All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Final Appraisal Report

Epoetin alfa (Binocrit®▼)

Sandoz Limited

Advice No: 1210 - August 2010

Recommendation of AWMSG

Epoetin alfa (Binocrit®▼) is recommended as an option for restricted use within NHS Wales in accordance with NICE Clinical Guideline 39 for the treatment of symptomatic anaemia associated with chronic renal failure in adult and paediatric patients:

- Treatment of anaemia associated with chronic renal failure in paediatric and adult patients on haemodialysis and adult patients on peritoneal dialysis.

- Treatment of severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing dialysis.

Epoetin alfa (Binocrit®▼) is not suitable for shared care within NHS Wales for the above indications.

Epoetin alfa (Binocrit®▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

This report should be cited as:

1.0 RECOMMENDATION OF AWMSG:

The AWMSG recommendation is based on: the Preliminary Appraisal Report, the Company Response to this, medical expert opinion, lay perspective and discussions at the AWMSG meeting.

Date: Wednesday 18th August 2010

The recommendation of AWMSG is:

Epoetin alfa (Binocrit®▼) is recommended as an option for restricted use within NHS Wales in accordance with NICE Clinical Guidance 39 for the treatment of symptomatic anaemia associated with chronic renal failure in adult and paediatric patients:

- Treatment of anaemia associated with chronic renal failure in paediatric and adult patients on haemodialysis and adult patients on peritoneal dialysis

- Treatment of severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing dialysis

Epoetin alfa (Binocrit®▼) is not suitable for shared care within NHS Wales for the above indications.

Epoetin alfa (Binocrit®▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

Additional note:

In accordance with European Medicines Agency (EMA) guidance, the licence for the use of epoetin alfa (Binocrit®▼) in paediatrics, patients receiving peritoneal dialysis or those not receiving dialysis was granted on the basis of assumed bioequivalence.

Due to the potential for small differences between biosimilars from different manufacturers and/or the reference product (Eprex®) post-marketing pharmacovigilance is essential and will be facilitated by the Risk Management Plan.

2.0 PRODUCT DETAILS

Licensed indication[1]	Treatment of symptomatic anaemia associated with chronic renal failure (CRF) in adult and paediatric patients: - Treatment of anaemia associated with chronic renal failure in paediatric and adult patients on haemodialysis and adult patients on peritoneal dialysis. - Treatment of severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing dialysis. Treatment of anaemia and reduction of transfusion requirements in adult patients receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, and at risk of transfusion as assessed by the patient's general status (e.g. cardiovascular status, pre existing anaemia at the start of chemotherapy). To increase the yield of autologous blood from patients in a predonation programme. Its use in this indication must be balanced against the reported risk of thromboembolic events. Treatment should only be given to patients with moderate anaemia (haemoglobin [Hb] 10-13g/dl [6.2-8.1mmol/l], no iron deficiency), if blood saving procedures are not available or insufficient when the scheduled major elective surgery requires a large volume of blood (four or more units of blood for females or five or more units for males). To reduce exposure to allogeneic blood transfusions in adult non-iron deficient patients prior to major elective orthopaedic surgery, having a high perceived risk for transfusion complications. Use should be restricted to patients with moderate anaemia (e.g. Hb 10-13g/dl) who do not have an autologous predonation programme available and with an expected blood loss of 900 to 1,800ml.
Dosing	In patients with CRF the medicinal product has to be administered by the intravenous (IV) route[1]. Refer to the summary of product characteristics (SPC) for dosing guidance according to indication[1].
Market authorisation date	Original market authorisation was granted 28 August 2007. Market authorisation for an extension of the indication to increase the yield of autologous blood from patients in a predonation programme was granted 21 November 2008[2].
UK Launch date	11 March 2008[3].

3.0 DECISION CONTEXT

3.1 Background

Anaemia is a common complication in patients with CRF, and although its pathogenesis is multifactorial, the loss of peritubular cells in the kidney responsible for the synthesis and secretion of erythropoietin (EPO) is considered the key aetiologic factor[4]. The main impact of anaemia on organ function is reduced oxygen delivery to tissues leading to debilitating symptoms such as: fatigue, exercise intolerance, impaired cognitive function, sleep disorder, altered haemostasis, and depressed immune function[4].

