

Original Article

Evaluation of prescriptions of medicines not included in Iran medicine list: A cross-sectional study

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Received: May 2016
Accepted: June 2016

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ABSTRACT

Objective: Iran Food and Drug Administration (IFDA) has the mission to regulate all aspects of pharmaceutical market including registration of the new medicines. Iran Drug Selection Committee has the responsibility to maintain and revise Iran Medicine List (IML). The National law has banned production, importation, distribution, and prescription of medicines not included in IML. Although, IFDA policy makers have created a mechanism to provide medicines not included in the list but might be essential for the treatment of specific patients.

Methods: A cross-sectional study was carried out on prescription of out of IML medicines during the year 2015. This study was conducted on a total of 1375 application forms received by Secretariat of Iran Drug Selection Committee for prescription of out of IML medicines.

Findings: It has been shown that among 402 specialist physicians, the most out of IML medicine were prescribed by oncologist/hematologist. Antineoplastic and immunomodulating agents were the most frequently prescribed medicines both in terms of number and diversity. According to the collected data, more than 76% of all medicines were supplied by only 4 out of 25 pharmaceutical companies in 1 year.

Conclusion: Results of this study show that despite its early intention this mechanism is easily abused by some pharmaceutical companies as an unethical way of induced demand and marketing of their products. Therefore, IFDA decision makers should revise this mechanism and decide based on its real benefits and harms both to the patients and Iran national health system.

Keywords: Drug selection committee; induced demand; Iran medicine list; national regulation

INTRODUCTION

The Islamic Republic of Iran's pharmaceutical market is a fully regulated market. Iran Food and Drug Administration (IFDA) as part of Iran Ministry of Health and Medical Education has the mission to regulate all aspects of pharmaceutical market including registration of the new medicines. To establish and

update a national medicine list, IFDA has created a national drug selection committee. Iran Drug Selection Committee, which consists of pharmacists and medical specialists, has the responsibility to maintain and revise Iran Medicine List (IML). According to the law, IML is the main base for any pharmaceutical activity in Iran. Only medicines on the list could be registered for entering into Iran market. National law has banned

Access this article online



Website: www.jrpp.net

DOI: 10.4103/2279-042X.192456

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How to cite this article: Zargaran M, Nikfar S, Cheraghali AM. Evaluation of prescriptions of medicines not included in Iran medicine list: A cross-sectional study. *J Res Pharm Pract* 2016;5:234-7.

production, importation, distribution, and prescription of medicines out of the IML. Breach of the law could result to penalties. Iran Drug Selection Committee has adapted a generic-based list of the medicines. Currently, there are more than 2900 items on the IML, including a variety of molecules with different dosage forms and strength. Previous investigations show that more than 90% of the population of Iran has accessed to the affordable essential medicines during the last decades.^[1]

Although IFDA policy makers believe diversity of the medicines on IML covers majority of medical needs of Iranian patients to the safe and effective medicines, they have created a mechanism to provide medicines not included in the list but might be essential for the treatment of a specific patient. According to this approach, physicians could prescribe such medicine for a specific patient if they have evidences to prove that patient's medical need could not be satisfied by the medicines already on IML. IFDA has established clear criteria for evaluation of such requests to grant permission for the importation of such medicines. Under the provisions of these criteria, physician should complete the application form of "Specific Patient Prescription" and explain the reasons of prescription. The applications will be assessed by the experts of the secretariat of Iran Drug Selection Committee and in the case of approval, the pharmaceutical company will import specifically the requested medicine for the patient. In this study, a 1 year data for 1375 "Specific Patient Prescription" during 2015 have been analyzed and evaluated. The main objective of this study is to provide information regarding the types of medicines and specialists prescribing drugs of nonincluded in the national list.

METHODS

This cross-sectional study conducted on a total of 1375 application forms received by Secretariat of Iran Drug Selection Committee in 2015. This includes all requests for prescription of medicines not included in the IML. Collected data including medicines' name, dosage form, strength, brand name, the importer pharmaceutical company, quantity of prescribed medicines, physician's name and specialty, diagnosis, patient's name, and medication history were obtained from requests received by the committee's secretariat. According to the designed application form, doctors are allowed to prescribe medicines out of the IML only based on following conditions:

1. There is not any medicine in IML to manage diagnosed patient medical problem
2. There is a history of lack of patient's response to the medicines already on IML or incidence of

serious side effects due to the administration of other medicines.

In any case, the doctor should document the history of prescription of the medicines existed on IML and explained the reason for prescription of the new medicines. The exact quantity of the prescribed medicine and the duration of treatment should be determined by the physician.

All application forms from physicians were collected by the Secretariat of Iran Drug Selection Committee from January to December 2015. All the registered medicines were coded using the World Health Organization's Anatomical Therapeutic Chemical (ATC) classifications^[2] and the data were analyzed.

RESULTS

A total number of 1375 application forms were analyzed. Results are summarized in Tables 1 and 2. These 1375 prescriptions were issued by 402 physicians. However, oncologists and hematologists showed the highest rate (28.9%) of prescribing out of IML medicines followed by cardiologists (12.4%), rheumatologists (11.2%), neurologists (8.2%), ophthalmologists (5.5%), infectious disease specialists (4.2%), urologist (3.7%), nephrologists (3.5%), gastroenterologists (3.0%), pulmonologists (2.7%), endocrinologists (2.5%), psychiatrists (2.2%), dermatologists (1.7%), and gynecologists (1.5%).

