

High Insurance Coverage and Financial Support for Effective Cancer Drugs in I.R. Iran

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A B S T R A C T

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Background: In recent years, financial coverage and availability of new and expensive cancer drugs have changed into one of the challenges of the health system, especially in low-income and middle-income countries. We studied the availability of anticancer drugs, insurance coverage and the financial burden of these drugs in Iran.

Methods: In this cross-sectional descriptive study, first, we listed effective cancer drugs according to the World Health Organization's Model List of Essential Medicines and previous studies. Then, we evaluated financial burden of these drugs by using the available data in Iran pharmaceutical Pharmacopoeia, the national pharmaceutical sales statistics database (pharmaceutical Amarnameh), and inquiry of the insurance organizations, the availability, insurance coverage in Iran. Excel software was used for data analysis.

Results: All of the medicines incorporated into the latest version of the WHO Model List of Essential Medicines were available in Iran, and, except for Bendamustine and Anastrozole all medicines were covered by insurance. In addition, of the 19 drugs, those were not on the WHO Model List of Essential Medicines, there were seven drugs in Iran, insurance covered that six drugs. The total Dollar sales of the studied cancer drugs amounted to US\$350.85 million in 2015 and US\$384.96 million in 2016.

Conclusion: It seems that the status of access to effective cancer drugs in Iran is better than many low and middle-income countries. However, since the cost of cancer drugs is rising, health policy makers inevitably need to prioritize cancer drugs by using the results of health technology assessment methods and provide patients with access to drugs that are cost-effective in order to the optimal allocation of limited resources and provide maximum access to cancer drugs throughout the country.

Keywords: Accessibility, insurance coverage, financial burden, cancer drugs



INTRODUCTION:

Many advances in cancer treatment have taken place in recent years, and new therapies have been invented. Although many of these new drugs and methods have had a significant impact on improving the quality of life or survival of the patients, they impose high costs on patients and health systems¹. The cost of cancer drugs has increased more than double over the past decade, and from an average of \$ 5,000 per month has reached to more than \$ 10,000 per month. For example, the price of 11 cancer drugs among 12 drugs that approved by the FDA in 2012, was more than \$ 100,000 per year².

Studies in the United States in 2009 have shown that in the years leading to this year, the cost of cancer drugs has increased 14% annually. Also, out-of-pocket expenses have significantly increased for cancer patients, especially among the low-income patients, so that these families have spent about 27% of their annual revenues for cancer treatment³. Increasing out-of-pocket expenses makes patients prevent expensive treatments or discontinue their treatment because they do not want their family pulled down below the poverty line because of them⁴. What is important about new cancer drugs, which has led to many discussions about it in recent years, is that many of these drugs have limited clinical benefits, in contrast to their high costs, and some of them only add a few months to the lifespan of the patient. This has led to concerns among policy-makers and clinicians about the cost-effectiveness of these drugs^{5,6}. For example, in 2013, a group of more than 100 experts in chronic myeloid leukemia (CML) from different countries published an article about the price of drugs used in the treatment of CML and stated that the cost of drugs used to treat CML was high and reduces the access by patients. In addition, it endangers the financial sustainability of health insurance².

The high out-of-pocket costs of patients increase financial pressure and influence the choice of drug type, the quality of life and the outcome of the disease⁷. The incidence of cancer is increasing worldwide, especially in low- and middle-income countries (LMCs) such as Iran. It is estimated that the proportion of diagnosed cancers in LMCs will increase over the next two decades so that 70% of new cancer cases worldwide will relate to these countries. Therefore, these countries will face several challenges in the future to reduce the impact of cancers, including providing effective cancer drugs and providing all patients with access to these drugs. After cardiovascular diseases and accidents, cancer is the third leading cause of death in Iran. Annually, about 50,000 Iranians die from cancer. It is estimated 100,000 new cases of cancer occur annually in the country. With an increase in life expectancy and an increase in the percentage of aging in the country's population, it is expected the incidence of cancer increase to twice as many of the current level in the next two decades⁸⁻¹⁰. The results of previous studies in Iran indicate that a significant portion of the cost of cancer treatment is related to drug costs^{11,12}. The price of cancer drugs in Iran has almost doubled over the past decade, due to an increase in the incidence and prevalence of cancer and the entry of new and expensive drugs. According to the increasing trend of cancer incidence and prevalence and the entry of new and costly cancer drugs, the cost of cancer drugs will rise further and will impose significant economic burdens to the country in the future^{13,14}. Since most countries, including Iran, are facing severe financial constraints and the cost of cancer drugs is high, it is not possible to cover the cost of all cancer drugs by government and insurance agencies. Therefore, to increase the access of cancer patients to essential and useful cancer drugs, it is necessary to prioritize cancer drugs, and then the drugs that are more effective and