Anaemia is also associated with a high prevalence of cardiovascular disease in renal patients, and their consequent increased morbidity and mortality[4]. It has been reported that cardiovascular disease accounts for more than 50% of deaths in these patients[4]. Exogenous replacement therapy of EPO by recombinant hormone epoetin is a well accepted therapy for the treatment of anaemia in patients with chronic kidney disease (CKD) and is reported to be effective in about 90-95% of such patients[4].

Binocrit®▼ has been developed as a similar biological medicinal product (biosimilar), i.e. a new biological product similar to an existing, authorised reference product[5]. The reference product for Binocrit®▼ is Eprex® (epoetin alfa) manufactured by Janssen-Cilag.

A biological medicine is a medicine whose active substance is made by or derived from a living organism[5]. Biological products are fundamentally different from standard chemical products in terms of their complexity; it is unlikely that a biosimilar product will have an identical structure to that of the reference product, thereby requiring comparative evidence of safety and efficacy before European Medicines Agency (EMA) approval. In this regard, biosimilars are different to generic products[6]. Generic products only require confirmation that the product is chemically identical and has similar pharmacokinetic properties to the reference product[7].

The company have submitted clinical data based on the information provided to the EMA for market authorisation. At the Welsh Medicines Partnership's (WMPs) request, the company have submitted clinical and cost-effectiveness data for anaemia associated with CRF. The use of epoetin alfa for cancer treatment-induced anaemia is covered by the National Institute for Health and Clinical Excellence (NICE) multiple technology appraisal 142 and therefore is not considered within this report[8]. The remaining indications (orthopaedic surgery and autologous predonation) may be considered as a separate appraisal in the future. No data has been provided for the use of Binocrit®▼ in paediatrics. Prevalence data is detailed in section 8.

3.2 Comparators

The following erythropoiesis stimulating agents (ESAs) are currently licensed in the UK:
Short acting:

- Epoetin alfa (Eprex®)[9]
- Epoetin beta (NeoRecormon®)[10]
- Epoetin theta (Eporatio®▼)[11]
- Epoetin zeta (Retacrit®▼)[12] (refer to section 3.3)

Longer acting:

- Darbepoetin alfa (Aranesp®)[13]
- Methoxy polyethylene glycol-epoetin beta (Mircera®▼)[14]

3.3 Guidance and related advice

- NICE: Anaemia management in people with CKD (CG39; 2006); which recommends that the management of anaemia should be considered if the Hb level is ≤11g/dl (or 10g/dl if under two years of age)[15].
- NICE: Early identification and management of CKD in adults in primary and secondary care (CG73; 2008)[16]
- UK Renal Association: Clinical Practice Guideline 4th edition (2007)[17]; which recommends that treatment with ESAs should be offered to patients with anaemia of CKD and Hb consistently below 11g/dl who are likely to benefit in terms of quality of life and physical function, and to avoid transfusion in patients considered suitable for transplantation.
- National Collaborating Centre for Chronic Conditions, Royal College of Physicians: Anaemia management in CKD (2006)[18].

- Joint speciality committee on renal medicine of the Royal College of Physicians and the Renal Association: UK guidelines for identification, management and referral of CKD in adults (2006)[19].
- Scottish Intercollegiate Guidelines Network (SIGN): Diagnosis and management of CKD (2008)[20].
- All Wales Medicines Strategy Group (AWMSG): Methoxy polyethylene glycol-epoetin beta (Mircera®▼) was recommended in October 2009 as an option for use within NHS Wales for the treatment of adults with symptomatic anaemia associated with CKD[21].
- AWMSG: Epoetin zeta (Retacrit®▼) was not recommended for use within NHS Wales for the treatment of anaemia associated with CKD, reduction of transfusion requirements in adult patients receiving chemotherapy or to increase the yield of autologous blood from patients in a predonation programme[22].

