not responded to at least three months therapy at the maximum tolerated dose of cyclosporin alone or in combination with another agent; or
  - 5.2 Patient has tried and not responded to at least three months therapy at the maximum tolerated dose of leflunomide alone or in combination with another agent; and
- 6 Either:
  - 6.1 Patient has persistent symptoms of poorly controlled and active disease in at least 20 active, swollen, tender joints; or
  - 6.2 Patient has persistent symptoms of poorly controlled and active disease in at least four active joints from the following: wrist, elbow, knee, ankle, and either shoulder or hip; and
- 7 Either:
  - 7.1 Patient has a C-reactive protein level greater than 15 mg/L measured no more than one month prior to the date of this application; or
  - 7.2 C-reactive protein levels not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months.

**Initial application – (Crohn's disease)** only from a gastroenterologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following

- 1 Patient has severe active Crohn's disease; and
- 2 Any of the following:
  - 2.1 Patient has a Crohn's Disease Activity Index (CDAI) score of greater than or equal to 300; or
  - 2.2 Patient has extensive small intestine disease affecting more than 50 cm of the small intestine; or
  - 2.3 Patient has evidence of short gut syndrome or is having an ileostomy or colostomy, and has intestinal inflammation; and
- 3 Patient has tried and not responded to, or has experienced intolerable side effects from, prior systemic therapy with immunomodulators (including a trial of at least two of azathioprine, 6-mercaptopurine or methotrexate at maximum tolerated doses) and corticosteroids; and
- 4 Surgery (or further surgery) is considered to be clinically inappropriate.

**Initial application – (severe chronic plaque psoriasis)** only from a dermatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

- 1 Either:
  - 1.1 Patient has "whole body" severe chronic plaque psoriasis where lesions have been present for at least 6 months from the time of initial diagnosis; or
  - 1.2 Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, where the plaque or plaques have been present for at least 6 months from the time of initial diagnosis; and

- 2 Patient has tried, but had an inadequate response (see Note) to, at least three of the following (at maximum tolerated doses): phototherapy (UVB or PUVA), methotrexate, cyclosporin, or acitretin; and
- 3 A Psoriasis Area and Severity Index (PASI) assessment has been completed for each prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course; and
- 4 The most recent PASI assessment is no more than 1 month old at the time of application.

Note: "Inadequate response" is defined as: for whole body severe chronic plaque psoriasis, a PASI score of greater than 15, as assessed preferably while still on treatment but no longer than 1 month following cessation of the most recent prior treatment; for severe chronic plaque psoriasis of the face, hand or foot, a at least 2 of the 3 PASI symptom subscores for erythema, thickness and scaling are rated as severe or very severe, and the skin area affected is 30% or more of the face, palm of a hand or sole of a foot, as assessed preferably while still on treatment but no longer than 1 month following cessation of the most recent prior treatment.

**Initial application – (ankylosing spondylitis)** only from a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

- 1 Patient has a confirmed diagnosis of ankylosing spondylitis present for more than six months; and
- 2 Patient has low back pain and stiffness that is relieved by exercise but not by rest; and
- 3 Patient has bilateral sacroiliitis demonstrated by plain radiographs, CT or MRI scan; and
- 4 Patient's ankylosing spondylitis has not responded adequately to treatment with two or more non-steroidal anti-inflammatory drugs (NSAIDs), in combination with anti-ulcer therapy if indicated, while patient was undergoing at least 3 months of an exercise regime supervised by a physiotherapist; and
- 5 Either:
  - 5.1 Patient has limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 2 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI); or
  - 5.2 Patient has limitation of chest expansion by at least 2.5 cm below the average normal values corrected for age and gender (see Notes); and
- 6 A Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 6 on a 0-10 scale; and
- 7 Any of the following:
  - 7.1 An elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour; or
  - 7.2 A C-reactive protein (CRP) level greater than 15 mg per litre; or
  - 7.3 ESR and CRP not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months.

