Anagrelide versus hydroxyurea in Essential thrombocythemia

Health Technology Appraisal

Issued: June 2016

- **بيانات المستحضر محل الدراسة:**

Intervention	Thrombonorm (Anagrelide)
Company name	Marcyrl
Comparator	Hydrea (Hydroxyurea)

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر Anagrelide مقابل مستحضر Hydroxyurea في علاج مرضي Essential thrombocythemiaوذلك 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:**

١. في ضوء متابعة إجراء دراسة جدوي إقتصادية (cost effectiveness study) لتحديد القيمة العلاجية المضافة مقابل التكلفة لمستحضرات **Thrombonorm (Anagrelide)و Hydrea (Hydroxyurea) في الاستخدام العلاجي Thrombocythemiaوهي كالأتي:**

-خلصت الدراسة إلي ان مستحضر Anagrelide يعتبر ليس الأكفأ من حيث الفعالية لقاء التكلفة (not cost effective) مقارنة بمستحضر Hydroxyurea في علاج مرض Thrombocythemia. وذلك في ضوء السعر المقترح من الشركة وهو ١٠ جنيه مصري للقرص الواحد.

حيث يحقق مستحضر Anagrelide عدد أكبر من serious event مثل bleeding و thrombosis وبتكلفة اكبر عن نظيره Hydroxyurea

-وقد تم مراجعة النتائج النهائية للدراسة والإفادة بصلاحيتها Validation من ناحية الجودة العلمية في منهج الدراسة والتحليل الإحصائي المتبع وذلك بحضور المتخصصين في مجال الاقتصاد وتقييم الدليل العلمي والاحصاء.

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات التي تم تجميعها من هيئة التأمين الصحي بالاضافة 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 الناتجه عن جودة الحياه المعيشية للمريض ونسبة الحالات المستجيبة للعلاج من الدراسات المنشورة عالميًا .

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English Summary:

Cost effectiveness analysis of Anagrelide versus Hydroxyurea in Essential thrombocythemia from the health insurer perspective :

- **Introduction**

Essential thrombocythemia is characterized by an increased platelet count, megakaryocytic hyperplasia, and a hemorrhagic or thrombotic tendency. Symptoms and signs may include weakness, headaches, paresthesias, bleeding, splenomegaly, and erythromelalgia with digital ischemia. Diagnosis is based on a platelet count > 450,000/μL, normal RBC mass or normal Hct in the presence of adequate iron stores, and the absence of myelofibrosis, the Philadelphia chromosome (or BCR-ABL rearrangement), or any other disorder that could cause thrombocytosis [1].

The principal feature of essential thrombocythemia, a clonal hematologic stem-cell disorder, is thrombosis, with arterial events being more common than venous events? Hemorrhage also occurs, particularly if the platelet count is very high. In the long term, some cases transform to myelofibrosis, myelodysplasia, or acute myeloid leukemia. Factors that increase the risk of thrombosis are an age of more than 60 years, prior thrombosis, and, to a lesser extent, cardiovascular risk factors. The importance of the platelet count as a risk factor is unclear, but a reduction in platelet count reduces the frequency of thrombosis, and aspirin relieves the microvascular symptoms of essential thrombocythemia. [2].

Medical therapy is targeted toward reducing risk of thrombosis and hemorrhage and is indicated in Patients who are at increased risk of thrombotic events, based on age or history of thrombosis. While cytoreductive therapy, with or without low-dose aspirin, is the mainstay of thrombosis risk reduction, optimal choice of agent is less clear. Several agents, including hydroxyurea, anagrelide, interferon and busulfan are in use for this purpose [3].

Hydroxycarbamide (also known as hydroxyurea) is the only cytoreductive agent proven to reduce thrombotic events in a randomized controlled trial and remains the recommended first-line therapy for the majority of patients requiring treatment [4].