4.0 SUMMARY OF EVIDENCE ON CLINICAL EFFICACY[23]

The company has provided efficacy and safety results from a multicentre phase III study, INJ-9[24], which was designed to evaluate a 1:1 dose conversion from IV Eprex® to IV Binocrit®▼ with respect to efficacy based on Hb assessment in CRF patients on haemodialysis. The efficacy data in healthy volunteers within the company submission has not been considered as there is data available in the relevant patient population. Study INJ-9 consisted of two parts: Part one was a 28 week double-blind, randomised equivalence study consisting of an initial 24 week phase of dose adjustment and maintenance of Hb levels, followed by a four week evaluation phase during which the primary efficacy endpoint was measured. Part two was a 28 week study to determine long-term safety whereby all patients received open-label Binocrit®▼. Adult (≥18 years) patients were randomised 2:1 to switch to IV Binocrit®▼ (n=314) or to continue receiving IV Eprex® (n=164) three times weekly. Dose adjustments were permitted every other week as necessary.

The primary endpoint was defined as the mean absolute change in Hb levels from baseline to the end of the evaluation phase for the per-protocol (PP) patient population (i.e. all patients who completed the double-blind part of the study [part one] without any major protocol violations [Binocrit®▼: n=207; Eprex®: n=118]). This equated to 0.147g/dl and 0.063g/dl for the Binocrit®▼ and Eprex® groups respectively; treatment difference of 0.084g/dl, 95% confidence interval (CI) -0.170 to 0.338. Since the 95% CI fell within the predefined range of ±0.5g/dl, therapeutic equivalence was confirmed. The same measurement in the intention-to-treat (ITT) population was defined as a secondary endpoint and therapeutic equivalence was again confirmed. No significant differences were found between the treatment groups for any of the other secondary endpoints. Assessments of quality of life (QoL) using 10cm linear analogue self-assessment scales relating to energy level, ability to work and overall QoL revealed little change in either treatment group during the study.

5.0 SUMMARY OF EVIDENCE ON COMPARATIVE SAFETY

The clinical safety assessment of Binocrit®▼ included a phase III study, INJ-9, conducted in adult haemodialysis patients and five phase I studies conducted in healthy volunteers. These studies collectively consisted of 478 CRF patients and 98 healthy volunteers valid for safety analysis[2]. The adverse event profile (including immunogenicity) in the pivotal study INJ-9 was consistent with the advanced dialysis

patient population and comparable between treatment groups. There were no serious, significant or treatment-related severe adverse events in the healthy volunteers[2].

The EMA has recently reviewed the safety of ESAs partially as a result of data indicating that treatment of anaemia in CKD to a relatively high target Hb level (>12g/dl) has been associated with an increased risk of mortality and cardiovascular morbidity. The EMA concluded that the benefits of treatment outweigh the risks but have suggested changes to the product information[25]. The EMA recommend that healthcare professionals should use ESAs in accordance with their approved indication and dosing[25].

6.0 SUMMARY OF CLINICAL EFFECTIVENESS ISSUES

- Therapeutic equivalence of Binocrit®▼ to Eprex® has been demonstrated only for IV administration in anaemic CRF adult patients on haemodialysis (study INJ-9). The EMA has, however, extrapolated equivalence to other indications as the mechanism of action is the same[2,26].
- In contrast to other ESAs, Binocrit®▼ is only licensed for IV administration for the treatment of symptomatic anaemia associated with CRF in adult and paediatric patients. The extent to which ESAs are administered via the subcutaneous (SC) route in clinical practice may therefore affect the uptake of this product in NHS Wales.
- No data has been provided for the use of Binocrit®▼ in paediatrics, patients receiving peritoneal dialysis or those not receiving dialysis.
- For market authorisation, the EMA requires that biosimilar ESAs are assessed in at least two adequately powered randomised parallel group trials versus the reference product[26]. However, at the time of the clinical development of Binocrit®▼, the temporary contraindication of the SC route of administration in CKD patients for the reference product precluded the conduct of such a study[2].
- The target primary efficacy endpoint in the clinical development programme for Binocrit®▼ was 10-13g/dl, in contrast to the Medicines and Healthcare Products Regulatory Agency (MHRA) recommended target of 10-12g/dl[27] and the NICE recommended target of between 10.5 and 12.5g/dl for adults and children older than two years of age[15].
- The lowest approved dose of ESAs should be used to adequately control anaemia and its symptoms; with overcorrection of Hb levels in patients with CKD potentially increasing the risk of mortality and cardiovascular morbidity[25,27].
- NICE clinical guideline on anaemia management in people with CKD (CG39) states that there is no evidence to distinguish between ESAs in terms of efficacy[15].
- The company have identified two ongoing studies of Binocrit®▼: study 2006-66-INJ-14 and study 2007-22-INJ-17. The former is a cohort study to monitor the incidence of relevant drug-related adverse events and epoetin-related loss of efficacy in patients with CKD receiving Binocrit®▼ as an IV injection. The latter is a randomised, controlled, double-blind, multicentre study designed to achieve market authorisation for Binocrit®▼ administered via the SC route by evaluating the safety and immunogenicity of SC Binocrit®▼ versus Eprex® for the treatment of anaemia associated with CKD in predialysis patients. This study is on hold as a precautionary measure since one patient was diagnosed with pure red cell aplasia and another developed positive neutralising antibodies, subsequently dying of unrelated causes[23].
- In line with NeoRecormon®[10], Eporatio®▼[11], Retacrit®▼[12] and Aranesp®[13], Binocrit®▼ syringes are chemically and microbiologically stable for two years[1], as compared to 18 months for Eprex®[9] and three years for Mircera®▼[14].

