Policies to improve access to pharmaceutical products in shortage: the experience of Iran food and drug administration

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Abstracts

Background In the past decades, economic sanctions imposed on Iran for its nuclear program. The embargo made difficulty in foreign trade and led to lack of timely access to medicines. As the internationally-led sanctions caused to the shortage of medicine there, healthcare systems need to applied the new policies for maintaining health service quality especially in pharmaceutical sector.

Objectives This paper is about policies applied in Iran health system during the crisis reached its peak in 2012 as a good experience for guarantying access to pharmaceutical products.

Methods Through interviewing experts and managers in pharmaceutical regulatory system, the implemented policies in targeted historical period were extracted, then quantitative data were analyzed to show the impact of the policies on the access and affordability of medicines before and after their implementation in Iran food and drug administration (IFDA). This paper tries to show strategies employed by to tackle the crisis caused by sanctions and to offer practical policies to make medicines more accessible at the time of crisis.

Results In order to reduce the harmful effects of this crisis, IFDA proposed some changes at different levels ranging from organizational procedures to parliament legislations. The main achievements of IFDA were making drugs easily available are as follows, significantly reducing prices, decreasing the share of market regarding the imported medicines, facilitating the manufacture of domestic medicines, encouraging foreign investment in manufacturing drugs domestically, controlling the shortage of drugs, and finally giving financial support to all patients in general and to those patients who had problem paying for drugs in particular.

Conclusion These experiences which made the Iran pharmaceutical sector survive during the international sanctions, can be considered as a good example of resilience strategies in similar situations.

Keywords Healthcare access · Supply and distribution · Embargo · Pharmaceutical policy · Iran · Sanction

Introduction

Crisis history in Iran

In the past decades, economic sanctions whose main objective is to interrupt a country's diplomatic or economic relations have been frequently used on a worldwide scale for political intentions [1]. Owing to international sanctions imposed on Iran for its nuclear program, it has faced declining economy as well as difficulty in foreign trade. In particular, after 2012, Iran's GDP declined by 9% [2]. Although according to the National Defense Authorization Act and the Iran Threat Reduction and Syria Human Rights Act, medicines are not included in sanctions [3], the sanctions against Iran have caused increasing pain and suffering for Iranian patients due to lack of timely access to medicines, in general and lifesaving medicines such as chemotherapy medicines, in particular [4]. The impact of sanctions on the population health mainly refers to drug shortage caused

Key Messages, detailing concisely the main points made in the paper

- 1- Flexible legislations can help Pharmaceutical market in crisis
- 2- Inter and intra cooperation is helpful in managing pharmaceutical market crisis
- 3- Resiliency should be noted in pharmaceutical system

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by limitations of money transactions [1]. These limitations included foreign banks reluctance to opening a letter of credit, which is a payment term used for international commercial transaction. Thus, the money transaction was limited to cash transfer. In addition, these limitations increased with the direct sanction of the Central Bank of Iran. Therefore, the country had a hard time in receiving the money from exporting goods, and also paying for imported ones [4]. Accordingly, Health policymakers sought protective policies to alleviate the above-mentioned concerns to retain accessibility to qualified medicines with affordable prices.

This paper explains the Iranian Food and Drug Administration (IFDA) strategy, which helped Iran's pharmaceutical system to overcome the crisis. This strategy aimed at increasing access to medicines, including the main pharmaceutical policies and procedures employed at different levels to manage the crisis effectively. Following sections describes Iran pharmaceutical market and policy changes, as well as advantages and disadvantages of these implemented policies.

Iranian pharmaceutical Market

Iran has a population of about 80 million and its pharmaceutical market value is approximately 4 billion USD with about 5% average annual growth rate in five years ending to 2015.

After Iran's the Islamic Revolution in 1979, many medicines consumed in Iran are manufactured under a generic scheme [5], being highly successful in providing accessible and affordable medicines [6]. As the Iranian pharmaceutical market trend ending to 2010 shows, the financial value of the market share of domestic products is 61% [7]. However, most of the active pharmaceutical ingredients (API) used in domestic industry were imported [8].

