

Darbepoetin for Maintaining Haemoglobin Target Level versus Epoetin in Hemodialysis Patients in Egypt

Health Technology Appraisal

Issued: November 2015

- بيانات المستحضر محل الدراسة:

Intervention	Darbepoetin alfa prefilled syringe
Company name	Amgen
Comparator	Epoetin alfa (Sedeco Co.)

- الهدف:

تقييم الفعالية لقاء التكلفة لمستحضر Darbepoetin في البقاء على مستويات الهيموجلوبين بمرضى الغسيل الكلوي وذلك في مقابل مستحضر Epoetin. وذلك لضمان أفضل النتائج العلاجية بالنسبة للمريض وبأقل تكلفة ممكنة من خلال الإلتزام بالخطوط العلاجية الاسترشادية العالمية وفي ضوء الممارسة الإكلينيكية المحلية.

- توصية لجنة اقتصاديات الدواء:

في ضوء متابعة دراسة قائمة المستحضرات ذات الأولوية القصوي لإجراء دراسة جدوي إقتصادية لها (**cost effectiveness study**) لتحديد القيمة العلاجية المضافة مقابل التكلفة و بناء علي اجتماع لجنة وحدة إقتصاديات الدواء بتاريخ ٨-٧-٢٠١٥ بالسادة مديري قطاعات الصيدلة بالتأمين الصحي والمؤسسات العلاجية والأمانة العامة للمستشفيات ومستشفيات الهيئة التعليمية. وبتقييم الدراسة الإقتصادية التي أجرتها وحدة اقتصاديات الدواء لأدوية **Darbepoetin Alfa** و **Epoetin Alfa** بغرض دراسة التكلفة لقاء الفعالية والميزة العلاجية المضافة لهم في الاستخدام العلاجي **treatment of anemia due to chronic kidney disease (CKD)** تبين ان مستحضر الـ **Darbepoetin Alfa** هو الأكفأ من حيث الفعالية مقابل التكلفة مقارنة بـ **Epoetin Alfa** ، وذلك بناءً على السعر المقترح من كلا الشركتين. حيث انه يحقق وفراً في التكلفة بمقدار **853,862 L.E/QALY** .(ICER= -853,862).

- علماً أن الدراسة التي قامت بإجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات التي تم تجميعها من التأمين الصحي بالإضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة عن علاج الحالات الغير مستجيبة لاستخدام كل مستحضر على حدة.
- كما تم تجميع البيانات الخاصة بالقيمة العلاجية الناتجة عن جودة الحياة المعيشية للمريض ونسبة الحالات المستجيبة للعلاج بالإضافة إلى الدراسات المنشورة عالمياً.

English Summary

EVALUATION OF USING DARBEPOETIN ALFA FOR HAEMODIALYSIS PATIENTS VERSUS EPOETIN ALFA IN EGYPT

• **Introduction**

Anaemia is a common consequence of chronic kidney disease (CKD) because of the inability of the kidney to produce enough erythropoietin to stimulate the production of red blood cells [1]. This deficiency results in lower haemoglobin (Hb) levels and oxygen availability [2]. The anaemia of CKD is associated with increased mortality, cardiovascular disease, sleep abnormalities, loss of cognitive function, and impaired quality of life [3-6].

Currently chronic anemia is managed by treating patients with erythropoiesis-stimulating agents (ESAs) and iron. Epoetin alfa (EPO, a recombinant human erythropoietin containing the identical amino acid sequence as endogenous erythropoietin) and darbepoetin alfa (a modified recombinant erythropoietin analogue) are two ESAs available to treat anemia in dialysis patients. Darbepoetin alfa has a longer half-life than EPO [7 & 8], and is indicated for less frequent administration in patients with chronic renal failure. Clinical studies indicate that dialysis patients receiving darbepoetin alfa weekly (QW) or every-other-week are able to maintain hemoglobin (Hb) levels within the study-specified target ranges [9-11].

Extending the darbepoetin alfa dosing interval may have advantages for both patients and their healthcare providers. Benefits for patients include increased convenience, as a result of fewer trips to the clinic for treatment, and greater comfort, owing to the reduced number of injections. These benefits may result in better treatment compliance. Advantages for healthcare providers include decreased health-resource utilization and a reduced logistical burden, leading to increased operational efficiency.

• **Objective**

Decision-making based on clinical and economic evidence is essential in order to optimize resource use and service delivery for haemodialysis patients. The objective of this study was to evaluate the cost-effectiveness of darbepoetin alfa versus epoetin alfa in adult haemodialysis patients.