7.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

7.1 Cost-effectiveness evidence

7.1.1 Context

The company submission[23] describes a cost minimisation analysis (CMA) of Binocrit®▼ compared against Eprex®, NeoRecormon® and Aranesp® for the treatment of symptomatic anaemia associated with CKD (haemodialysis patients and IV administration only). A one-year treatment period of use in CKD is assumed on the basis that treatment would be lifelong but outcomes are not considered to differ over time. The analysis relates to adult patients weighing an average of 74.39kg, which the company suggests is the mean weight of patients enrolled in the phase III studies of Binocrit®▼[24]. Costs included in the analysis relate to drug acquisition cost (based on list prices) and administration costs. Further details are provided in Appendix 1.

The analysis excludes Mircera®▼ and Retacrit®▼, with the former recommended by AWMSG as a treatment option in NHS Wales[21] and the latter not recommended[22]. An economic analysis has not been provided specifically for the use of Binocrit®▼ in paediatric patients. NICE has issued guidance on the use of ESAs in the management of CKD-related anaemia[15], and the economic evidence submitted for Binocrit®▼ should be considered within the context of that guidance.

7.1.2 Results

The results of the main analysis, including administration costs, as presented in the company submission are displayed in Table 1. Binocrit®▼ is estimated to be the least costly ESA of those considered in the analysis[23].

Table 1. Company-estimated ESA treatment costs from base case analysis[23]

Indication	Binocrit®▼	Eprex®	Aranesp®	NeoRecormon®
Adult patients suffering from CKD – 1 year of treatment	£3,333	£3,623	£3,711	£4,438
Cost difference versus Binocrit®▼	-	+£290	+£378	+£1,106

The company has conducted a sensitivity analysis to explore the impact of a 35% reduction in ESA dose requirements. The cost difference between Binocrit®▼ and the other ESAs narrows (to within £15 against darbepoetin alfa [Aranesp®]), but Binocrit®▼ remains the least costly.

A scenario analysis in which patients are able to self administer via SC injection (i.e. no resource use associated with nurse administration) is also considered. Binocrit®▼ remains the least costly ESA[23], and the cost difference increases against darbepoetin alfa (Aranesp®) as the advantage of less frequent administration with the latter is lost in this scenario. It should be noted that Binocrit®▼ is not licensed for SC injection in patients with CKD[1].

7.1.3 WMP critique of the company's economic evidence

Strengths of the economic evidence include:

- A pragmatic approach to the base case analyses has been taken.
- The analyses appropriately use current list prices for costing the ESA products.