Notes: The BASDAI must have been determined at the completion of the 3 month exercise trial, but prior to ceasing NSAID treatment. The BASDAI, ESR and CRP measures must be no more than 1 month old at the time of initial application. Average normal chest expansion corrected for age and gender:

18-24 years – Male: 7.0 cm; Female: 5.5 cm  
 25-34 years – Male: 7.5 cm; Female: 5.5 cm  
 35-44 years – Male: 6.5 cm; Female: 4.5 cm  
 45-54 years – Male: 6.0 cm; Female: 5.0 cm  
 55-64 years – Male: 5.5 cm; Female: 4.0 cm  
 65-74 years – Male: 4.0 cm; Female: 4.0 cm  
 75+ years – Male: 3.0 cm; Female: 2.5 cm

**Initial application – (psoriatic arthritis)** only from a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following

- 1 Patient has had severe active psoriatic arthritis for six months duration or longer; and
- 2 Patient has tried and not responded to at least three months of oral or parenteral methotrexate at a dose of at least 20 mg weekly or a maximum tolerated dose; and
- 3 Patient has tried and not responded to at least three months of sulphasalazine at a dose of at least 2 g per day or leflunomide at a dose of up to 20 mg daily (or maximum tolerated doses); and

- 4 Patient has persistent symptoms of poorly controlled and active disease in at least four active joints from the following: wrist, elbow, knee, ankle, and either shoulder or hip; and
- 5 Any of the following:
  - 5.1 Patient has a C-reactive protein level greater than 15 mg/L measured no more than one month prior to the date of this application; or
  - 5.2 Patient has an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour; or
  - 5.3 ESR and CRP not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months.

**Renewal – (rheumatoid arthritis)** only from a rheumatologist or Practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:

Both:

- 1 Treatment is to be used as an adjunct to methotrexate therapy or monotherapy where use of methotrexate is limited by toxicity or intolerance; and
- 2 Either:
  - 2.1 Following 4 months initial treatment, the patient has at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
  - 2.2 On subsequent reapplications, the patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician.

**Renewal – (Crohn’s disease)** only from a gastroenterologist or Practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications where the treatment remains appropriate and the patient is benefiting from treatment.

**Renewal – (severe chronic plaque psoriasis)** only from a dermatologist or Practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:

Both:

- 1 Either:
  - 1.1 Both:
    - 1.1.1 Patient has “whole body” severe chronic plaque psoriasis; and
    - 1.1.2 Following each prior adalimumab treatment course the patient has a PASI score which is reduced by 75% or more, or is sustained at this level, when compared with the pre-adalimumab treatment baseline value; or
  - 1.2 Both:
    - 1.2.1 Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot; and
    - 1.2.2 Either:
      - 1.2.2.1 Following each prior adalimumab treatment course the patient has a reduction in the PASI symptom subscores for all 3 of erythema, thickness and scaling, to slight or better, or sustained at this level, as compared to the treatment course baseline values; or
      - 1.2.2.2 Following each prior adalimumab treatment course the patient has a reduction of 75% or more in the skin area affected, or sustained at this level, as compared to the pre-adalimumab treatment baseline value; and
- 2 Photographic evidence demonstrating improvements in psoriasis symptoms (as outlined above) is included in the patient's notes.

Note: An adalimumab treatment course is defined as a minimum of 12 weeks of adalimumab treatment.

**Renewal – (ankylosing spondylitis)** only from a rheumatologist or Practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

- 1 Following 12 weeks of adalimumab treatment, BASDAI has improved by 4 or more points from pre-adalimumab baseline on a 10 point scale, or by 50%, whichever is less; and
- 2 BASMI has improved by at least one category over baseline; and

- 3 Either:
  - 3.1 ESR or CRP is within the normal range; or
  - 3.2 ESR and CRP not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months; and
- 4 Physician considers that the patient has benefited from treatment and that continued treatment is appropriate.

**Renewal – (psoriatic arthritis)** only from a rheumatologist or Practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:

Either

- 1 Following 4 months initial treatment, the patient has at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the treating physician; or
- 2 The patient demonstrates at least a continuing 50% improvement in active joint count from baseline and a clinically significant response to prior adalimumab treatment in the opinion of the treating physician.