Newly Defined Role of Pharmacoeconomics in Iran National Medicine Policy

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Unlimited and mostly competing demands in health care systems even in developed societies, always force decision makers to choose among the priorities for allocation of resources. However, recent developments in health technology assessment (HTA) have created a better opportunity for allocation of limited resources available in health care systems. Although this tool has been used more frequently in developed countries, which have substantially more resources available in their health sector, there are increasing efforts in developing countries for using this tool in order to prioritize demands in their national health sector (1). The fact that HTA evaluates both short and long term impacts of medical interventions for their health outcomes and resource use could provide a clear picture for the real value of health technologies. This could obviously help with better availability and distribution of resources and improve health care system performance and equity in the society. Therefore, this function provides the opportunity to compare the value of different interventions from the society or health care providers' perspective.

Pharmacoeconomics is one of the HTA sub disciplines, which solely deals with cost effectiveness evaluation of medicines and their real value for the health care system. Although many scientists believe it could provide a rational ground for decision makers, since pharmacoeconomic analysis identifies, measures and values costs and outcomes of the pharmaceutical interventions simultaneously, some health care professionals feel uncomfortable about putting a monetary value on the patients' medical problems and their suffering.

Iran is a Middle Eastern country with a population of more than 78 million people with most being young. Iran gross domestic product (GDP) per capita, which mainly depends on the oil revenue, in 2014, was reported to be about 4200 USD. In Iran, the ministry of health and medical education (MOH) is the main stewardship of the health care system. According to the Iran constitutional law, the Iran government has the mandate to provide the highest attainable level of the health care for all Iranians. Therefore, the Iran government in the past decades has invested heavily on the national health care system and has created an opportunity for all Iranians to have fairly equitable access to the health care system. The government believes that this investment will bring valuable return to the society in the long term. As a result, the Iran health care system has advanced to a degree that its indicators have substantially improved and now in addition to the presence of a primary health care system, the most advanced medical interventions and high tech equipment are also available to the patients (2). Although the Iran health system consists of both public and private sectors, currently all Iranians have access to a government-supported health insurance system. However, due to the lack of sufficient resources in public health sectors and national health insurance schemes, in the past years and up to 2012, out of pocket payments of patients have substantially increased and has topped to over 60% of the costs of medical services (3). Since early 2013, the Iran government implemented a national health reform program mostly targeted at reduction of out of pocket payment by the patients. According to the MOH report, the program was successful to reduce out of pocket spending share in total health care spending to about 20% and to about 10% for medicines for inpatient services.

In 2014, the Iran pharmaceutical market was valued at about 4.2 billion USD. Despite the fact that promoting the national pharmaceutical industry is one of the main objectives of the Iran national medicine policy, share of the national pharmaceutical industry in Iran pharmaceutical market is about 60%. All aspects of medicines regulation including production, importation, distributions, and sale of medicines in Iran are fully controlled by the Iran food and drug administration (IFDA). All medicines

should receive registration and marketing authorization before entering the Iran market. Traditionally, the Iran drug selection sommittee, responsible body for developing and revising the medicine list, used to request acceptable safety, quality and efficacy data for including new medicines to the list. Recently, in shadow of pressures from limited available resources in the national health care system, Iranian policy makers have considered pharmacoeconomics to evaluate benefit of medicines in comparison with the extra costs they impose to the health care system. Therefore, the committee now requires pharmacoeconomics evaluation of any submission for new medicine application (4).

In 2014, the IFDA has published its first version of the guideline for pharmacoeconomics analysis of medicines. Since then, all pharmaceutical companies (local and international) are required to submit pharmacoeconomics evaluation data for their candidate medicine. However, based on the national policy of supporting local pharmaceutical industry, the Iran national health care system considers medicines produced locally "cost effective". Based on this policy, local pharmaceutical companies exempted from submitting a full pharmacoeconomics evaluation, dossier for their medicines. The local pharmaceutical industry requested only to submit a concise file, which mainly includes a review of published data regarding cost effectiveness of candidate medicine. However, it should be mentioned that locally-produced generic medicines in Iran, are mostly priced based on "cost plus" method.

Based on published national guidelines for submission of pharmacoeconomics evaluation dossier, the file should include at least data related to the following topics:

1. Introduction: In this section the applicant should provide reliable data regarding the disease in question, including epidemiology of the disease, burden of disease and available interventions currently in use of the country.