Iran has a well-established medicine registration system for both domestic and imported pharmaceutical products including dossier review as the common technical document (CTD), Good Manufacturing Practice (GMP) inspections, laboratory testing, and post marketing surveillance. Registration application is sent only by official representative of marketing authorization holder and registered medicine should be imported from the original company with its original quality and shipment documents [9]. In addition, the IFDA approval letter sent to the importing company, custom and related bank after reviewing the original documents of each batch is mandatory for all further processes including custom release, banking payment, and distribution of products.

Since some economic, legal, regulatory, policy, and clinical decisions [10], which are effective and mandatory in ordinary situation may not be appropriate in crisis, the IFDA started to modify some policies implemented before the sanctions to reduce the adverse effect of the sanctions on the health system. Therefore, the IFDA suspended many of its routines and official procedures and implemented some new ones to facilitate

and accelerate manufacturing and importing procedures. These new policies, which are explained in the following sections, were significantly effective to maintain the quality level of services in the Iranian pharmaceutical system.

Method

This paper is aimed to provide an overview of some policy changes in the Iran pharmaceutical market as a response to the economic crisis following the international sanction which may be relevant to any other country in similar conditions.

Two main strategies were employed in this study for addressing the aim of study. First, analysis the associated documents, reports and published literature to collect appropriate data. Among various methodology for literature review, the scoping review which was the most relevant methodology for our purpose was selected for reviewing literature. Scoping review introduce a methodology to assessment of emerging evidence. It is a suitable methodology for addressing more general question and exploration its related literature; however, it may not proper for focusing on providing answers to a narrow question [11]. Although in a systematic review, investigators usually start with a clearly defined question, analyze high quality research studies, and focus on narrow parameters. In contrast, a scoping review has less depth but a broader conceptual scope [12]. Although there is no generally accepted definition of a scoping review, it is generally proposed as the best method when a body of literature is heterogeneous and not qualified for a precise systematic review. So, scoping review methodology is well suited to the education and policy issues [13].

The literature review initiated by a question on other countries policies in pharmaceutical sector during crisis. The review has been done by 3 researcher in different databases including PubMed, Google Scholar, and Scopus using keywords such as "pharmaceutical access" AND ("policy" OR "Crisis").

Not only the literature about Iran pharmaceutical market, but also the other countries' experience in the same situation has been reviewed. After extracting published policies and their impacts on pharmaceutical access. In the qualitative step, after purposeful sampling, the interviews have been done with some key managers of IFDA and other stakeholders to screen and complete relevant policies in Iranian context. The interviewees had at least 3- year experience in healthcare system and had direct involvement in decision making during crisis. Data saturated by 10 interviews. Then, policies are categorized during qualitative coding and thematic analysis.

To validate the findings, the focus group discussion has been done in IFDA with 5 experts in the different level of involvement.

Finally, quantitative data gathered from documented evidences in IFDA, before and after each policy implementation to show the impact of flexible policies and regulations on maintaining service quality in crisis.

Results

Following the sanctions imposed by the United States and the European Union against Iran, which was exacerbated by acting Iran under Chapter VII of the Charter of the United Nations, pharmaceutical market experienced a shock so that procurement and importation of medicines and medical devices became a major concern for the Iranian Ministry of Health (MOH) in general, and the IFDA in particular [14]. The crisis reached its peak in 2012, when the US Congress voted new sanctions against Iran, targeting the banking system and banning any transactions with Iranian banks and financial institutions. Due to these sanctions, the access of the Iranian banking system to the Society for Worldwide Interbank Financial Telecommunication (SWIFT), a Belgium-based company facilitating transfer of money across international borders was blocked. Therefore, the transferring process became slow, costly and unreliable [2]. Although medicines were exempted from sanctions, sanctions in financial and banking services made procurement of imported medicines more difficult, leading to reduction in availability and affordability of medicines. Accordingly, the 2012 web-based survey conducted by the Ministry of Health revealed the pharmaceutical issue as the top priority of society's concern.

