Cost-Effectiveness of Cabergoline versus bromocriptine in treatment of Hyperprolactinemic amenorrhea

Health Technology Appraisal

Issued: February 2016

- **بيانات المستحضر محل الدراسة:**

Intervention	Cabergoline
Trade name	Dostinex
Company name	Pfizer
Comparator	Bromocriptine Mesylate

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر Cabergoline مقابل مستحضر Bromocriptine Mesylate في علاج مرضي Hyperprolactinemic amenorrhea 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 اجراء دراسة جدوي إقتصادية (cost effectiveness study) لتحديد القيمة العلاجية المضافة مقابل التكلفة لمستحضر Cabergoline:

- فقد تبين ان مستحضر Cabergoline يحقق فائدة علاجية افضل في ضبط مستوي هرمون البرولاكتين لمدة أطول بفارق ١٣ شهر عن نظيره Bromocriptine.

وقد خلصت الدراسة إلي ان مستحضر Cabergoline ليس الأكفأ من حيث الفعالية لقاء التكلفة مقارنة بمستحضر Bromocriptine في علاج مرض Hyperprolactinemia. وذلك في ضوء السعر المقترح من الشركة وهو ٥٣ جنيه للقرصين ،علما بأن مستحضر Cabergolineسيكون الأكفأ من حيث الفعالية لقاء التكلفة اذا تم تخفيض السعر الى ٣١ جنيه للقرصين للتأمين الصحى او مشاركة المريض في تحمل جزء من التكاليف.

- وعليه تقترح اللجنة ان يتم دراسة الاليات المناسبة لتوفير مستحضر Cabergoline للمرضى نظرا لما يحققه من فائدة علاجية . ودراسة مدى امكانية تطبيق (patient copayment).

- 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 .

English Summary:

Cost-Effectiveness of Cabergoline versus bromocriptine in treating Hyperprolactinemic amenorrhea Patients from the Insurer perspective: A Decision tree Model

Introduction

Hyperprolactinemia is defined as the elevation of prolactin levels above 25ng/ml in women of child bearing age group and above 20ng/ml in men and postmenopausal women. Hyperprolactinemia is mainly due to enlargement of the pituitary gland or due to a pituitary tumour or can occur without any obvious reason. Hyperprolactinemia is also frequently associated with secondary hypogonadotropic hypogonadism. This gonadotropic deficiency has been proposed to result from direct suppression of prolactin (PRL) on gonadotrophin-releasing hormone (GnRH) release. Increased serum prolactin levels decreases the secretion of gonadotropin-releasing hormone (GnRH) in the hypothalamus, thus causing decreased secretion of LH and follicle-stimulating hormone (FSH) in the pituitary gland leading to decreased production of estrogen and progesterone by the ovaries. Decreased hormone production in the ovaries leads to disruption of the normal follicular development causing atresia of the dominant follicle [1].

It is a common endocrine disorder of the hypothalamic-pituitary axis. It occurs more commonly in women. The prevalence of hyperprolactinemia ranges from 0.4% in an unselected adult population to as high as 9-17% in women with reproductive diseases. Its prevalence was found to be 5% in a family planning clinic, 9% in women with adult onset amenorrhea, and 17% among women with polycystic ovary syndrome [2].

Bromocriptine still the most widely used dopamine agonist, is given orally starting with a low dose. The dose should be increased until prolactin levels are returned to normal. Bromocriptine treatment normalizes serum prolactin levels in 80% of patients with idiopathic hyperprolactinemia or microprolactinoma with a pregnancy rate of 60–80% provided there are no other infertility factors [3]

Cabergoline is new, selective, potent, and long lasting dopamine agonist that inhibits prolactin secretion in both normal subjects and those with hyperprolactinemia [4]. It has an extremely long plasma half – life of about 65 hours allowing once- or twice – weekly administration. Unlike bromocriptine, cabergoline has low affinity for D1 receptors, Cabergoline is more expensive than bromocriptine, and some physicians may reserve the medication for use in patients who are resistant to or intolerant of bromocriptine.

Cabergoline has the advantage over bromocriptine in terms of both efficacy and tolerability, and therefore it is preferred in the treatment of hyperprolactinemic amenorrhea [5].

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

- **Objective**

The objective of this study was to evaluate the cost-effectiveness of Cabergoline versus bromocriptine for treatment of hyperprolactinemic amenorrhea over a time horizon of eight months.

