Taxanes in Egyptian Patients with Early Breast Cancer

Health Technology Appraisal
Issued: March 2015

- **بيانات المستحضر محل الدراسة:**

Intervention	Weekly paclitaxel and 3 weekly docetaxel
Company name	Docetaxel (taxotere) by Sanofi-aventis Paclitaxel (taxol) by Bristol-Myers Squibb
Comparator	3-weekly paclitaxel

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر weekly paclitaxel and 3 weekly docetaxel في علاج حالات سرطان الثدي المبكر. 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 معهد الأورام لسرطان الثدي لعمل دراسة "Pharmacoeconomics" للمقارنة بين الجدوي الاقتصادية للعلاج التقليدى 3-weekly paclitaxel وبين مستحضر weekly paclitaxel و مستحضر 3 weekly docetaxel فى حالات سرطان الثدي المبكر . فقد تبين من الدراسة التي قامت بها وحدة اقتصاديات الدواء و بناء على رأي اساتذة و خبراء الاورام، ان كل بروتوكول على حدى weekly paclitaxel و 3 weekly docetaxel هما الأكفأ من حيث الفعالية مقابل التكلفة بالمقارنه مع 3-weekly paclitaxel ولكن مستحضر weekly paclitaxel هو الأكثر كفاءه من حيث الفعالية مقابل التكلفة.

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات التي تم تجميعها من قسم المناقصات بمستشفي الأورام لسرطان الثدي بالاضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة عن علاج الحالات الغير مستجيبة والحالات الطارئة لاستخدام كل بروتوكول 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 weekly paclitaxel and 3 weekly docetaxel versus 3-weekly paclitaxel in Egyptian patients with early breast cancer from health care provider perspective

- **Introduction**

Breast cancer is the second most common cause of death from cancer [1]. Postoperative adjuvant chemotherapy for regionally invasive breast cancer reduces the risk of recurrence and death. Outcomes for breast cancer vary depending on the cancer type, extent of disease, and person's age [2]. Survival rates in the developed world are high [3], with between 80% and 90% of those in England and the United States alive for at least 5 years [4, 5]. In developing countries survival rates are poorer [6]. Worldwide, breast cancer is the leading type of cancer in women, accounting for 25% of all cases [7]. In 2012, breast cancer resulted in 1.68 million cases and 522,000 deaths.

Until the early 1990s, adjuvant chemotherapy was most commonly based on cyclophosphamide, methotrexate and fluorouracil, but such regimens have largely been superseded by anthracycline-based regimens (doxorubicin or epirubicin) because of their greater effectiveness. The taxanes, paclitaxel and docetaxel, were introduced in the late 1990s and were found to improve survival in the adjuvant setting when used sequentially with anthracycline- based regimens compared with the anthracyclines based regimens alone [8]. Guidelines recommend that a taxane should be considered in all cases where adjuvant chemotherapy is contemplated for women with early breast cancer [9].

Paclitaxel and docetaxel differ in terms of their pharmacokinetic and toxicity profiles. However, most guidelines do not specify which taxane is preferred for adjuvant treatment of early breast cancer because they have conventionally been considered to be similarly effective [9, 10, 11]. However, a number of cost-effectiveness analyses have shown that the adjuvant treatment of early breast cancer with docetaxel is cost effective compared with non-taxane-containing regimens [12–13], whereas cost-effectiveness data have been less convincing for adjuvant standard 3-weekly paclitaxel [14, 15].

The cost-effectiveness of taxanes in the Egyptian health system context has not been studied yet and as we have limited resources to PTES (Pay-at-The-Expense-of-the-State), an insurance system, can't cover all the interventions, we should only reimburse the cost effective drug to better allocate our resources.

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Objective:

The aim of this study was to evaluate the cost-effectiveness of weekly paclitaxel and 3 weekly docetaxel versus 3-weekly paclitaxel in Egyptian patients with early breast cancer.