Limitations of the economic evidence include:

- The analysis assumes a standard IV epoetin dose for all ESA products. Binocrit®▼ is licensed only for IV administration in CKD patients, but other ESA products are licensed for SC administration in CKD patients (e.g. epoetin beta [NeoRecormon®][9]). SC administration may enable lower epoetin doses to be used compared with the IV route in the same patient population, and the difference in costs between Binocrit®▼ and other ESAs will be influenced by the extent to which other ESAs are administered via the SC route in the same patient population in practice. The economic evidence therefore relates only to situations in which SC administration of any ESA is not considered to be an option.
- It should be noted that actual acquisition costs of the available ESAs may differ in practice from current list prices due to contracting arrangements.
- The CMA approach does not consider the potential for greater convenience of, or preference for, a once weekly injection regimen with darbepoetin alfa (Aranesp®) compared with thrice weekly injection for other ESAs. However, differences in administration costs are accounted for within the analysis.

7.2 Review of published evidence on cost-effectiveness

Standard literature searches conducted by WMP have not identified any published evidence on the cost effectiveness of Binocrit®▼.

8.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

8.1 Budget impact evidence

8.1.1 Context and Methods

The budget impact analysis relates to the treatment of patients with anaemia due to CKD only. UK renal registry data for 2008[28] are used to estimate the number of haemodialysis (HD; 1,064) and peritoneal dialysis (PD; 259) patients in Wales. It is assumed that 70% of HD patients receive IV ESA (745 patients), although the basis of that assumption is unclear. The number of patients eligible for ESA treatment is assumed to be constant over the next five years.

UK sales figures for 2009 have been used to estimate the current market share of ESAs (NeoRecormon® 39.07%, Aranesp® 36.80%, Eprex® 18.45%, others 5.68%)[23]. The company assumes market uptake of Binocrit®▼ at 4% in Year 1, 8% in Year 2, 12% in Year 3 and 14% in Years 4 and 5[1], with equal displacement rates across other ESAs. The costs included in the analysis are based on the drug list prices and administration costs, as per the CMA in section 7, which considered ESA therapy for one year in patients with anaemia of CKD[23].

8.1.2 Results

The company-estimated annual budget impact, based on drug acquisition and administration costs, is summarised in Table 2. The company estimates that the use of Binocrit®▼ will result in cost savings compared with the assumed current use of ESAs[23]. No sensitivity analyses have been conducted.

Table 2. Company estimates of budget impact in the management of anaemia in CKD[23]

	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5
Anaemia in CKD					
Eligible population	745	745	745	745	745
Current ESA costs*	£2,806,431	£2,806,431	£2,806,431	£2,806,431	£2,806,431
Cost with Binocrit®▼ uptake	£2,793,465	£2,780,498	£2,767,532	£2,761,049	£2,761,049
Net budget impact	**–£12,966**	**–£25,933**	**–£38,899**	**–£45,383**	**–£45,383**
* Includes NeoRecormon®, Aranesp®, Eprex®, but excludes the 'other' ESAs that account for 5.68% of the current ESA market					

8.1.3 WMP critique

The budget impact estimates are based upon the drug acquisition and administration costs as estimated in section 7. Limitations of these estimates are discussed in section 7.1.3. It should be noted that treatment of anaemia related to CKD is potentially lifelong and would therefore extend beyond one year for many patients. However, it is assumed in the budget impact analysis that patient numbers are constant each year, which does not take into account the cumulative number of ESA-eligible CKD patients with each successive year. In addition, actual acquisition costs of the available ESAs may differ in practice from current list prices due to contracting arrangements. It is therefore uncertain whether the company-estimated cost savings would be realised in practice. The net budget impact estimates would therefore seem subject to significant uncertainty and should be interpreted with caution.

8.2 Comparative unit costs

Table 3 includes example annual costs of relevant comparators in the management of CKD-related anaemia, which is the indication common to all ESAs. Doses must be individualised according to Hb response; those in Table 3 are example doses that may be encountered in the maintenance phase of treatment and should not be interpreted as direct dose equivalents. Costs relate only to acquisition costs derived from BNF list prices[29].

