NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

5 August 2014

Decision to award sole supply to Eprex (erythropoietin alfa)

PHARMAC is pleased to announce the award of Sole Subsidised Supply Status in the community, and Hospital Supply Status in DHB hospitals, to Janssen-Cilag's brand of erythropoietin, Eprex (erythropoietin alfa). In summary, the effect of the decision is that:

- Eprex (erythropoietin alfa) will be the only funded brand of erythropoietin in the community and the only brand of erythropoietin able to be used in DHB hospitals, subject to a 5% Discretionary Variance (DV) limit, from 1 March 2015 to 28 February 2018; and

- Access to erythropoietin will be widened to include:

    - patients with myelodysplasia; and
    - patients for whom blood transfusion is not a viable treatment option (hospital only).

This decision was the subject of a consultation letter dated 20 June 2014 which can be found on PHARMAC's website at: http://www.pharmac.health.nz/assets/consultation-2014-06-20-erythropoietin.pdf.

Several changes were made following consideration of consultation feedback, including:

- Access was widened to include patients with myelodysplasia intermediate risk.
- Removal of the definition of transfusion dependence.
- Removal of reference to the Cockcroft-Gault equation.
- The application of the wastage rule to dispensing of erythropoietin.

Details of the decision

From 1 September 2014 Janssen's brand of erythropoietin alfa (Eprex) will be listed in Section B and Part II of Section H of the Pharmaceutical Schedule at the current subsidies and prices (ex-manufacturer and excluding GST) as follows;

Pharmaceutical	Brand	Form and strength	Pack Size	Subsidy/price
Erythropoietin alfa	Eprex	Inj 1,000 iu in 0.5 ml syringe	6	$48.68
Erythropoietin alfa	Eprex	Inj 2,000 iu in 0.5 ml syringe	6	$120.18
Erythropoietin alfa	Eprex	Inj 3,000 iu in 0.3 ml syringe	6	$166.87
Erythropoietin alfa	Eprex	Inj 4,000 iu in 0.4 ml syringe	6	$193.13
Erythropoietin alfa	Eprex	Inj 5,000 iu in 0.5 ml syringe	6	$243.26
Erythropoietin alfa	Eprex	Inj 6,000 iu in 0.6 ml syringe	6	$291.92
Erythropoietin alfa	Eprex	Inj 10,000 iu in 1 ml syringe	6	$395.18

- Eprex will be subject to a confidential rebate.

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- There will be a 6-month transition period between 1 September 2014 and 28 February 2015 where both erythropoietin alfa (Eprex) and Roche's brand of erythropoietin beta (NeoRecormon) will both be listed, fully funded, on the Pharmaceutical Schedule.

- Eprex will have Sole Subsidised Supply Status (the only funded brand of erythropoietin in the community) and Hospital Supply Status (the only available brand of erythropoietin in DHB hospitals, subject to a 5% DV limit) from 1 March 2015 to 28 February 2018.

- Roche's brand of erythropoietin beta (NeoRecormon) will be delisted from Section B and Part II of Section H of the Pharmaceutical Schedule from 1 March 2015.

- The chemical erythropoietin beta will remain listed on Part II of Section H of the Pharmaceutical Schedule for the purpose of the DV limit. The following note will be added to make it clear that other types of erythropoietin could be used by hospitals as a DV pharmaceutical.

  Note: Erythropoietin beta is considered a Discretionary Variance Pharmaceutical for erythropoietin alfa.

- Access criteria for erythropoietin will be amended in Section B and Part II of Section H from 1 September 2014 as follows (additions in bold, deletions in strikethrough):

Section B

Initial application – (chronic renal failure) from ~~a relevant~~ **any** Specialist. Approvals valid for 2 years for applications meeting the following criteria:
Both:
Restricted (chronic renal failure)
Both:
1 Both:
1.1 Patient in chronic renal failure; and
1.2 Haemoglobin ≤ 100g/L; and
2 Any of the following:
2.1 Both:
2.1.1 Patient ~~is not diabetic~~ **does not have diabetes mellitus**; and
2.1.2 Glomerular filtration rate ≤ 30ml/min; or
2.2 Both:
2.2.1 Patient ~~is diabetic~~ **has diabetes mellitus**; and
2.2.2 Glomerular filtration rate ≤ 45ml/min; or
2.3 Patient is on haemodialysis or peritoneal dialysis.