Anagrelide was developed as an inhibitor of platelet aggregation but was later found to reduce the platelet count at doses lower than the amount required to inhibit platelet aggregation. The drug blocks megakaryocyte differentiation and proliferation and inhibits the action of cyclic AMP phosphodiesterase.Despite the lack of evidence of efficacy reported in a randomized trial, anagrelide is commonly used as first-line therapy for high-risk patients with essential thrombocythemia, even though it is substantially more expensive than hydroxyurea [2].

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Objective

The aim of this study is to evaluate the cost-effectiveness of the Anagrelide versus hydroxyurea from health insurer perspective in treatment of essential thrombocythemia in Egypt.

Economic evaluation Key Features:

Key Features:	
year of the document	June 2016
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Evaluate the cost-effectiveness of the Anagrelide versus hydroxyurea in treatment of essential thrombocythemia from health insurer perspective.
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Public, Healthcare Industries
Perspective	Health insurer perspective
Indication	Treatment of essential thrombocythemia.
Target population	Those who are insured and not insured by the Egyptian health care system.
Subgroup analysis	No subgroup analysis
Choice of comparator	Hydroxyurea
Time horizon	Over 39 months' time horizon
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 lab tests done for monitoring.
Source of costs	Health insurance hospitals.
Modeling	Decision tree
Systematic review of evidences	yes
Preference for effectiveness over efficay	yes
outcome measure	The outcomes of the two treatments were measured in terms of Number of events avoided.
Preferred method to derive utility	We depend on surrogate outcome
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	Not done.
Discounting outcomes	Not done.

Sensitivity analysis-parameters and range	Critical component(s) in the calculation is total events avoided in Anagrelide versus Hydroxyurea
Sensitivity analysis-methods	One-way sensitivity analysis is performed.
Presenting results	Hydroxyurea is more cost effective
Incremental analysis	Not done
Total costs vs. effectiveness (cost/effectiveness ratio)	Not done
Portability of results (Generalizability)	The generalizability and extent to which the clinical efficacy data and the economic data are representative is identified and discussed.

- **Committee Discussion**

The leukocyte-lowering effect of hydroxyurea reduced the strength of the association between leukocytosis and thrombosis in this investigation. The cytoreductive effect of hydroxyurea on leukocyte counts may explain the advantage of this drug with respect to the prevention of arterial thrombosis over the selective platelet-lowering compound anagrelide in the UK-PT1 trial, a randomized phase III trial in a cohort of high-risk ET patients. Based on the superiority of hydroxyurea combined with aspirin over anagrelide combined with aspirin in this trial, current guidelines for cytoreductive therapy favor hydroxyurea as first-line therapy for ET [5].

The objective of this analysis was to evaluate the cost-effectiveness of the Anagrelide versus hydroxyurea from health insurer perspective in treatment of essential thrombocythemia in Egypt. The results of the CE study indicated that Anagrelide is high costly and less effective than hydroxyurea in treatment of essential thrombocythemia based on the intention-to-treat analysis [3].

The clinical data of the cost effectiveness study were derived from meta-analysis of two phase III randomized controlled clinical trials that compared Anagrelide versus hydroxyurea in treatment of essential thrombocythemia on 809 and 259 patients. The outcomes of interest, including arterial thrombosis, venous thrombosis, all thrombosis, major bleeding, minor bleeding [3].

The current cost effectiveness study measured efficacy in terms of intermediate outcome (total events avoided) in anagrelide versus hydroxyurea, the time horizon for the cost effectiveness model was 39 months to reflect the events costs calculated.

Several assumptions were made in this study leading to uncertainties in the results. To assess the impact of other model structures and assumptions on the cost -effectiveness estimates, one-way sensitivity analysis was performed and revealed that the key driver of the results was the total events avoided in anagrelide versus hydroxyurea in ITT scenario and cost of anagrelide; these parameters have the major impact on the analysis result.

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- **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:

Dr. Gihan Hamdy, Head of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

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