- **Economic evaluation Key Features:** [5]

Key Features:	
Title and year of the document	February 2016
Affiliation of authors	Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs
Purpose of the document	Evaluation the cost-effectiveness of using Cabergoline versus bromocriptine For treating Hyperprolactinemic amenorrhea Egyptian patients
Standard reporting format included	yes
Disclosure	yes
Target audience of funding/ author's interests	Public and private payers, healthcare industries and clinicians
Perspective	The Insurer Perspective
Indication	Treatment of Hyperprolactinemic amenorrhea
Target population	Those who are insured and uninsured by the Egyptian health care system.
Subgroup analysis	No subgroup analysis
Choice of comparator	Bromocriptine Mesylate
Time horizon	over eight months period ' time horizon
Assumptions required	yes
Preferred analytical technique	Cost-effectiveness analysis
Costs to be included	Direct medical costs only included and include the cost of therapy and cost of lab tests done for monitoring.
Source of costs	Official sources of unit cost data for products (e.g. Tender lists)
Modeling	Decision tree model
Systematic review of evidences	yes
Preference for effectiveness over efficacy	yes
Preferred outcome measure	The outcomes of the two treatments were measured in terms of Number of months controlled prolactin level
Preferred method to derive utility	No utility was measured
Equity issues stated	The outcomes are valued equally, regardless of age, gender, or socioeconomic status of individuals in the population

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

Discounting costs	Not done.
Discounting outcomes	Not done.
Sensitivity analysis-parameters and range	Critical components in the calculation were chosen
Sensitivity analysis-methods	One-way sensitivity analysis was performed.
Presenting results	Cabergoline is not cost-effective compared to the use of Bromocriptine treatment of Hyperprolactinemic amenorrhea inspite of the better outcomes of Cabergoline.
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.
Financial impact analysis	Not done
Mandatory or recommended or voluntary	Recommended in the meantime but expected to be mandatory in few years

- **Committee Discussion**

The main objective of this study was to evaluate the cost-effectiveness of cabergoline versus bromocriptine for treating Hyperprolactinemic amenorrhea from the insurer perspective. The results of the CE study indicated that cabergoline is not cost effective compared to bromocriptine in treatment of Hyperprolactinemic amenorrhea at ICER value of 114.000 L.E for each extra month prolactin controlled.

The clinical data of the cost effectiveness study were derived from randomized controlled trial that compared cabergoline to bromocriptine in the treatment of hyperprolactinemic amenorrhea on 459 women aged 16-45 years.

The efficacy of treatment was assessed with clinical criteria and biochemical measurement. The complete clinical success was defined as the occurrence of at least two consecutive menses with biochemical evidence of ovulation and complete biochemical success was defined as serum prolactin value within the normal range after week 6 of treatment [4].

The current cost effectiveness study measured efficacy in terms of intermediate outcome (Number of months controlled prolactin level) in cabergoline versus bromocriptine, the time horizon for the cost effectiveness model was 8 months in which cost of managing side effects was calculated. As in all modeling exercises, 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 Number of months controlled prolactin level in Cabergoline and cost of cabergoline; these parameters have the major impact on the results.

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

- **Conclusion**

It is important to address both the clinical and the economic implications of a new therapy from the payer perspective before deciding on public reimbursement of new therapies. We conclude that compared with our willingness to pay threshold stated by WHO (3times GDP/CAPITA): Cabergoline is not cost-effective compared to the use of Bromocriptine treatment of Hyperprolactinemic amenorrhea in spite of the better outcomes of cabergoline**.**

- **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.

Prof. Ahmed Hassouna, Consultant for clinical trials.

Prof. Heba Nassar, Economics Professor, Faculty of Economics and Political Sciences, Cairo University.

Dr. Souad Abd Al Aleem, Manager of Hospital Pharmacy Administration, Central Administration for Pharmaceutical Affairs, Ministry of Health.

Dr. Rasha Hassan, Director of pricing administration, Central Administration for Pharmaceutical Affairs, Ministry of Health

- **PEU project team**

- **Gihan Hamdy El-sisi**, Head of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.
- **Zeinab Ahmed El-shafei,** Team member of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.
- **Asmaa Saad,** Team member of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

- **References:**

[1] Kalaivani, vidhyalakshmi Incidence of Hyperprolactinemia in Infertile Women *(IOSR-JDMS)* 2279-0861.Volume 13, Issue 11 Ver. VII (Nov. 2014), PP 07-10.

[2] Abha Majumdar and Nisha Sharma Mangal Hyperprolactinemia J Hum Reprod Sci. 2013 Jul-Sep; 6(3): 168–175.

[3] P.G. Crosignani Management of hyperprolactinemic infertility Middle East Fertility Society Journal Volume 17, Issue 2, June 2012, Pages 63–69

[4] Jonathan Webster, Gabriella piscitelli, Anna polli, et al Comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea New England Journal of Medicine oct.6,1994 Vol.331 No.14

[5] Ahmed J Al-Husaynei, Isam H. Mahmood, Zena S. Al-Jubori, Comparison of the effects of cabergoline and bromocriptine in women with hyperprolactinemic amenorrhea Middle East Fertility Society Journal Vol. 13, No. 1, 2008

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg