

PUBLIC SUMMARY DOCUMENT

Product: EPOETIN LAMBDA, injection, 1,000 units in 0.5 mL, 2,000 units in 1.0 mL, 3,000 units in 0.3 mL, 4,000 units in 0.4 mL, 5,000 units in 0.5 mL, 6,000 units in 0.6 mL, 8,000 units in 0.8 mL and 10,000 units in 1.0 mL, pre-filled syringe, Novicrit[®]

Sponsor: Novartis Pharmaceuticals Australia Pty Ltd

Date of PBAC Consideration: July 2010

1. Purpose of Application

The submission sought a Section 100 (Highly Specialised Drugs Program) listing for treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g per L, where intrinsic renal disease, as assessed by a nephrologist, is the primary cause of the anaemia.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background

This drug had not previously been considered by the PBAC.

3. Registration Status

Epoetin lambda (Novicrit[®]) was TGA registered on 27 January 2010 for:

- treatment of patients with symptomatic or transfusion requiring anaemia associated with chronic renal failure to improve their quality of life by improving energy levels, exercise performance, fatigue and sleep patterns and by reducing the need for blood transfusions.
- treatment of anaemia in patients with non-myeloid malignancies where anaemia develops as a result of concomitantly administered chemotherapy, and where blood transfusion is not considered appropriate.
- adult patients with mild to moderate anaemia (haemoglobin > 100 to less than or equal to 130g/L) scheduled for elective surgery with an expected moderate blood loss (two to four units or 900 to 1,800mL) to reduce exposure to allogeneic blood transfusion and to facilitate erythropoietic recovery.
- augment autologous blood collection and to limit the decline in haemoglobin in anaemic adult patients who are scheduled for major elective surgery and who are not expected to pre-deposit their complete perioperative blood needs.

4. Listing Requested and PBAC's View

Section 100 (Highly Specialised Drugs Program)

Private hospital authority required

Treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g per L, where intrinsic renal disease, assessed by a nephrologist, is the primary cause of the anaemia.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Chronic kidney disease (CKD) is marked by long-term and usually irreversible loss of kidney function and may further deteriorate into end-stage kidney disease, and renal replacement

therapy in the form of dialysis or transplantation is required for survival. Anaemia is a complication of chronic kidney disease.

Epoetin lambda would provide an alternative treatment for anaemia associated with CKD.

6. Comparator

The submission nominated epoetin alfa as the comparator. The PBAC considered this appropriate.

7. Clinical Trials

The submission presented the results of Study INJ-9 as the basis of the evidence in support of listing. Details of the published trial presented in the submission are in the table below.

Trial ID / First Author	Protocol title / Publication title	Publication citation
Study INJ-9 Haag-Weber M, et al	Therapeutic equivalence, long-term efficacy and safety of HX575 in the treatment of anaemia in chronic renal failure patients receiving hemodialysis.	Clin Nephrol 2009; 72(5):380-90

8. Results of Trials

Study INJ-9 evaluated the therapeutic equivalence of epoetin lambda with epoetin alfa in the long-term intravenous treatment of anaemia in chronic renal failure patients on haemodialysis only.

The primary efficacy outcome was mean absolute change in Hb level between the screening/baseline period and the evaluation period. Major secondary efficacy outcomes were:

- Percentage of patients with Hb within the target range of 10.0 – 13.0 g/dL;
- Frequency of patients with Hb values > 10.0 g/dL;
- Frequency of patients with changes in the epoetin dosage (adaptation of more than 25% at any visit);
- Development of the weekly epoetin dose (in IU and per kg);
- Frequency of responders (PP)% (95% CI); and
- Red blood cell transfusions.

For the primary endpoint, the difference between treatment groups of 0.084 g/dL (95% CI [-0.170; 0.338]) was within the pre-defined boundaries of -0.5 and 0.5 g/dL, therefore meeting the criteria to confirm, with statistical significance, therapeutic non-inferiority of epoetin lambda and epoetin alfa.

Regarding safety, the submission stated that no relevant differences between treatment groups, with regard to adverse events, serious adverse events and death were observed.

The submission claimed that Study INJ-9 showed epoetin lambda to be therapeutically non-inferior to epoetin alfa with respect to mean absolute change in Hb levels, and to have a comparable safety profile in the IV treatment of anaemia in patients with chronic kidney disease.