• Economic evaluation Key Features [12]:

Key Features:	
year of the document	November 2015
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Assess the cost-effectiveness of darbepoetin alfa versus epoetin alfa in haemodialysis patients.
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Health insurance
Perspective	Health insurance perspective
Indication	Haemodialysis patients
Target population	insured patients the Egyptian health care system.
Subgroup analysis	Not done in the study
Choice of comparator	Epoetin alfa
Time horizon	5 years was the best time for the study when outcomes are measured and compared.
Assumptions required	Yes
Analytical technique	Cost-effectiveness analysis
Costs to be included	Direct medical costs only included and include the cost of therapy, and the cost of AEs treatment, cost of hospitalization, lab tests done for monitoring.
Source of costs	Hospital costs.
Modeling	Markov model of four health states represent the normal pathway of the disease: low-Hb-level status, target-Hb-level status, high-Hb-level status, and death.
Systematic review of evidences	Yes
Preference for effectiveness over efficacy	Yes
Outcome measure	QALY
Method to derive utility	Kidney Disease Quality of Life-Short Form, the Short-Form 36, and EuroQol EQ-5D
Equity issues stated	All lives, life years, or QALYs are valued equally, regardless of age, gender, or socioeconomic status of individuals in the population
Discounting costs	A discount rate of 3.5 % per year
Discounting outcomes	A discount rate of 3.5 % per year
Sensitivity analysis-parameters and range	Critical component(s) in the calculation is varied

	through a relevant range or from worst case to best case.
Sensitivity analysis-methods	One-way deterministic sensitivity analysis is performed.
Presenting results	With the commonly accepted willingness-to-pay thresholds (3 GDP), using darbepoetin alfa is cost-saving compared with epoetin alfa.
Incremental analysis	Yes
Total costs vs. effectiveness (cost/effectiveness ratio)	Yes
Portability of results (Generalizability)	The generalizability and extent to which the clinical efficacy data and the economic data are representative is identified.

- **Committee Discussion**

The present study found that Darbepoetin alfa is cost-saving compared to Epoetin alfa, making it the dominant treatment for the management of anaemia in chronic haemodialysis patients.

Dosage regimens for both strategies were derived from KDIGO Clinical Practice Guidelines for Anemia in Chronic Kidney Disease [13]. However, there is currently insufficient evidence to suggest the superiority of any ESA formulation based on available safety and efficacy data.

This long-term five-year cost-utility model focuses on the impact of anaemia in haemodialysis patients such as costs associated, dosage regimens, adverse events treatment costs allowing the economic evaluation of both alternatives that have been assessed in treat-to-target studies.

Results of the analysis have shown that for this population of haemodialysis patients, darbepoetin alfa will provide an extra 0.3 QALYs compared to best supportive care with lesser cost of EGP 257,969. This results in an ICER value of -853,862 EGP/QALY.

These results indicate that darbepoetin alfa is a cost-dominant therapy for anaemia suffered by haemodialysis patients in comparison to Egypt's willingness-to-pay threshold as that stated by WHO (3 times GDP per capita). Also, these results were consistent with other technology appraisal studies.

In March 2003, a complete haemodialysis unit switched its patients from epoetin alfa to darbepoetin alfa, as it maintained similar haemoglobin levels at a substantially reduced cost [14]. A brief report from a haemodialysis clinic in Japan indicated that a savings of 34% could be obtained by using darbepoetin alfa instead of epoetin alfa [15]. Another Russian study on the economic evaluation of darbepoetin alfa stated that it is a more cost-effective treatment option compared with other alternative ESAs [16].

Utility data of different health states was derived from Manns 2003 [17] and Clement 2009 [18]. Costs were adapted from health insurance hospitals lists.

The current cost effectiveness study measured efficacy in terms of Quality Adjusted Life Years (QALY) which is a final outcome, the time horizon for the cost effectiveness model was 5 years in which direct medical costs of interventions and treatable adverse events were monthly calculated.

One-way sensitivity analyses of various parameters were performed and showed that the key driver of the results was the utility score of the high haemoglobin level. Other key drivers were the other utility scores of target haemoglobin, low haemoglobin, and blood transfusion.

- **Conclusion**

Darbepoetin alfa is cost saving compared to epoetin alfa in anaemia treatment of haemodialysis patients.

- **Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

- **Appraisal Committee members**

Each technology appraisal is appraised by the PE Committee, which is one of CAPA's standing advisory committees and consist of members who represent different specialties such as statistics, clinical evidence, economics, medicine, clinical pharmacy and pharmacoeconomics. A list of the Committee members who took part in the discussions for this appraisal appears below:

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- **PEU project team**

- **Gihan Hamdy El-sisi**, Head of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.
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