necessary are placed at the top of the financial coverage by the government and the insurance organizations. The World Health Organization (WHO) has developed its Model Lists of Essential Medicines, to help countries prioritize and select the medicines to include in their national essential medicines lists and, increasingly, national reimbursable medicines lists. WHO published its first Model List in 1977. The general list has since been updated every two years based on the recommendations of an expert committee, the last edition of the list of essential cancer drugs is related to 2017¹⁵. In addition to the WHO, some international medical associations such as European Society for Medical Oncology (ESMO) and American Society of Clinical Oncology (ASCO) also have developed tools to help clinicians and policymakers to evaluate the clinical benefits of new cancer treatments and prioritize them. For example, the European Society for Medical Oncology (ESMO) has developed a tool to assess the extent of the clinical benefits of new cancer treatments in 2015. By using this tool, the extent of the clinical benefits of new cancer treatments is rated at zero to five. Based on this score, therapies with a score of more than 4 have a high clinical benefit, if the score is 3, they have a modest clinical benefit and, if it is less than 2, they have little clinical benefit^{16,17}. Health Policymakers and planners need to be aware of the status of access to cancer drugs and the financial burden of these drugs in the country in order to develop and implement a cancer control program in the country. Therefore, the present study is conducted to evaluate the availability, insurance coverage and financial burden of essential and effective cancer drugs in Iran.

METHODS:

In this descriptive cross-sectional study, first a list of essential and useful cancer drugs is prepared and then the availability, insurance coverage and finan-

cial burden of these drugs are investigated in Iran in 2015 and 2016. In this study, the purpose of essential and useful cancer drugs were medications that were either listed on the WHO Model List of Essential Medicines, or by using a developed tool by ESMO to assess the extent of the clinical benefits of cancer drugs, have been identified to has a moderate or high clinical benefit (effectiveness rating higher than 2). In order to determine the essential cancer drugs by using the WHO Model List of Essential Medicines, the latest edition of the essential drugs for cancer (edition 2017) has been used¹⁸. Also, the list of cancer drugs with moderate or high clinical benefits was extracted from a paper published by Cherny et al. in 2017¹⁹. In the next step, we looked for the names of these drugs in Iran pharmaceutical Pharmacopoeia to determine whether or not these drugs are available. Iran pharmaceutical Pharmacopoeia was extracted from the Iran food and drug administration website²⁰ in 2017. Considering that in Iran the Supreme Council of Health Insurance decides on the insurance coverage of drugs, so the insurance coverage of the under-study drugs also evaluated through the inquiry of the Supreme Council of Insurance and basic insurance organizations such as Iran Health Insurance Organization and the Social Security Insurance Agency. Finally, the Dollar sale of these drugs in the years 2015 and 2016 was extracted from the national pharmaceutical sales statistics database (pharmaceutical Amarnameh), which is published every year by the Food and Drug Administration^{21,22}. We converted Iranian rials into US dollars (US \$) using the average annual 2015 exchange rate (US\$1=Rial 31,410).