Table 1 shows that prescribed medicines belong to which ATC code and their share from total medicines prescribed. According to these results, antineoplastic

Table 1: The percentage of prescribed medicines based on Anatomical Therapeutic Chemical classifications

Anatomical Therapeutic Chemical category	Number of prescribed medicines (%)
Antineoplastic and immune-modulating agents	450 (32.7)
Musculoskeletal system	324 (23.6)
Sensory organs	158 (11.5)
Cardiovascular system	158 (11.5)
Nervous system	86 (6.3)
Genitourinary system and sex hormones	60 (4.4)
Antiinfectives for systemic use	59 (4.3)
Anti-parasitic products	27 (2.0)
Alimentary tract and metabolism	16 (1.2)
Respiratory system	14 (1.0)
Systemic hormonal preparations	7 (0.5)
Blood and blood forming organs	5 (0.4)
Dermatologicals	3 (0.2)

Table 2: Top ten out of Iran medicine list medicines prescribed by different medical specialties in Iran in 2015

Out of Iran medicine list prescribed medicines	Number of prescription (%)
Denosumab, injection	289 (21)
Metolazone, tablet	121 (8.8)
Enzalutamide, capsule	66 (4.8)
Bendamustine, injection	63 (4.6)
Aflibercept, injection	52 (3.8)
Pilocarpine, tablet	45 (3.3)
Ranibizumab, injection	43 (3.1)
Dihydrotestosterone, topical gel	43 (3.1)
Azacitidine, injection	32 (2.3)

and immunomodulating agents (L) are the most frequently prescribed medicines. The medicines classified as musculoskeletal system (M) have the second highest prescription rate among all the categories. Table 2 shows top ten most frequently out of IML medicines prescribed by different specialties. Among all medicines prescribed by physicians, denosumab injection was the most frequently prescribed medicine.

Since physicians are requested to explain the reasons they prescribed out of IML medicines about 81% of all 1375 applications declared a lack of patient's response to the other medicines on IML or a history of serious side effects as the main reason to justify out of IML prescription. However, other 19% claimed that there is not any medicine in the IML to cover the diagnosed therapeutic indications. Analysis of data for out of IML medicines prescribed from pharmaceutical companies showed that more than 76% of all requested out of IML medicines belongs to four importer pharmaceutical companies; while the rest belongs to other 21 pharmaceutical companies.

DISCUSSION

In this study, data regarding prescription of out of IML medicines have been elaborated. Results of this investigation show that oncologists are the main cause of prescribing such medicines. Despite the fact that there are several medicines for the management of osteoporosis in IML, there are still other medicines available for the patient management. Denosumab, a fully human monoclonal antibody for the treatment of osteoporosis, is one of these medicines. Denosumab is the most frequently out of IML medicine prescribed by physicians.

The hypothesis of supplier-induced demand is one of the controversial themes in the health economic

system.^[3] Based on this theory, the health services providers utilize more information about healthcare advantages for persuading the patients to use unnecessary health-care commodities.^[4,5] There are a lot of studies that confirm the phenomenon of induced demand in health economic systems.^[6-8] The results of this study show that about 54.8% of the all 129 requested medicines were pertaining to the first ten medicines [Table 1]. The other 119 prescribed medicines were accounted for less than half of all prescriptions. According to the collected data, since more than 76% of all medicines were supplied by four numbers of all 25 pharmaceutical companies in 1 year, it seems that some of the pharmaceutical companies have played an important role to motivate the physicians to prescribe the medicines not included in the IML. It seems that some pharmaceutical companies use this opportunity as their marketing strategy for introducing their products into the Iran market. However, it should be mentioned that despite the presence of nationwide medical insurance this national insurance scheme does not cover costs attributed to the medicines out of IML. Therefore, patients have to pay full costs of these medicines. Although we did not consider cost-effectiveness of the prescribed medicines not included in the IML from patients or national health perspective, it seems this approach obviously imposes substantial out of pocket costs to the patients.^[9,10] On the other hand, it seems that this approach could be used by some pharmaceutical companies to induce demands for new medicines not already on IML.^[3]

The results of this study indicated that more than one-third of all requested medicines both in term of frequency and diversity were belonged to the antineoplastic and immunomodulating agents. More reviews on the diagnosed disease mentioned in the application forms showed that about 55% of all the antineoplastic and immunomodulating medicines were prescribed for the patients who were in advanced stages of metastatic cancers. It is clear that this group of patients has no choice but to try the new medicines and are forced to pay out of pocket exorbitant fees for more survival.

Although Iran policy makers have created a mechanism for responding to possible therapeutic needs of some specific patients who might need medicines not included in IML for their life-threatening medical conditions, it seems that this mechanism easily abused by some physicians and pharmaceutical companies. It was previously shown that health provider's professional behavior can be influenced by the different methods of payment.^[11,12] In fact, an inappropriate relationship between the physicians and pharmaceutical companies will lead

to induce the imposed demands on patients^[13,14] and forced them to buy medicines which are not financially supported by the health insurance in public and private sectors.

This study has revealed that in more than 80% of the all applications, the physician asserts that all of the indicated medicines from IML have been administrated for the patient already. Indeed, based on the physician's claim, there is not any other choice to cure the diagnosed disorder. Results of this study show that despite early intention of policy makers for implementation of this mechanism as a relieve for patients in desperate need of some very specific medicines, this mechanism could be abused by some pharmaceutical companies as an unethical way of marketing. Therefore, IFDA decision makers should seriously revise this mechanism and decide based on its real benefits and harms both to the patients and Iran national health system.

AUTHORS' CONTRIBUTION

All the authors were involved in collection and analyzing the data and preparing the manuscript.

Financial support and sponsorship
Nil.

Conflicts of interest

There are no conflicts of interest.

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