Note
Erythropoietin ~~beta/alpha~~**alfa** is indicated in the treatment of anaemia associated with chronic renal failure (CRF) where no cause for anaemia other than CRF is detected and there is adequate monitoring of iron stores and iron replacement therapy.
~~The Cockroft Gault Formula may be used to estimate glomerular filtration rate (GFR) in persons 18 years and over:~~
~~GFR (ml/min) (male) = (140 – age) x Ideal Body Weight (kg) / 814 x serum creatinine (mmol/l)~~
~~GFR (ml/min) (female) = Estimated GFR (male) x 0.85~~

Initial application – (myelodysplasia)* from any Specialist. Approvals valid for 2 months for applications meeting the following criteria:
All of the following:
1. Patient has a confirmed diagnosis of myelodysplasia (MDS)*; and
2. Has had symptomatic anaemia with haemoglobin <100g/L and is red cell transfusion-dependent; and

3. Patient has very low, low or intermediate risk MDS based on the WHO classification based prognostic scoring system for myelodysplastic syndrome (WPSS); and
4. Other causes of anaemia such as B12 and folate deficiency have been excluded; and
5. Patient has a serum erythropoietin level of <500 IU/mL; and
6. The minimum necessary dose of erythropoietin would be used and will not exceed 80,000 iu per week.
***Indication marked with * is an Unapproved Indication**

Renewal – (chronic renal failure) from ~~a relevant~~ **any** Specialist. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

Note
Erythropoietin ~~beta/alpha~~**alfa** is indicated in the treatment of anaemia associated with chronic renal failure (CRF) where no cause for anaemia other than CRF is detected and there is adequate monitoring of iron stores and iron replacement therapy.
~~The Cockroft Gault Formula may be used to estimate glomerular filtration rate (GFR) in persons 18 years and over:~~
~~GFR (ml/min) (male) = (140 - age) x Ideal Body Weight (kg) / 814 x serum creatinine (mmol/l)~~
~~GFR (ml/min) (female) = Estimated GFR (male) x 0.85~~

Renewal application – (myelodysplasia)* from any Specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:
1. The patient's transfusion requirement continues to be reduced with erythropoietin treatment; and
2. Transformation to acute myeloid leukaemia has not occurred; and
3. The minimum necessary dose of erythropoietin would be used and will not exceed 80,000 iu per week.
***Indication marked with * is an Unapproved Indication**

Section H

Restricted (chronic renal failure)
Both:
1 Both:
1.1 Patient in chronic renal failure; and
1.2 Haemoglobin ≤ 100g/L; and
2 Any of the following:
2.1 Both:
2.1.1 Patient ~~is not diabetic~~ **does not have diabetes mellitus**; and
2.1.2 Glomerular filtration rate ≤ 30ml/min; or
2.2 Both:
2.2.1 Patient ~~is diabetic~~ **has diabetes mellitus**; and
2.2.2 Glomerular filtration rate ≤ 45ml/min; or
2.3 Patient is on haemodialysis or peritoneal dialysis.

Initiation (myelodysplasia)*
Re-assessment required after 2 months
All of the following:
1. Patient has a confirmed diagnosis of myelodysplasia (MDS); and
2. Has had symptomatic anaemia with haemoglobin <100g/L and is red cell transfusion-dependent; and
3. Patient has very low, low or intermediate risk MDS based on the WHO classification-based prognostic scoring system for myelodysplastic syndrome (WPSS); and
4. Other causes of anaemia such as B12 and folate deficiency have been excluded; and

5. Patient has a serum erythropoietin level of <500 IU/mL; and
6. The minimum necessary dose of erythropoietin would be used and will not exceed 80,000 iu per week.