RESULTS:

The findings of the study were reported separately from the incorporated drugs in the WHO Model List of Essential Medicines and drugs that by

using ESMO tools, had moderate or high clinical benefits, but not included in the WHO list. Drugs included in the WHO Model List of Essential Medicines

According to the latest edition of the WHO Model List in 2017, 47 drugs were introduced as essential drugs for cancer, all of which were available in Iran (**Table 1**). All of the essential cancer drugs were under insurance coverage except Bendamustine and Anastrozole. Of the 45 available drugs, the insurance organizations covered 90% of the price for 36 drugs and 70% for seven other drugs. In 2016, the highest Dollar sales of these drugs were respectively related to trastuzumab with US\$64.97 Million dollars (19.40%), Triptorelin with US\$32.18 Million dollars (9.61%) and Rituximab with US\$31.39 Million dol-

lars (9.37%). The lowest Dollar sales of drugs were respectively related to Dasatinib with US\$4.14 Thousand dollars (0.00%), Procarbazine with US\$67.18 Thousand dollars (0.02%) and Daunorubicin with US\$265.52 Thousand dollars (0.08%) (**Table 1**). Effective drugs that were not included in the WHO Model List of Essential Medicines:

Based on the developed tools by ESMO, in addition to the existing drugs in the list of WHO essential cancer drugs, by the year 2016, 19 drugs were introduced as drugs with moderate or high clinical benefits, of which seven drugs were available in Iran (**Table 2**). Also, only 6 drugs of these drugs were covered by insurance. The percentage of insurance coverage for two drugs was 90% and the percentage coverage for the 4 other drugs was 70%. In 2016, the highest Dol-

Table 1. Dollar Sales, Percentage of Total Sales, and insurance Coverage of Essential Cancer Drugs (included in the WHO Model List of Essential Medicines) in Iran

Drug name	Dollar Sale in 2015		Dollar Sale in 2016		Percentage of insurance coverage
	Total Amount (Million US dollars)	The percentage of all these drugs	Total Amount (Million US dollars)	The percentage of all these drugs	
<u>Trastuzumab</u>	64.39	21.68	64.97	19.40	90%
<u>Triptorelin</u>	33.59	11.31	32.18	9.61	90%
<u>Rituximab</u>	27.24	9.17	31.39	9.37	90%
<u>Docetaxel</u>	20.59	6.94	20.42	6.10	90%
<u>Pegfilgrastim</u>	15.13	5.09	17.39	5.19	90%
<u>Tretinoin</u>	0.19	0.06	17.02	5.08	70%
<u>Paclitaxel</u>	11.67	3.93	14.58	4.35	90%
<u>Filgrastim</u>	17.91	6.03	14.07	4.20	90%
<u>Imatinib</u>	11.69	3.94	12.66	3.78	90%
<u>Nilotinib</u>	5.92	1.99	12.37	3.70	70%
<u>Oxaliplatin</u>	12.05	4.06	10.10	3.02	90%
<u>Methotrexate</u>	5.15	1.73	9.37	2.80	90%
<u>Gemcitabine</u>	8.60	2.90	9.34	2.79	90%
<u>Irinotecan</u>	4.73	1.59	9.13	2.73	90%
<u>Capecitabine</u>	9.57	3.22	9.06	2.70	90%

Table 1. Continue...

