Bortezomib Plus Dexamethasone in previously untreated Multiple Myeloma patients

Health Technology Appraisal

Issued: June 2014

- **بيانات المستحضر محل الدراسة:**

Intervention	Bortezomib Plus Dexamethasone
Trade name	Velcade
Company name	Takeda
Comparator	Vincristine+Adriamycin+Dexamethasone

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر **Bortezomib** في علاج مرضي Multiple Miloma. 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 طلب الادارة الفنية لمناقصات الادوية بعمل دراسة "Pharmacoeconomics" لبيان الجدوى الاقتصادية "CEA" لمستحضر Velcade Tablet . وفي ضوء السعر المقترح من الشركة فقد تبين من الدراسة الاقتصادية التي قامت بها الوحدة، ان البروتوكول العلاجي Velcade + Dexamethasone ليس الأكفأ من حيث الفعالية مقابل التكلفة مقارنة بالبرتوكول العلاجي Vincristine+ Adriamycin+ Dexamethasone (VAD).

وعليه توصي لجنة اقتصاديات بالتفاوض مع الشركة على السعر او عمل Risk sharing agreement.

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات والتي تم تجميعها من تسعيرة الادارة الفنية لمناقصات الادوية ومناقصات هيئة التأمين الصحي، بالاضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة والناتجة عن استخدام كل بروتوكول على حدة، وطبقا لتسعيرة نفقة الدولة. كما تم تجميع البيانات الخاصة بالقيمة العلاجية الناتجة عن جودة الحياة المعيشية للمريض "QUALITY OF LIFE" ونسبة الحالات المستجيبة للعلاج من الدراسات المنشورة عالميًا .

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English Summary:

Economic Evaluation of Bortezomib Plus Dexamethasone Versus to Vincristine Plus Adriamycin Plus Dexamethasone in previously untreated Multiple Myeloma patients

- **Introduction**

Multiple myeloma (MM) is a neoplastic plasma cell disorder that characterized by low blood counts, bone and calcium problems, infections, light chain amyloidosis and other hazardous and its incidence is strongly related to age (1). However MM isn't curable, it's treatable by chemotherapy combinations that aim to improve survival and quality of life.

Induction therapy is recommended before stem cell transplant to reduce tumor burden.
Vincristine, adriamycin, and dexamethasone (VAD) has been a standard for induction therapy before HDT-ASCT (high dose melphalan therapy followed by autologous stem cell transplantation); however, it typically results in lower Complete response rates (2). Improving very good partial response (VGPR) rates by new induction regimens may improve VGPR rates post transplantation and avoid second transplantation.

A recent clinical trial IFM 2005-01 Phase III demonstrated that Bortezomib plus dexamethasone significantly improved postinduction and post-transplantation Complete Response/near Complete Response and at least VGPR rates compared with VAD and resulted in a trend for longer PFS (3).

- **Objective**

The objective of the current analysis was to assess the cost-effectiveness of Bortezomib Plus Dexamethasone Versus to Vincristine Plus Adriamycin Plus Dexamethasone in previously untreated Multiple Myeloma patients from the third party payer perspective over a time horizon of ten years.

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Economic evaluation Key Features: [4]

Key Features:	
year of the document	June 2014
Affiliation of authors	Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs
Purpose of the document	Assess Cost effectiveness analysis of Bortezomib Plus Dexamethasone (Vel Dex) versus VAD As Induction Treatment Prior to Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma.
Standard reporting format included	yes
Disclosure	yes
Target audience of funding/ author's interests	Public and healthcare industries
Perspective	Health care system
Indication	Induction Treatment Prior to Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma
Target population	Both those who are insured and uninsured 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	Vel Dex it is the routinely used intervention for this indication in such patients.
Time horizon	10 years was chosen to capture long term health and economic outcomes
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 and cost of hospitalization
Source of costs	Official sources of unit cost data for products (e.g. Tender lists)
Modeling	Markov model
Systematic review of evidences	yes
Preference for effectiveness over efficacy	yes
Outcome measure	Primary outcome measures are progression free survival (PFS), and overall survival (OS)
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

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Discounting costs	A discount rate of 3.5 % per year is used for costs.
Discounting outcomes	A discount rate of 3.5 % per year is used for outcomes.
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	Bortezomib plus dexamethasone is not clearly cost-effective compared to VAD
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**

Understanding multiple myeloma disease has led to rapid expansion of available options for treatment, such as thalidomide, lenalidomide and bortezomib. Although these options have proved to increase response rate and prolong patient survival, they are more costly which creates the need to assess the incremental cost effectiveness ratio versus traditional intervention.

The main objective of this study was to evaluate the cost-effectiveness of Bortezomib plus dexamethasone Versus VAD from the Egyptian insurer perspective (PTES). Our analysis was a 3 health state Markov chain model over a 10 year time horizon concluded that bortezomib/dexamethasone improve survival times over VAD. However, the additional QALY gained didn't justify the increased costs upon using BTZ/Dex instead of VAD resulting in ICER equal to 942, 291 which is far above the willingness to pay threshold value of QALY gain in Egypt .

As in all decision models, there are uncertainties around the parameters used in the model need to be taken into account. One-way sensitivity analyses of various parameters were performed and showed that bortezomib/dexamethasone overall survival has the major impact on the analysis result.

While the National Institute of Care Excellence uses a threshold of £ 30,000 per QALY [5], the Egyptian threshold value still uncertain to conclude whether the new intervention is cost effective against current intervention or not. WHO proposed many approaches to approximate this threshold. The most common approach is based on GDP per capita, where an intervention that, per disability-adjusted life-year (DALY) avoided, costs less than three times the national annual GDP per capita is considered cost–

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effective, whereas one that costs less than once the national annual GDP per capita is considered highly cost–effective.[6] Based on WHO recommendation the calculated threshold was about EGP 70000 for 2005-2009.[7]

As most economic analysis studies, our analysis herein has limitations need to be highlighted. First, being based on one clinical trial due to lack of other head to head phase III trials comparing Bortezomib plus dexamethasone versus VAD at the time of the analysis. Second, dose modifications were required as response to hematologic and non-hematologic adverse events (AEs) but we couldn't include this in our analysis as the insurer doesn't pay for the consumed doses of drug but paying the whole dosing regimen. Finally, the modeling represents an extrapolation beyond the observed trial period.

- **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. Since a recent clinical trial demonstrated that Bortezomib plus dexamethasone significantly improved post-induction and post-transplantation CR/nCR and at least VGPR rates compared with VAD and resulted in a trend for longer PFS. Bortezomib plus dexamethasone should therefore be considered a standard of care in this setting.

Compared with commonly accepted willingness-to-pay threshold using Bortezomib plus dexamethasone is not clearly cost-effective; and most likely to result in an ICER somewhat higher than the societal willingness-to-pay threshold.

So this cost effectiveness study helps inform the health care decision in allocation of health care system resources and achieving better health for the Egyptian population. However, we are in a great need for local trials to build our local data. More accurate localized data will help a lot in running the model and reaching health care decisions with the best available evidence for our population so a risk sharing agreement could be a solution until we have our local data.

- **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,

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economics, medicine, clinical pharmacy and pharmacoeconomics. A list of the Committee members who took part in the discussions for this appraisal appears below:

- **Prof. Ahmed Hassouna**, Consultant of clinical trials.
- **Prof. Ashraf Nabhan**, Associate Editor, Cochrane Collaboration.
- **Prof. Randa El-Desoki**, Scientific director of global initiatives of the Organization of the economics of medicine management and research outputs.
- **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.

- **PEU project team**

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

- **References:**

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