PHARMAC
Pharmaceutical Management Agency

30 June 2009

Approval of proposals relating to adalimumab, leuprorelin and levothyroxine and other autoimmune biologic funding applications

Abbott adalimumab, leuprorelin and levothyroxine proposal

PHARMAC is pleased to announce its decision to widen funded access to adalimumab for the "last-line" treatment of ankylosing spondylitis, Crohn's disease, severe chronic plaque psoriasis and psoriatic arthritis from 1 August 2009.

PHARMAC has also approved widening of access to, and reference pricing of, leuprorelin and funding of a new brand of levothyroxine.

Key aspects of the decisions in relation to these pharmaceuticals are detailed on the following pages, followed by a summary of some of the common themes raised during consultation.

Decline of autoimmune biologic funding applications

PHARMAC has declined all outstanding community funding proposals 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). It is important to note that future proposals or applications for these medicines could still be made and would be considered in accordance with PHARMAC's Operating Policies and Procedures.

This decision will not affect the current community funding of etanercept for juvenile idiopathic arthritis, which will continue to be available subject to Special Authority criteria.

The decision will also not prevent DHB hospitals from funding infliximab, abatacept or rituximab, should they choose to, for use in the treatment of autoimmune disorders within DHB hospitals. As previously indicated, PHARMAC intends to undertake further economic assessment with the aim of issuing advice to DHB hospitals on the cost-effectiveness of the use of these pharmaceuticals.

DHB hospitals currently funding patients on infliximab, adalimumab or etanercept for any of the newly funded adalimumab indications may apply directly to PHARMAC (care of the Medical Director) for consideration of an adalimumab Special Authority approval where:

- the patient was taking infliximab, adalimumab or etanercept at the date of this notification letter and had been doing so for a period of at least 1 month;
- the patient would have met the criteria for adalimumab funding at the time they were initiated on the hospital-funded treatment; and
- supporting evidence for both of the above points is provided.

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Details of the decision

Adalimumab (Humira and HumiraPen)

- Access to adalimumab in Section B of the Pharmaceutical Schedule will be widened to include "last-line" treatment of ankylosing spondylitis, Crohn's disease, chronic severe plaque psoriasis and psoriatic arthritis from 1 August 2009. The Special Authority criteria are attached at the end of this consultation letter. Note that several changes to the originally proposed Special Authority criteria have been made as a result of points raised during consultation.
- Adalimumab will be subject to a confidential rebate, reducing its net price.
- Adalimumab will have protection from delisting and subsidy reduction until 1 August 2012.

Leuprorelin (Lucrin Depot, Lucrin Depot PDS, Eligard)

- The Special Authority criteria will be removed from leuprorelin from 1 August 2009.
- A new, prefilled syringe presentation of leuprorelin (Lucrin Depot PDS), including a 6-month (30 mg) preparation, will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 August 2009 at the following prices and subsidies (ex-manufacturer, excluding GST):

Chemical	Brand	Form and Strength	Strength	Pack Size	Price and subsidy
Leuprorelin	Lucrin Depot PDS	Solution for injection (prefilled syringe)	3.75 mg (for monthly administration)	1	$221.60
Leuprorelin	Lucrin Depot PDS	Solution for injection (prefilled syringe)	11.25 mg (for 3-monthly administration)	1	$591.68
Leuprorelin	Lucrin Depot PDS	Solution for injection (prefilled syringe)	30 mg (for 6-monthly administration)	1	$1,109.40

- Lucrin Depot and Lucrin Depot PDS will have protection from delisting and subsidy reduction until 1 August 2012.
- A rebate will apply to Lucrin Depot and Lucrin Depot PDS which will reduce the net price by 25%.
- The subsidy for Eligard will be reduced to the net effective price of Lucrin Depot and Lucrin Depot PDS through the application of reference pricing as outlined in the following table (prices/subsidies expressed ex-manufacturer, excluding GST) from 1 October 2009:

Chemical	Brand	Presentation	Pack Size	Current price and subsidy	New 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 means that if Hospira New Zealand Limited, 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 Depot PDS brands to remain on a fully funded brand of leuprorelin.

Levothyroxine (Synthroid)

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

Pharmaceutical	Brand	Form and Strength	Pack Size	Price and subsidy
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

Feedback received during consultation

We appreciate all the feedback we received and acknowledge the time people took to respond. All consultation responses received by 6 July 2009 were considered in their entirety in making a decision on the proposed changes. The majority of responses were supportive of the proposal. Several responders proposed changes to the adalimumab Special Authority criteria, many of which were incorporated.

Common themes that emerged during consultation, that we are able to publicise, are outlined in the table on the following pages, along with our response.

