Aprepitant in Egyptian Patients Receiving Highly Emetogenic Therapy

Health Technology Appraisal

Issued: May 2014

- **بيانات المستحضر محل الدراسة:**

Intervention	Aprepitant
Company name	MSD
Comparator	Dexamethazone+Ondosterone

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر Aprepitant في علاج حالات القئ الشديد الناتج من العلاج الكميائى للسرطان. 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:**

بناء علي الطلب المحول من إدراة الفنية لمناقصات الادوية لعمل دراسة "Pharmacoeconomics" للمقارنة بين الجدوي الاقتصادية للعلاج التقليدى(Dexamethazone+ Ondosterone) وبين إضافة دواء ال Aprepitant اليه فى حالات القئ الشديد الناتج من العلاج الكميائى للسرطان .
قد تبين من الدراسة التي قامت بها وحدة اقتصاديات الدواء و بناء على رأي اساتذة و خبراء الاورام، ان مستحضر الـ Aprepitant ليس الأكفأ من حيث الفعالية مقابل التكلفة ، ومع العلم انه إذا تم تخفيض السعر سوف يكون هو الأكفأ من حيث الفعالية مقابل التكلفة "Cost effective Therapy" .

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات التي تم تجميعها من تسعيرة الادارة الفنية لمناقصات الادوية بالاضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة عن علاج الحالات الغير مستجيبة والحالات الطارئة لاستخدام كل بروتوكول على حدة، وطبقا لتسعيرة نفقة الدولة .

- 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 OF APREPITANT IN EGYPTIAN PATIENTS RECEIVING HIGHLY EMETOGENIC THERAPY FROM THE THIRD PARTY PAYER PERSPECTIVE

- **Introduction**

In chemotherapy treatment for malignancy, chemotherapy-induced nausea and vomiting (CINV) is one of the major adverse effects that hinder patient compliance with further chemotherapy treatment and affect patient's quality of life [1]. 90% or more of the patients who receive highly emetogenic chemotherapeutic agents such as cisplatin and cyclophosphamide will experience acute emesis [2]. Aprepitant is a substance P neurokinin 1 receptor antagonist [3] that proves efficacy in the treatment of acute and delayed CINV associated with the use of highly emetogenic chemotherapeutic agents (HEC).

Aprepitant demonstrated efficacy in clinical trials on end points related to CINV when used in combination with a serotonin receptor antagonist (5-HT3 RA) and dexamethasone compared with a standard care regimen (combination of 5-HT3 RA and dexamethasone) [4]. That is why international organizations recommend aprepitant in their guidelines as a part of the antiemetic treatment for patients who receive HEC. For instance, Association of Supportive Care in Cancer, the European Society for Medical Oncology, the National Comprehensive Cancer Network, and the American Society of Clinical Oncology include aprepitant in their antiemetics guidelines [2,5,6]. In Asia-pacific markets such as New Zealand, South Korea and Australia, aprepitant has been assessed and listed for patients who are receiving HEC [7,8,9]. In Singapore, aprepitant is recommended for CINV prophylaxis in patients who are receiving HEC or moderately emetogenic chemotherapy in any type of cancer [10].

Several studies have been conducted to assess the cost-effectiveness of aprepitant. In Belgium, aprepitant-based regimen is found to be more effective and less expensive compared to standard anti-emetic regimen in the treatment of (CINV) [11]. Moreover, aprepitant showed to be cost-effective in the treatment of (CINV) compared to standard therapy in similar studies conducted in Germany, USA and Singapore [12, 13, 14].

The cost-effectiveness of aprepitant in the Egyptian health system contest has not been studied yet. Decision analysis is a quantitative method for synthesizing data from numerous sources for the evaluation of treatment alternatives and was developed to determine the cost-effectiveness of aprepitant as add on therapy to 5-HT3 RA and dexamethasone.

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Objective

The aim of this study was to evaluate the cost-effectiveness of aprepitant as add-on therapy to the standard Egyptian regimen (5-HT3 RA and dexamethasone) in patients receiving HEC .