Continuation (myelodysplasia)*
Re-assessment required after 12 months
All of the following:
1. The patient's transfusion requirement continues to be reduced with erythropoietin treatment; and
2. Transformation to acute myeloid leukaemia has not occurred; and
3. The minimum necessary dose of erythropoietin would be used and will not exceed 80,000 iu per week.

Restricted (all other indications)
Haematologist
For use in patients where blood transfusion is not a viable treatment alternative.

***Note: Indications marked with * are Unapproved Indications**

- A Brand Switch Fee will apply to dispensings of Eprex from 1 March 2015 until 31 May 2015.

- The wastage rule will apply to the listing of erythropoietin in Section B of the Pharmaceutical Schedule from 1 September 2014. For the avoidance of doubt the wastage rule will apply to erythropoietin beta (until it is delisted) and also to erythropoietin alfa (this will be ongoing post the transition period).

Transition timelines

- **1 September 2014** – Funded access to erythropoietin will be widened to include patients with myelodysplasia (in hospitals and in the community) and patients for whom blood transfusion is not a viable treatment alternative (in hospitals only).

- **1 September 2014 to 28 February 2015** – Eprex (erythropoietin alfa) and NeoRecormon (erythropoietin beta) will remain listed in both Part II of Section H and Section B fully funded. During this 6-month period patients who had been receiving funded NeoRecormon will need to be transitioned to the Eprex brand of erythropoietin in order to remain on a fully funded brand from 1 March 2015.

  Whilst erythropoietin alfa and beta are considered therapeutically equivalent, the two medicines are not generically substitutable, so the transition to erythropoietin alfa will need to be managed by the prescribing clinician (see the **Managing the change** section below for more information).

- **1 March 2015** – NeoRecormon will be delisted from Section B, and Part II of Section H, of the Pharmaceutical Schedule. Other types of erythropoietin can be used by hospitals as a DV pharmaceutical.

- **1 March 2015 to 28 February 2018** – Eprex will be the sole subsidised brand of erythropoietin in the community and the only available brand in DHB hospitals, subject to a 5% DV limit.

- Other types of erythropoietin will only be funded in the community from 1 March 2015 if funding was approved in accordance with PHARMAC's Named Patient Pharmaceutical Assessment (NPPA) Policy.

Managing the change

PHARMAC received clinical advice from specialists and the Pharmacology and Therapeutic Advisory Committee (PTAC) that erythropoietin alfa and beta can be considered therapeutically equivalent and dose equivalent. The erythropoietin change will be managed by each patient's treating clinician (specialist or GP) as a new prescription will be required.

We recommend that prescriptions for erythropoietin should be written generically in full i.e. erythropoietin alfa or erythropoietin beta. Special Authority approvals for existing patients will allow a pharmacy to claim for erythropoietin alfa (Eprex) and will not be affected by the change.

The syringe injector for erythropoietin alfa (Eprex) differs to that of erythropoietin beta (NeoRecormon). Training resources for health professionals will be provided, where required, about the different syringe injector so that they can confidently advise patients who need to change.

PHARMAC will work with health professionals to provide support with managing patients who are required to change erythropoietin. Resources and activities to support the move to sole supply will include:

- Support materials on the PHARMAC website via http://www.pharmac.health.nz/medicines/my-medicine-has-changed/erythropoietin
- Patient information leaflets in various languages (e.g English, Maori, Samoan, Tongan, Cantonese and Mandarin). A PDF copy of the leaflet is available and paper copies may be ordered from www.pharmaconline.co.nz.
- A video of the new injection device to show people what to do. This provides a visual representation of the patient leaflets.
- Communications and support to health professionals involved in the change.

As with all medicines, PHARMAC is able to consider funding an alternative type of erythropoietin for patients in the community for whom Eprex is not appropriate for clinical reasons and this would be done in accordance with PHARMAC's NPPA Policy. PHARMAC is aware that Eprex is not indicated for anaemia of prematurity. Clinicians may consider using an alternative erythropoietin product for such patients via the 5% DV limit.