Theme	Response
Responses relating to autoimmune biologics	
A number of consultation responders requested changes to the proposed Special Authority criteria for adalimumab.	Many of the suggested changes have been incorporated into the approved Special Authority. These changes are too numerous to detail in this notification letter, so please refer to the consultation document (which can be accessed on www.pharmac.govt.nz/consultation) for comparison. We would welcome applications for further alterations to the criteria. We note that we intend to monitor the working of the current criteria for at least 6 months before considering any changes. Where requested changes would result in additional patients accessing treatment, applicants should refer to the application guidelines on PHARMAC's website, which can be found at: www.pharmac.govt.nz/DecisionMakingProcess
Some responders were concerned that the proposal would restrict the ability of DHB hospitals to provide funding for the hospital administered treatments (infliximab, rituximab, abatacept), or that it would restrict access to etanercept for juvenile idiopathic arthritis.	The decision will not prevent DHB hospitals from choosing to provide funding for infliximab, abatacept or rituximab for use in the treatment of autoimmune disorders within DHB hospitals. This decision also will not affect the current community funding of etanercept for juvenile idiopathic arthritis, which will continue to be available.
Several consultation responders considered that there was a need for a second funded biologic treatment for use in patients in whom adalimumab was not effective.	PHARMAC welcomes funding applications for autoimmune biologics in their registered indication(s) for use as a second-line treatment following adalimumab failure. Guidelines on how to make funding applications can be found on PHARMAC's website at: www.pharmac.govt.nz/DecisionMakingProcess
Responses relating to levothyroxine	
Several consultation responders called for PHARMAC to stop funding the current Eltroxin formulation and/or re-fund the original Eltroxin formulation.	It is not possible to re-fund the original Eltroxin formulation because it is no longer available. This is because the manufacturer, GlaxoSmithKline, has stopped making it. We note that the new Eltroxin formulation is currently used by around 80% of patients talking levothyroxine, and we are not aware of any information to indicate that it is unsafe.

Several consultation responders requested funding of whole thyroid extract as another alternative treatment for patients who have difficulties with Synthroid and/or the other funded brands of levothyroxine.	Whole thyroid extract is not registered by Medsafe for use as a therapeutic product in New Zealand. We understand that it is currently being purchased by patients under Section 29 of the Medicines Act 1981 on a named patient basis. We have not received an application for funding from the manufacturer nor, as far as we can tell, has an application for registration been submitted to Medsafe. If whole thyroid extract gains Medsafe registration, PHARMAC would welcome a funding application. Guidelines on how to make funding applications can be found on PHARMAC's website at www.pharmac.govt.nz/DecisionMakingProcess.
Responses relating to leuprorelin	
Some responders were concerned that the proposal would result in no fully funded 6-month preparation of leuprorelin.	There will be no break in full funding for a 6-month preparation of leuprorelin as a result of this decision. The 6-month leuprorelin preparation of Lucrin Depot PDS will be available fully funded from 1 August 2009. From 1 October 2009 the subsidy for the 6-month preparation for Eligard will be reduced, so a manufacturer's surcharge could apply if the supplier does not decrease its price. The 6-month Lucrin Depot PDS formulation will continue to be available fully funded from 1 October 2009.
Some responders were concerned that the proposal would further restrict access to goserelin (Zoladex) in some way.	This decision does not restrict access to goserelin (Zoladex), which will continue to be available, subject to Special Authority criteria, as it is currently. We note that there are differences between the registered indications for leuprorelin and goserelin, and clinicians should refer to the registered datasheets for more information. These can be found at www.medsafe.govt.nz.

New 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 3 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 would be at risk of short gut syndrome with further bowel resection; or
- 2.4 Patient has an ileostomy or colostomy and has intestinal inflammation; and

3 Patient has tried but had an inadequate response to, or has experienced intolerable side effects from, prior systemic therapy with immunomodulators at maximum tolerated doses (unless contraindicated) 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 4 months for applications meeting the following criteria:

All of the following:

1 Either:

- 1.1 Patient has "whole body" severe chronic plaque psoriasis with a Psoriasis Area and Severity Index (PASI) score of greater than 15, 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, or has experienced intolerable side effects from, at least three of the following (at maximum tolerated doses unless contraindicated): phototherapy, methotrexate, cyclosporin, or acitretin; and

3 A PASI assessment has been completed for at least the most recent prior treatment course (but preferably all prior treatment courses), 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, 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 1 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 Either:

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.

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 Either:
    4.1 Patient has persistent symptoms of poorly controlled and active disease in at least 20 active, swollen, tender joints; or
    4.2 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
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 rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:
1 Either:
    1.1 Applicant is a rheumatologist; or
    1.2 Applicant is a Practitioner and confirms that a rheumatologist has provided a letter, email or fax recommending that the patient continues with adalimumab treatment; 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 Either:
    3.1 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
    3.2 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 gastroenterologist. Approvals valid for 6 months for applications meeting the following criteria:
Both:
1 Either:
    1.1 Applicant is a gastroenterologist; or
    1.2 Applicant is a Practitioner and confirms that a gastroenterologist has provided a letter, email or fax recommending that the patient continues with adalimumab treatment; and
2 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 dermatologist. Approvals valid for 6 months for applications meeting the following criteria:
Both:
1 Either:
    1.1 Applicant is a dermatologist; or
    1.2 Applicant is a Practitioner and confirms that a dermatologist has provided a letter, email or fax recommending that the patient continues with adalimumab treatment; and
2 Either:
    2.1 Both:
        2.1.1 Patient has "whole body" severe chronic plaque psoriasis; and

2.1.2 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

2.2 Both:

2.2.1 Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot; and

2.2.2 Either:

2.2.2.1 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

2.2.2.2 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.

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 rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1 Either:

1.1 Applicant is a rheumatologist; or

1.2 Applicant is a Practitioner and confirms that a rheumatologist has provided a letter, email or fax recommending that the patient continues with adalimumab treatment; and

2 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

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 rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:

Both:

1 Either:

1.1 Applicant is a rheumatologist; or

1.2 Applicant is a Practitioner and confirms that a rheumatologist has provided a letter, email or fax recommending that the patient continues with adalimumab treatment; 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 treating physician; or

2.2 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.