- **Economic evaluation Key Features:[15]**

Key Features:	
year of the document	May 2014
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Evaluate the cost-effectiveness of aprepitant as add-on therapy to the standard Egyptian regimen in patients receiving highly emetogenic therapy
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Public, Healthcare Industries And Clinicians
Perspective	Health care system, Third Party payer
Indication	Treatment of severe emesis induced by chemotherapy
Target population	Those who are insured by the Egyptian health care system.
Subgroup analysis	Only for those whom clinical and cost effectiveness may be expected to differ from that of the overall population.
Choice of comparator	Standard therapy (ondosterone+Dexamethazone).
Time horizon	5 days 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	Official sources of unit cost data for products (e.g. The Ministry of Health Hospitals)
Modeling	Decision tree
Systematic review of evidences	yes
Preference for effectiveness over efficacy	yes
Outcome measure	Primary outcome measures are complete response (no emesis and no rescue therapy) on days 1 to 5

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Method to derive utility	The direct use of 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 sensitivity analysis is performed.
Presenting results	Adding aprepitant to the standard regimen is cost effective
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 and discussed.

- **Committee Discussion**

Chemotherapy-induced nausea and vomiting (CINV) has been identified as one of the most distressing adverse effects for patients who are being treated with chemotherapy for malignancy, with patients rating the nausea or vomiting as low as 0.2 on a visual acuity scale [1]. Aprepitant has demonstrated a clinically important improvement of patients protection from acute or delayed emesis after treatment with HEC [7,8,9]. Our results support that achieving this clinical improvement with aprepitant is also cost-effective in the context of the Egyptian health system, with a favorable cost per emetic event avoided and cost per QALY result.

In this context, our analysis of the use of aprepitant for cisplatin based chemotherapy regimens (Protocols 052/054and801) indicate that an aprepitant-containing regimen is cost-effective (with ICERs close to 66004.78 EGP/QALY) for use in these patients compared with standard regimens including ondansetron[14].

Our results are also consistent with those published elsewhere in the literature. Lordick and colleagues [12] developed a decision analytic model to assess the cost-effectiveness of aprepitant in Germany based on the clinical trial evidence from Protocols 052 and 054(cisplatin-based regimens). An article from Belgium reported the findings from a cost-utility analysis based on the results of Protocols 052/054 (cisplatin-based regimen) [11]. An additional used data from a longitudinal hospital database to provide information on real-world resource use in

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CINV. In both scenarios, the authors found the aprepitant to be cost saving (less costly and more effective) than standard care in both highly and moderately emetic chemotherapy regimens[11].

The cost-effectiveness of aprepitant in the United States was assessed by using a Markov model to compare an aprepitant-containing regimen with a standard regimen of ondansetron and dexamethasone over five cycles of chemotherapy [6,13]. The resultant ICER was high (US $96,300); however, it should be noted that the costs of the antiemetic treatment regimens were more than double those used in our analysis.

There are some limitations to our approach. First, the resource use data were drawn from those reported in clinical trials (Protocols 052/054, cisplatin-based regimens) rather than Egyptian-specific resource use. Although it would be preferable to use country-specific data, this is not routinely reported for Egypt and, in the absence of good information, making assumptions would have introduced uncertainty. Second, the clinical data were derived from another clinical trial that its data were collected by using patient diaries and therefore this information is subjective in nature. However, because there are no objective measures for CINV end points, the diaries are valuable in that they capture the severity of CINV for an individual. Third, there was little Information in form the utility estimates for health states in the model because health-related quality-of-life data were not collected in the clinical trials. Therefore, the best available estimates included were drawn from the literature, and these were a key focus of the sensitivity analysis.

Finally, we did not undertake probabilistic sensitivity analysis to quantify the level of confidence in the ICERs. Instead, one-way sensitivity analysis was conducted for our study by simultaneously varying the inputs that had produced the greatest change. These results represent a “worst-case” and a “best-case” analysis, which may not be representative of the current situation in Egypt.

- **Conclusion**

The present study concludes that adding aprepitant to the standard regimen is cost effective based on the threshold stated by world health organization (3xGDP/capita) for patients with severe vomiting after chemotherapy.

- **Declaration of interest**

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

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- **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 pharmacoeconomic. A list of the Committee members who took part in the discussions for this appraisal appears below:

Dr. Mahmoud El-Mahdawy, General director of Hospital pharmacy administration, Central Administration for Pharmaceutical Affairs, Ministry of Health.

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

Prof. Ahmed Hassouna, Consultant of clinical trials.

Dr. Abd Allah Mohammed, Expert at National Authority for the control of Biopharmaceuticals.

- **PEU project team**

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

- **References:**

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