Table 3. Example annual costs of relevant comparators in the management of CKD-related anaemia

ESA	Example maintenance dose	Annual cost of example maintenance dose (£)
Biosimilar Epoetin alfa (Binocrit®▼)	8,000-16,000IU weekly in three divided doses	2,117 – 4,236
Epoetin alfa (Eprex®)	8,000-16,000IU weekly in three divided doses	2,380 – 4,760
Epoetin beta (NeoRecormon®)	8,000-16,000IU once weekly	3,116 – 6,234
Epoetin theta (Eporatio®▼)	8,000-16,000IU once weekly	2,492 – 4,984
Darbepoetin alfa (Aranesp®)	40-80 micrograms once weekly	3,115 – 6,231
Methoxy polyethylene glycol-epoetin beta (Mircera®▼)	200 micrograms once monthly	3,594
This table does not imply therapeutic equivalence of drugs or the stated doses Prices based on pre-filled syringes, no rounding of doses and no vial wastage assumed		

9.0 ADDITIONAL INFORMATION

9.1 Shared care arrangements

- Treatment with Binocrit®▼ must be initiated under the supervision of physicians experienced in the management of anaemia associated with CKD[1].
- Binocrit®▼ is not considered suitable for shared care within NHS Wales.

9.2 Ongoing studies

Refer to section 6.0.

9.3 Other

The UK Renal Registry (established by the Renal Association) provides a focus for the collection and analysis of data on the incidence, clinical management and outcome of renal disease. Currently there is a concentration of data concerning renal replacement therapy, including transplantation, but the Registry will extend to other forms of treatment of renal disease in the future. It is considered a source of comparative data, for audit/benchmarking, planning, clinical governance and research; providing data for bodies such as NHS Trusts, and commissioning authorities[30].

The Pharmacovigilance working party (PhVWP) of the EMA has recommended that the product information for all ESAs includes a request that the trade name of the ESA used is recorded in the patient notes. This will be used to aid assessment of cases of pure red cell aplasia in relation to any quality specifications of an individual ESA. This request was transmitted to the reference member state for Eprex® and the Committee of Medicinal Products for Human Use (CHMP) for all other ESAs[31].

Patient organisation and medical expert opinion was sought.

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Appendix 1. Additional Health Economic Analysis Information

Table 1A. Health economic analysis detail[23]

Base Case Model		Appropriate?
Comparator(s)	Binocrit®▼ is compared against Eprex® brand of epoetin alfa, epoetin beta (NeoRecormon®) and darbepoetin alfa (Aranesp®).	Model comparators appropriate; however, the analysis fails to consider methoxy polyethylene glycol beta (Mircera®▼) which has recently been recommended by AWMSG as a treatment option in Wales[1]
Population	Analysis relates to 74.39kg adult with anaemia due to CKD	Considers a subset of the entire licensed population. ESA costs are determined by patient weight, which the company suggests is the mean weight of patients in the phase III trials.
Analysis type	Simple CMA - assumes all dimension of health outcomes are equivalent.	NICE considered there to be no evidence to distinguish between epoetin alfa, epoetin beta and darbepoetin in terms of efficacy, which the company assumes to mean that outcomes with ESAs are equivalent.
Perspective	Considers direct medical costs only, from perspective of NHS Wales	Yes
Time Horizon	One year time horizon used for CKD patients	Treatment is likely to be lifelong in most patients with CKD. CMA approach assumes all dimension of health outcomes are equivalent, but cost differences may vary over time.
Discount rate	Not applicable due to short time horizon of analysis	N/A
Efficacy	ESA efficacy assumed equivalent	Same approach adopted by NICE in 2006 clinical guideline of anaemia in CKD[15]. The pivotal phase III Binocrit®▼ trial[24] demonstrates comparable efficacy and dosing requirements for Binocrit®▼ and Eprex®. Binocrit®▼ is licensed as a biosimilar epoetin alfa, for which Eprex® was the reference product.
Adverse effects	Not considered in analysis.	Yes, if accept CMA approach
Utility values	Not applicable in CMA	N/A
Resource use	Relates to drug acquisition and administration costs. ESA dose for patients in the CKD indication taken from UK Renal Registry[28].	Yes, if accept CMA approach.
Unit costs	Drug costs based on BNF list prices. Administration costs based on published unit costs for nursing time	Yes. There is a slight discrepancy in the assumed cost per 1,000IU of darbepoetin alfa, which does not materially change the overall conclusions.
Model Provided?	Yes	-

AWMSG: The All Wales Medicines Strategy Group; CKD: Chronic kidney disease; CMA: Cost minimisation analysis; ESA: Erythropoiesis stimulating agent; N/A: Not applicable; NICE: The National Institute for Health and Clinical Excellence.