- **Economic evaluation Key Features:[16]**

Key Features:	
year of the document	March 2015
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Evaluate the cost-effectiveness of weekly paclitaxel and 3 weekly docetaxel versus 3-weekly paclitaxel in Egyptian patients with early breast cancer.
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Public, Healthcare Industries
Perspective	Health care system perspective
Indication	Treatment of early breast cancer in adjuvant with anthracyclines – based regimen.
Target population	Those who are insured and not 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 (3-weekly paclitaxel).
Time horizon	Over a 30 Year period.
Assumptions required	yes
Analytical technique	Cost-effectiveness analysis
Costs to be included	Direct medical costs only included the cost of therapy, and the cost of AEs treatment, cost of lab tests done for monitoring.
Source of costs	Tender department from oncology institution.
Modeling	Markov model
Systematic review of evidences	yes
Prference for effectiveness over efficay	yes
outcome measure	The outcomes of the two treatments were measured in terms of quality-adjusted life-years (QALYs)

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Preferred method to derive utility	Methods of deriving utility varied: 51% of authors used direct elicitation (standard gamble, time tradeoff, or rating scale), 32% estimated QOL based on their own expertise or that of others, and 17% used health status instruments.[17]
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	Both weekly paclitaxel and 3-weekly docetaxel are cost effective versus 3 weekly paclitaxel.
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:

Adjuvant chemotherapy substantially reduces the risk of recurrence and death among women with operable breast cancer. The addition of a taxane to an anthracycline- containing regimen reduces the risk of relapse. There have been recent important changes to adjuvant regimens and costs of taxanes for the treatment of early breast cancer, requiring a re-evaluation of comparative cost effectiveness. In particular, weekly paclitaxel is now commonly used but has not been subjected to cost effectiveness analysis. The results of our study showed that both weekly paclitaxel regimen and 3 weeky docetaxel regimen were cost effective versus 3 weekly paclitaxel regimen but the weekly paclitaxel was more cost effective at ICER EGP362.9 /QALY while the ICER of 3 weekly docetaxel was EGP 739.2/QALY versus 3 weekly paclitaxel regimen.

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One of the key strengths of the current study is that the clinical evidence was derived from randomized clinical trial comparing the efficacy of two different taxanes, docetaxel and paclitaxel, given either weekly or every 3 weeks, in the adjuvant treatment of breast cancer on 4950 women with axillary lymph node–positive or high-risk, lymph node–negative breast cancer. The results of the study was comparable with that performed in New Zealand which stated that both weekly paclitaxel and docetaxel are likely to be cost effective compared with standard 3-weekly paclitaxel.

We fully acknowledge the limitations of this indirect comparison; the model was limited by the paucity of direct comparative data for docetaxel, weekly paclitaxel and 3-weekly paclitaxel. Given the importance of relatively small differences in survival effects in this analysis, further direct comparisons are needed if decision makers want to recommend one or other of docetaxel or weekly paclitaxel .In addition, dose reductions was not modeled in the analysis due to the complexity of incorporating these calculations. However, this is not likely to have significant effect on the results.

To test the stability of our results across variations in input model parameter estimates, we performed various one-way sensitivity analyses as recommended by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS): ISPOR Task Force report. The robustness of the model-to-model structures and assumptions was tested with one-way sensitivity analyses of the estimates of clinical parameters, health state utilities, costs of treatment, and discount rates for costs and health effects. One-way sensitivity analyses show that the disease free survival of the three regimens has the largest impact on the results.

- **Conclusion**

Compared with our willingness to pay threshold stated by WHO (3times GDP/Capita) both 3-weekly docetaxel and weekly paclitaxel are cost effective compared to 3- weekly paclitaxel (the standard regimen) for patients with early breast cancer but paclitaxel is more cost effective than 3-weekly docetaxel.

- **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 pharmacoeconomics. 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 for clinical trials and evidence based medicine.

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.
  - **Asmaa saad,** Team member of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

- **References:**

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