For PBAC's view, see Recommendation and Reasons.

9. Clinical Claim

The submission claimed that epoetin lambda is non-inferior in terms of efficacy and safety to epoetin alfa.

For PBAC's view, see Recommendation and Reasons.

10. Economic Analysis

The submission presented a cost-minimisation analysis. The equi-effective doses were 1000 IU epoetin lambda and 1000 IU epoetin alfa. The sponsor adopted a modified cost-minimisation approach where epoetin lambda was provided at a 10% lower price (ex-manufacturer) than the calculated equivalent price of the calculated equivalent dose of epoetin alfa.

11. Estimated PBS Usage and Financial Implications

The submission used a market share approach to estimate the financial impact of the requested listing for epoetin lambda. Anticipated utilisation of epoetin lambda was calculated based on substitution from the ESAs listed at the time of the submission (epoetin alfa, epoetin beta and darbepoetin alfa) and assumed that 50% of total current ESA usage is by intravenous administration.

The likely number of packs dispensed per year was estimated to be between 10,000 and 50,000 in Year 5.

The submission estimated net savings to the PBS of less than \$10 million in Year 5 of listing.

12. Recommendation and Reasons

The PBAC recommended the listing of epoetin lambda on the Pharmaceutical Benefits Scheme as a Section 100 Highly Specialised Drug for the treatment of anaemia requiring transfusion defined as a haemoglobin level of less than 100 g per L, where intrinsic renal disease, assessed by a nephrologist, is the primary cause of the anaemia. Listing was recommended on a cost-minimisation basis with epoetin alfa at the prices proposed in the submission, which the PBAC noted are 10% lower than the current PBS price for the corresponding strengths of epoetin alfa.

In making this recommendation, the PBAC noted that epoetin lambda had been approved by TGA under the Similar Biological Medicinal Product guidelines. When approving this product, the TGA had concluded although the amino acid sequence of epoetin lambda was the same as that of epoetin alfa, there were significant differences in the glycosylation pattern of this product and epoetin alfa which made it appropriate for the former to have the different Australian Biologic Name, epoetin lambda.

The PBAC was satisfied that the results of Study INJ-9 demonstrate that epoetin lambda is non-inferior to epoetin alfa in terms of efficacy and safety when used at the same doses for the long-term intravenous treatment of anaemia in chronic renal failure.

The PBAC agreed to advise the Minister and the Pricing Authority that it is appropriate to apply the same price reduction offered in this submission to the other PBS-listed erythropoiesis stimulating agents; epoetin-alfa, epoetin beta, darbepoetin and

methoxypolyethylene glycol-epoetin beta, all of which were recommended for listing on a cost-minimisation basis with epoetin alfa.

In accordance with Subsection 101 (3BA) of the *National Health Act 1953* the PBAC advised that on the basis of the material available to it at this time, the Committee is of the opinion that epoetin lambda should not be considered as interchangeable on an individual patient basis with another drug or medicinal preparation. This is because, according to the TGA approved Product Information, epoetin lambda can only be administered intravenously, whereas the other PBS-subsidised erythropoiesis stimulating agents can be administered intravenously and subcutaneously, and the subcutaneous route of administration accounts for a significant proportion of use of the PBS-subsidised erythropoiesis stimulating agents. This means that these drugs are not sufficiently similar in their clinical use.

Recommendation

EPOETIN LAMBDA, injection, 1,000 units in 0.5 mL, 2,000 units in 1.0 mL, 3,000 units in 0.3 mL, 4,000 units in 0.4 mL, 5,000 units in 0.5 mL, 6,000 units in 0.6 mL, 8,000 units in 0.8 mL and 10,000 units in 1.0 mL, pre-filled syringe, Novicrit[®]

Restriction: Section 100 (Highly Specialised Drugs Program)
Authority Required (STREAMLINED)
Private hospital authority required
Treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g per L, where intrinsic renal disease, as assessed by a nephrologist, is the primary cause of the anaemia.

NOTE:

Epoetin lambda should only be administered by the intravenous route.

Maximum quantity: 12
Repeats: 5

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Novartis Pharmaceuticals Australia welcomes the PBAC's recommendation to make Novicrit[®] available to patients with anaemia requiring transfusion.