Drug name	Dollar Sale in 2015		Dollar Sale in 2016		Percentage of insurance coverage
	Total Amount (Million US dollars)	The percentage of all these drugs	Total Amount (Million US dollars)	The percentage of all these drugs	
<u>Letrozole</u>	5.43	1.83	4.54	1.36	70%
<u>Doxorubicin</u>	4.53	1.53	4.43	1.32	90%
<u>Vinorelbine</u>	3.23	1.09	4.27	1.28	90%
<u>Fluorouracil</u>	3.03	1.02	4.16	1.24	90%
<u>Carboplatin</u>	6.00	2.02	4.08	1.22	90%
<u>Cytarabine</u>	1.41	0.47	3.17	0.95	90%
<u>Exemestane</u>	1.30	0.44	2.61	0.78	70%
<u>Ifosfamide</u>	3.08	1.04	2.41	0.72	90%
<u>Goserelin</u>	1.02	0.34	2.15	0.64	70%
<u>Calcium folinate</u>	2.71	0.91	2.11	0.63	90%
<u>Cisplatin</u>	1.69	0.57	1.73	0.52	90%
<u>Cyclophosphamide</u>	1.68	0.57	1.45	0.43	90%
<u>Mesna</u>	1.25	0.42	1.41	0.42	70%
<u>Bendamustine</u>	-	-	1.14	0.34	without coverage
<u>Hydroxycarbamide</u>	1.08	0.36	1.09	0.33	90%
<u>Chlorambucil</u>	0.62	0.21	1.06	0.32	90%
<u>Etoposide</u>	0.76	0.26	0.98	0.29	90%
<u>Bicalutamide</u>	0.89	0.30	0.87	0.26	70%
<u>Dacarbazine</u>	0.59	0.20	0.87	0.26	90%
<u>Anastrozole</u>	0.00	0.00	0.85	0.25	without coverage
<u>Dactinomycin</u>	0.88	0.29	0.78	0.23	90%
<u>Fludarabine</u>	1.01	0.34	0.71	0.21	90%
<u>Vincristine</u>	1.54	0.52	0.70	0.21	90%
<u>Tamoxifen</u>	0.59	0.20	0.60	0.18	70%
<u>Bleomycin</u>	0.96	0.32	0.60	0.18	90%
<u>Thioguanine</u>	0.53	0.18	0.48	0.14	95%
<u>Asparaginase</u>	0.66	0.22	0.46	0.14	90%
<u>Mercaptopurine</u>	0.11	0.04	0.42	0.12	90%
<u>Arsenic trioxide</u>	0.39	0.13	0.37	0.11	90%
<u>Daunorubicin</u>	1.22	0.41	0.27	0.08	90%
<u>Procarbazine</u>	0.34	0.11	0.07	0.02	90%
<u>Dasatinib</u>	0.00	0.00	0.00	0.00	without coverage
Total	296.96	100	334.86	100	

Table 2. Dollar Sales, Percentage of Total Sales, and Percent Coverage of Insurance of effective Cancer Drugs (not included in the WHO Model List of Essential Medicines) in Iran

Drug name	Dollar sale in 2015		Dollar sale in 2016		Percentage of insurance coverage	Included in the national medicines list
	Total Amount (Million US dollars)	The percentage of all these drugs	Total Amount (Million US dollars)	The percentage of all these drugs		
<u>Cetuximab</u>	27.13	50.34	21.53	42.97	90%	yes
<u>Sunitinib</u>	11.72	21.76	11.74	23.42	90%	yes
<u>Everolimus</u>	7.91	14.68	6.92	13.81	70%	yes
<u>Sorafenib</u>	5.24	9.71	6.76	13.49	70%	yes
<u>Erlotinib</u>	1.39	2.59	3.14	6.26	70%	yes
<u>Lapatinib</u>	0.22	0.41	0.02	0.04	-	no
<u>Pertuzumab</u>	0.27	0.49	-	-	-	no
<u>Crizotinib</u>	0.01	0.01	-	-	-	no
<u>Pazopanib</u>	0.00	0.01	-	-	-	no
<u>Panitumumab</u>	-	-	-	-	70%	yes
<u>Gefitinib</u>	-	-	-	-	-	yes
<u>(Trastuzumab emtansine) TDM-1</u>	-	-	-	-	-	no
<u>Afatinib</u>	-	-	-	-	-	no
<u>Axitinib</u>	-	-	-	-	-	no
<u>Temsirolimus</u>	-	-	-	-	-	no
<u>Ipilimumab</u>	-	-	-	-	-	no
<u>Vemurafenib</u>	-	-	-	-	-	no
<u>Abiraterone</u>	-	-	-	-	-	no
<u>Enzalutamide</u>	-	-	-	-	-	no
Total	53.89	100	50.10	100		

lar sales of drugs respectively related to Cetuximab with US\$21.53 Million dollars (42.97%) and Sunitinib with US\$11.74 Million dollars (23.42%). The lowest Dollar sales of drugs respectively related to Lapatinib at 0.02 Million dollars (0.04%) and Erlotinib with 3.14 Million dollars (6.26%) (**Table 2**). It is worth noting that although Panitumumab and Gefitinib, are

available in Iran Pharmaceutical List, because they were recently added to the list (2017), their Dollar sales were zero in the studied years (2015 and 2016). On the other hand, some drugs including Lapatinib, Pertuzumab, and Pazopanib appeared to have been on the drug list in 2015 and have entered the country, but they were removed from the list in 2016.