Since the early 2012, due to the sanctions debarring Iran from exporting oil and conducting financial transactions, the domestic currency, Iran Rial, devalued by two third of its previous value [15]. Then, the price of medicines raised significantly and availability and affordability of medicines were adversely affected [1], so that at its peak time, over 350 medicines including vital and essential medicines such as vaccines and orphan drugs were in short supply and the price of both imported and domestically manufactured medicines increased dramatically. As the past policies and procedures were inefficient in the current situation, to handle the crisis and reduce negative impact of the sanctions, some changes were applied by the IFDA at different policymaking levels from the parliament legislation to organizational procedures to manage shortage of drugs and price of medicines.

In order to protect Iranian citizens from negative impacts of the sanctions, some changes in policies were implemented by the IFDA to manage shortage of drugs and increasing price of medicines.

As sanctions and drug shortage can affect several agents in the health sector including essential raw ingredient suppliers, API and finished product manufacturers, distributors, clinicians [10] as well as pharmaceutical importers, all of these stakeholders were considered by the IFDA policymakers for policy changing during the sanctions.

As the past policies and procedures were inefficient in the current situation, to handle the crisis and reduce negative impact of the sanctions, some changes were applied at different policymaking levels from the parliament legislation to

organizational procedures. In following sections we explain different policy categories extracted from qualitative part of this study, then we show its outcomes in quantitative manner, based on analysis of historical quantitative data in IFDA.

National inter-sectorial policies

Anti-sanction action-committee

Based on the Iranian parliament act in 2012, anti-sanction action-committee, which is related to the Supreme National Security Council (SNSC), permitted immediate release of medicines from customs by minimum financial documents. As a result of this act, the routine procedure included review of original documents of each shipment by the IFDA and banking system was waived to accelerate the release procedure with the responsibility of the Ministry of Health and Medical Education (MOH). Thus, the large amount of imported drugs remaining in customs due to avoidance of foreign banks in providing them with the required documents, were released to the market.

Memorandum of understanding (MOU) between the IFDA and the central Bank of Iran

With exacerbating the crisis in Iran in 2012, currency allocation turn by the central bank, which is routinely based on the companies' requesting time was determined according to the IFDA priorities. Simultaneously, the Geneva Interim Agreement in 2013, which facilitated international money transfer augmented the outcomes of this new policy.

Memorandum of understanding (MOU) between the IFDA and health insurance organizations

Due to the sharp jump in exchange rate in 2012, the price of imported drug particularly those related to rare, chronic and incurable disease increased significantly. As some of these medicines were in basic insurance package, and health insurance organizations were not able to increase their resources via raising health insurance premium due to critical economic situation, extra financial resources were allocated by the Cabinet and Parliament in order to prevent raising patients' out of pocket payments. Following this, the MOU between the MOH and health insurance organizations was signed for extra financial protection of special, incurable and chronic patients with high pharmaceutical expenditures such as patients suffering from thalassemia, multiple sclerosis, hemophilia, cancer, diabetes, transplant patients, metabolic disorders, as well as dialysis patients. As the aim of this MOU was decreasing the patients' copayments, increasing pharmaceutical reimbursement coverage, and expanding the covered population and the allocated budget were applied to expand the level of

coverage in three dimensions including increasing population coverage, adding new pharmaceutical products and reducing direct payments [16].

In addition, to support patients at risk of catastrophic pharmaceutical expenditures, the additional budget was allocated by the MOH to over-compensate unaffordable pharmaceutical products based on the equity-based criteria. Approximately 800 million USD has been allocated to cover the cost of this scheme since 2013.

IFDA intra-sectorial policies

Support of local production

Although supporting domestic production was always one of the main goals of the Iranian national drug policy over the past decades, it considerably increased after the sanctions in order to improve availability and affordability of the medicines and to manage medicine shortage. The most important protectionism policies employed in the crisis were facilitating registration process for domestic manufacturers, granting temporary marketing authorizations to them, and supporting their innovative new medicines financially by pricing regulation revision.

Furthermore, for each medicine domestically manufactured, the restriction on the importation of equivalent drugs was applied. This import restriction was applied by the technical barrier, registration ban, higher tariff, and import volume restriction.