Reminders in prescribing and dispensing software will be used, where possible, to assist with managing the brand change.

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 4 July 2014 were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal, and the following issues were raised in relation to specific aspects of the proposal:

Theme	Comment
Patients with myelodysplasia intermediate risk should have access to erythropoietin treatment. Patients with a low blood transfusion requirement are the patients most likely to respond to erythropoietin treatment.	Patients with myelodysplasia intermediate risk will have access to erythropoietin as a result of this decision. We have removed the definition of transfusion dependence to allow the treating clinician to use their discretion to determine whether they consider the patient meets this criterion.

Theme	Comment
The Cockcroft –Gault equation is rarely used now in clinical practice and may cause confusion for health professionals. The Modification of Diet in Renal Disease (MDRD) equation and more recently the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas are now standard and are reported by all laboratories in New Zealand, hence negating the need for clinicians to do the calculations separately.	The Special Authority criteria no longer refers to the Cockcroft–Gault equation to measure renal clearance.
Resources should be provided to the DHBs to support the change.	PHARMAC will work with health professionals and produce resources to manage and support the change (see Managing the change section above). Some additional resources may be available from the supplier for new patients.
Patients who require erythropoietin as an alternative to blood transfusions prior to surgery may be outpatients at the time of treatment. Restricting erythropoietin for this use to hospitals is problematic.	PHARMAC consider it is appropriate to limit funding for this patient group to hospitals as the majority of patients will receive treatment on an inpatient basis or as an outpatient prior to surgery. PHARMAC note that the HML rules allow a DHB Hospital to dispense up to 30 days erythropoietin alfa treatment for use in the community. This provision would enable these patients to access erythropoietin alfa as outpatients. As with all medicines, PHARMAC is able to consider funding in erythropoietin in the community via the Named Patient Pharmaceutical Assessment (NPPA) pathway on a case by case basis if required.
The ability to prescribe erythropoietin as an alternative to blood transitions pre-surgery should not be restricted to a Haematologist as they would not be involved in treating these patients.	PHARMAC does not consider it is appropriate to amend the prescriber restrictions in Section H for erythropoietin. PHARMAC has received clinical advice that supports the Haematologist restriction and highlights concerns regarding the risk of hypertension and thrombosis if erythropoietin was used instead of blood transfusions inappropriately. We note that the Hospital Medicines List (HML) rules allow the development of protocols or guidelines that have been endorsed by the DHB hospital. Such protocols could allow other practitioners to prescribe erythropoietin. Refer to HML rule 5 for further details.
The prescribing and monitoring of erythropoietin in patients with chronic renal failure is complex and applications for the use of erythropoietin should be made by a Nephrologist.	PHARMAC note that other specialists including nephrologists and general practitioners have been able to make Special Authority applications for erythropoietin prior to this proposal. We expect that patients with chronic renal failure receiving erythropoietin will be initiated on treatment by a nephrologist, although ongoing care and monitoring could be by a general practitioner.

Theme	Comment
Patients could be changed from erythropoietin beta to alfa by their pharmacists via generic substitution over a shorter timeframe. It would also lessen the chance of part packs of erythropoietin beta being left unused in community pharmacy.	Clinical advice PHARMAC has received indicates that it is most appropriate for patients to be transitioned, if required, by their doctors. Erythropoietin alfa and erythropoietin beta are not considered generically substitutable.
An initial Special Authority application for a patient with myelodysplasia should be increased to three months, to coincide with normal prescribing practice. This would also minimise the risk to community pharmacy of being left with partly dispensed packs of medication.	Clinical advice supports the two month approval period for the myelodysplasia indication. The Wastage Rule has been applied to allow community pharmacy to claim for any partly dispensed packs of either erythropoietin alfa or beta that have to be disposed of.

More information

If you have any questions about this decision, you can email us at enquiry@pharmac.govt.nz or call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.