For this reason, their sales have been zero in 2016. The total Dollar sales of cancer drugs in 2015 was 350.85 Million dollars and in 2016 it was 384.96 Million dollars.

DISCUSSION:

The purpose of this study was to evaluate the availability of essential and effective cancer drugs, insurance coverage and the financial burden of these drugs in Iran. The results showed that all essential cancer drugs included in the WHO Model List are available in Iran. All of the drugs are covered by insurance, except Bendamustine which newly entered in Iran and Anastrozole. Also, a total of 19 drugs, based on ESMO-developed tools, were presented with moderate or high clinical benefits, but were not exist in the WHO list; 7 drugs were available in Iran, insurance covered 6 of which. The total Dollar sales of cancer drugs in 2015 amounted to 350.85 Million dollars and in 2016 it was 384.96 Million dollars.

The results of a study in 2017 by Cherny and colleagues to assess the availability and access to cancer drugs in non-European countries, showed that in high-income and middle-income countries, the majority of drugs that are recommended as essential cancer drugs by WHO existed and have been available to patients at little or no cost. While, in lower-middle-income countries, 5.2% of essential drugs were not available and 32% of drugs had no insurance coverage and the patients paid all of their expenses. Also, in low-income countries, 8.3% of essential drugs were not available and 57.7% of drugs had no insurance coverage. In addition, the findings of the study have shown that drugs that are not included in the WHO Model List have not been available in many LMCs, and in some countries where these drugs are available, a small percentage of them were covered by insurance²³.

The results of the study by Robertson et al., conducted in 2016 to evaluate the availability and insurance coverage of essential cancer drugs, according to the WHO Model List, in 135 countries with a per capita income of less than \$ 25,000, showed that there is a huge difference between low-income and high-income countries in terms of availability and access to essential cancer drugs, so that among 16 drugs that were added to the list of essential cancer drugs in 2015, the mean of the number of available drugs in the countries' national medicines list, in low-income countries was 1 (range: 0-10) and in the high-income countries was 10 (range: 2-15). In that study, there was a positive and significant correlation between the number of essential available drugs in the countries' drug list and national per capita income and per capita expenditure of the state in the health sector¹⁵. Other studies have also similar results such as Evans studies, and colleagues²⁴, Vitry et al.²⁵ and Bazargani et al.²⁶.

A comparison of this study with other studies suggests that the status of availability and access to essential cancer drugs is favorable in Iran according to the WHO Model List and is similar to high-income countries. For example, Trastuzumab was available in Iran and had the highest Dollar sales, while the results of the study by Robertson et al.¹⁵ showed that only 26 countries of the 135 studied countries had this drug in their country, but this drug has been available in all 18 European high-income nations²⁵. Triptorelin, which was available in Iran and had the second place drug regarding the largest Dollar sales, was available in only 53 countries of the 135 countries studied by Robertson et al.¹⁵. Rituximab drug which was available in Iran and had the third place drug in terms of the largest Dollar sales, was available in only 36 countries of the 135 countries studied by Robertson et al.¹⁵. Also, Bendamustine drug, which was available in Iran but insurance does

not cover it because of its new entrance in Iran, was available only in one country from 135 countries studied by Robertson et al.¹⁵.

Iran's health system is currently facing a severe financial constraint, and a significant share (about 40 percent) of health expenses is financed through direct payments of the people, which make some families suffer from catastrophic health expenditure²⁷. Due to resource constraints the government and social health insurance cannot provide financial coverage for all cancer drugs. So, the entry of these drugs to the country could increase direct payments by the people, thereby increasing the catastrophic health expenditure, as well as increasing inequity in health. Accordingly, given the limited available resources, in order to provide the most access to cancer drugs, policymakers and decision-makers are required to choose between cancer drugs and provide financial coverage only for the cost-effective drugs^{28,29}.