2. Medicine characterization: This section should include information related to the effectiveness and clinical performance of the intended medicine such as international non property name, anatomical therapeutic chemical classification, strength, dosage form and on-label and off-label clinical applications of the medicines.

3. Target population: Characteristics of the target population for which the intended medicine will be prescribed should be clearly defined. Items such as age, gender, socio-economic status, geographical distribution of the disease and the presence or absence of co-morbidities should be clarified. In presence of reliable data regarding better effects of the medicine in population subgroups of patients, the analysis of the subgroups should also be performed.

4. Perspective: Perspective of the study should be the third party payer and national health care system. However, separate presentation of the results from the perspective of society is also welcomed. The costs and benefits expressed in each analysis should be presented according to the perspective of the study.

5. Methods: Although different types of pharmacoeconomic methods could be used by the applicant, the choice of method must be fully justified. The selection of outcome parameters depends on the clinical use of the drug, research question and the economic evaluation method, which was used. Clinical parameters being used must be carefully selected and justified. Cost minimization analysis is only preferred when compared medicines provide equal health benefits. If the Cost Effectiveness method is used there must be a clear and validated correlation between the marker used and final health outcome. Obviously, use of this method for possible ranking of a broad set of medicines is not acceptable. Whenever measuring impact of the candidate medicine on quality of life of patients is feasible or is the only way of measuring health outcome, Cost Utility Analysis is the preferred analytical method. Therefore the results of the study can be measured and expressed in different units such as quality-adjusted-life-year (QALY), life years gained/saved, disability averted or utility.

6. Comparator: Although most of the time, clinical evaluation committee of the Iranian Drug Selection Committee recommends the most appropriate current practice as comparator for a given patient group, the selection of the comparator by the applicant has to be justified. The most relevant alternative should be selected based on the national standard clinical guidelines, whenever available. Although, comparing the new drug with its different alternatives is possible, for practical reasons, selecting one comparator is sufficient. In any case, the selected comparator must be approved by the drug selection committee, before performing the pharmacoeconomics study.

7. Outcomes: For measuring the clinical outcomes of the new drug, in the absence of domestic data, the clinical results related to the effectiveness and safety of the drug, which have been published in relevant academic journals (peer reviewed journals), could be used. The most common sources for extracting clinical data are randomized clinical trials (RCT) and systemic reviews or meta-analysis. In the absence of valid RCT studies, evidence must be extracted from the best existing studies. In any case, the method used to analyze or combine the data must be clearly expressed. The health outcomes of the clinical studies could be expressed as changes in the quality and/or quantity of life or changes in clinical surrogate outcomes. Changes in quality of life can be evaluated by either direct methods such as visual analogues scale, time trade off, standard gamble or indirect methods including questionnaire tools such as HUI, EQ-5D, and SF-36. In converting the results of the questionnaire to the local utility, numerical algorithms should be considered. Since the utility can be influenced by domestic cultural and social factors, the preferences extracted from the domestic target population will be preferred. If the domestic preference is not available, the preference of similar populations can be used.

8. Costs: Direct costs should mainly include the costs of the resources used in relation to the disease, including medical and non-medical costs such as the costs of medicine, diagnosis, treatment, monitoring, rehabilitation and hospital costs. They also include the costs of the treatment of side effects. Direct non-medical costs include expenses for personal items, travel, food, transportation, personal care, etc. The costs should always be expressed in the local currency (Iranian Rials) and presented in separately clarified tables. Any inclusion of indirect costs, including productivity loss needs justification based on local country perspectives. Currently, saving from indirect costs is not being considered as justified benefits for new treatment unless there are strong reasons to do so.

9. Models: The structure being used for analysis of the models should be clarified based on its logic and graphical scheme (decision tree or Markov model). There should be transparent justification for the population of the clinical studies used in the model, inclusion and exclusion criteria, duration of the study and the problem being investigated. The model must be as clear and simple as possible and all assumptions explicitly expressed. However, it should illustrate all aspects of disease and treatment options. Although any validated commercially-available software could be used for modeling, use of the Excel software in modeling is recommended. Items such as structure of the model, study assumptions, list of inputs including probabilities, costs and utilities along with the references should be provided.

10. Time horizon: Regardless of which analytical method is used, a suitable time horizon should be chosen. Appropriate time horizon should guarantee reflection of the treatment outcome and the resource consumption in the course of the disease.

11. Discount rates: For costs and benefits occurring beyond the one-year horizon, discount should be applied. A discount rate of 3% per year is proposed for both costs and health outcomes.