Of course, since health policymakers need to decide about the allocation of health system limited resources among different patients, such as cardiovascular, cancer patients, etc., it is also necessary to compare the existing interventions in the different domains. In other words, to decide on the insurance coverage of cancer drugs, these drugs should be compared not only with each other but with other interventions in the health sector, such as cardiovascular interventions or prevention interventions. As a result, new cancer drugs will be financially covered by government or social health insurance if they are cost-effective compared to other interventions in the health system³⁰.

If we assume that the resources of the health system are a fixed and stable amount, in order to provide financial coverage for new cancer drugs, policymakers are forced to reduce the resources allocated to other interventions, thereby losing the benefits that could

have been achieved by those interventions. In such a situation, the allocation of resources to new cancer drugs is only reasonable if the benefits gained by these drugs are greater than the benefits that will be lost due to lack of allocation of resources to other interventions. Even if we assume that the possibility of financial of new cancer drugs is possible through increasing the resources of the health system, the further increase of health resources means reducing the cost of government in other sectors or increasing the direct payments by the people. Given that the government and people's resources are fixed, the government and people are forced to reduce their costs in other sectors in order to provide the costs of cancer drugs. As a result, allocation of resources to cancer drugs is reasonable if the benefits of cancer drugs are greater than the benefits that the government and people are losing in other sectors³⁰.

According to Health Economic principles, if the benefits of a new cancer drug are greater than the benefits that are lost (due to extracting money from existing intervention to pay for new drug), then the drug is called cost-effective. Cost-effectiveness of an intervention can be expressed in different ways in which, in its most common mode, the cost is calculated for each additional outcome obtained by the new intervention, and if its value is less than a certain limit (the cost-effectiveness acceptance threshold) that intervention is called cost-effective³¹. For example, if a new cancer drug, compared to the previous drugs, increase the survival of patients by an average of 2 years and cost 50 thousand dollars more, the cost per additional year of life with this drug would be 25 thousand dollars. Now, if the cost to get one year of life in the health system (that is, through other existing interventions in the health system) is equal to or greater than 25 thousand dollars, this new drug will be cost-effective. Oth-

erwise, if the necessary cost to get one year of life in the health system is less than 25 thousand dollar, the new drug will not be cost-effective. For example, if the cost needed to get one year of life in the health system (including all diseases and interventions) is equal to 10 thousand dollar, then by using the interventions in the health system and with 50 thousand dollar, we can achieve 5 years of life, while using the new drug with this cost, we only get 2 years of life. Accordingly, based on this example, the threshold for accepting cost-effective would be 10 thousand dollars, and if the cost per additional year created by a new intervention is less than or equal to 10 thousand dollars, then that intervention is considered cost-effective. Since the cost per life year gained in health systems varies from each other, the threshold for accepting cost-effectiveness is not the same in different countries. Usually, the higher level of health of the country, the higher the cost-effectiveness threshold. Therefore, the cost-effectiveness thresholds in higher-income countries are higher than in low and middle-income countries³⁰.

Health Technology Assessment studies (HTA) as well as economic evaluation studies compare the costs and consequences of different interventions with each other and provide the required information for policymakers to decide on the financial coverage of interventions³⁰. Although in this study the status of availability, financial burden and insurance coverage of a major part of cancer drugs in Iran has been evaluated, but because all cancer drugs have not been studied in this study, it cannot show the total financial burden of all cancer drugs and the share of each drug from the total financial burden.

Based on the findings of this study, although the current status of access to cancer drugs in Iran is not as good as high-income countries, it seems to be better than many LMCs. However, in recent years, the cost of

cancer drugs in Iran has been rising, and with increasing incidence and prevalence of cancer, it is expected the cancer costs, in particular the cost of cancer drugs increase in the coming years. Therefore, health policy makers inevitably need to prioritize cancer drugs by using the results of health technology assessment studies and provide patients with access to drugs that are cost-effective in order to optimize allocation of limited resources and provide maximum access to cancer drugs throughout the country.

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