12. Sensitivity analysis: In order to show whether the study results are sensitive to the variable changes, uncertainty of the results should be presented through sensitivity analysis. For practical reasons, deterministic sensitivity analysis is preferred.

13. Threshold: Based on current national guidelines, IFDA considers drugs with cost/QALY of less than one national GDP per capita as "cost effective". However, for drugs with cost/QALY in the range of one to three times of the national GDP per capita there is room for negotiation with the national committee. Medicines with cost/QALY higher than this will be considered as unacceptable.

14. Presenting the results: Results of the evaluation must be presented clearly so that the quality, validity and relevance of the findings can easily be measured. Unless the newly introduced option dominates, the study results may be presented using incremental cost effectiveness ratio (ICER), to compare the difference between the costs and health outcomes of two alternative interventions. To provide a clear picture of the costs and benefits of different options, all costs and health outcomes of the alternatives considered in the study, must be separately tabulated and compared with the base options. To provide the necessary information about the new drug and its therapeutic alternatives, the costs and outcomes must be expressed separately and in total. The generalizability of foreign clinical study outcomes to the conditions within the country must be judged according to the similarity in the treatment methods being applied. The sources of the data being used, and the assumptions in the analysis must be clearly stated. Also, the limitations of the study must be discussed, and the results of the study must be compared with similar economic evaluations. Any possible conflict of interests should be clearly stated in the report.

15. Budget impact analysis: In order to evaluate the budget impact of use of new medicine on the country's national health budget, the applicant should also provide data for the impact of using the new medicine. A budget impact deals with the ability to pay for new interventions and its sustainability will help decision makers with regards to the overall impact of the intended intervention on the national health care budget. The model designed for the budget impact analysis must be transparent, and be based on local population data or a scenario, which can be generalized to the Iran population. In these studies, attention must be paid to the population, market share, growth rate, and costs in two scenarios with new drugs and current situation.

16. Conclusion: The Iran national health system is facing growing demands for new and mostly expensive medicines. However, due to limited resources available to this sector, the Iranian health system decision makers have decided to implement cost effectiveness analysis for all candidate medicines to be included in the medicine list. Therefore, since 2014, all pharmaceutical companies are requested to submit pharmacoeconomics analysis for their proposed medicines. The Iran national pharmacoeconomics evaluation committee is part of the IFDA and the director of the committee is appointed by the Minister of Health. Following approval of the committee for cost effectiveness of the candidate medicine, the application will be forwarded to the Iran drug selection committee for a final decision. In fact the pharmacoeconomics evaluation committee provides a positive list for the drug selection committee. In 2014, pharmacoeconomics evaluation committee has published its guideline for submission of files and its criteria for decision-making. Although the Iran pharmacoeconomics evaluation committee accepts transfer of certain HTA elements from other countries, local data especially in the cost section is absolutely necessary.

The Iranian authorities believe local production of pharmaceuticals will improve their accessibility and affordability. Therefore, supporting the national pharmaceutical industry is one of the fundamental objectives of

the Iran national health policy. The IFDA considers all locally-manufactured medicines as "cost effective". However, local pharmaceutical companies should submit pharmacoeconomics evaluation dossier for their candidate medicine in order to set a baseline price for the medicine. The base price will be set based on the ICER and cost/QALY whenever feasible. It should be emphasized that pharmacoeconomics evaluation of medicines in Iran is still at its early stage and lack of high quality data both in economic and clinical outcome parts could be considered as a major hurdle to this new field. However, decision makers of the Iran health system at its highest level are determined to implement HTA in the country's health sector and hope that in the near future the quality of pharmacoeconomics evaluation of medicines will be improved.

Acknowledgments

References

1. Babar ZU, Scahill S. Is there a role for pharmacoeconomics in developing countries? *Pharmacoeconomics*. 2010;**28**(12):1069–74. doi: 10.2165/11584890-000000000-00000. [PubMed: 21080732]
2. Bagheri Lankarani K, Alavian SM, Peymani P. Health in the Islamic Republic of Iran, challenges and progresses. *Med J Islam Repub Iran*. . 2013;**27**:42–9. [PubMed: 23479501]
3. Davari M, Haycox A, Walley T. The Iranian health insurance system; past experiences, present challenges and future strategies. *Iran J Public Health*. 2012;**41**(9):1–9. [PubMed: 23193499]
4. Cheraghali. Implications of Pharmacoeconomics for Iran National Health System. *Iran J Pharm Sci*. 2013;**9**:81–5.