For the domestic products, although the routine pricing policy is cost-plus, in order to reduce import dependence and also avoid exchange intensity, in the case of high-tech pharmaceutical products, the price was determined up to 70% of the imported ones. Furthermore, in the case of orphan drugs and products produced on low scales, price may be set even higher than the imported ones. Moreover, if imported medicine were manufactured by the domestic industry, the custom tariff of imported drugs would have increased from 4% to 32% and their market shares would have reached to 30% during one year. Before the crisis, the criterion for imposing such a tariff was 50% market share during 6 months.

Figure 1 shows that the trend of per capita consumption of domestic and imported medicines before policy changes. According to the market trend, the share of imported drugs was predicted to be higher than domestic medicines in coming years. While, protectionism policies of the IFDA increased share of domestically manufactured medicines to higher than the estimated one and decreased the share of imported medicines to lower than the estimated one.

Proactive inventory control

The drug shortage needs to be managed effectively to avoid its negative health impacts. An effective management strategy for drug shortage handling should include procedures for data

collection, decision-making, collaboration, and timely communication [17]. Therefore, to identify the drug shortage more rapidly during the sanctions, the routine market monitoring program was improved [18]. The proactive program includes an immediate warning system collecting shortage data through “Information Center of Medicine” in the IFDA, at universities of medical sciences and some referral pharmacies all over the country. The list of drugs in short supply was announced to all pharmaceutical companies regularly. This list was prepared based on the International Non-proprietary Name (INN) and the shortage of specific brands, which their generic alternatives were available on the market, was not defined as shortage. However, if the essential drug list had been developed previously in Iran, shortage management would have been more efficient with using less resources. The emergency companies established based on the law “emergency pharmaceutical companies”, are responsible for supplying medicines in shortage from registered foreign wholesalers in the IFDA [19]. The shortage monitoring program was improved to a proactive inventory program, which was implemented to avoid shortage, considering future demand by referring to past consumption [20]. The intense inventory control was implemented in the IFDA by holding monthly formal meetings between domestic producers, importers, and distributors/wholesalers to monitor medicines supply chain [14, 21]. Participation of all stakeholders in these meetings help them to maintain minimum inventory costs, while ensuring the availability of medicines.

Price reduction of imported medicines

One of the most common pharmaceutical cost-containment approaches which is used by policymakers to control price of medicines and also efficient use of limited health care resources is external reference-based pricing (ERFP). In this approach, the prices of a target medicine in determined countries are referenced as a benchmark. A systematic review of employing the ERFP in 16 countries shows that it has considerable effects on reducing patients out of pocket (OOP) and total expenditure of payers [22]. Turkey, Spain, Greece and country of origin are considered references for imported pharmaceutical pricing in Iran. Based on the IFDA regulation, importing companies have to set their price at the lowest level according to the reference countries. In spite of advantages of this mechanism in controlling price of medicines, the implicit agreement on the real price cannot be reached. In some situations, this strategy may not be applicable and efficient. For instance, during the sanction, the country faced the sharp decline of domestic currency value against the US dollar [15]. Therefore, the price of imported medicine increased dramatically. To enhance medicines affordability, price reduction of imported medicines was conducted through parallel import, and tendering as the main policies [23, 24].

Fig. 1 Trend of domestic and imported drugs market share before and after policy changes (source: the IFDA Annual Statistics, 2015)

Parallel import has been used in other countries such as European countries. In this strategy, importing medicines is limited to official agents of original producers and all importing companies are allowed to import requested medicines from the regulated market using free exchange. In this regard, Iran currently has two exchange rates, one formally fixed by the Central Bank of Iran and another informal, open market rate that is sold to the public which has been around 10% above the official rate. Using free exchange, emergency companies were exempted from banking bureaucracy and their importing process accelerated.

As a result of employing this strategy, we accessed real price in the target market. Therefore, it decreased the monopoly power of originators and increased the IFDA negotiation leverage, so that it led to price reduction of medicines and pushed originators to cut their prices [9].

The IFDA set prices for all imported medicines even emergency ones and these set prices remained constant at least for one year.

Tendering was the second policy, being successfully implemented in the IFDA in order to create price competition and reduce purchasing price for the procurement of subsidized public needed medicines. Continuous and intensive tender meetings were held in the IFDA to find the best proposed price. In this situation, participation in tender was not limited to agent companies and any importing companies. Therefore, emergency companies were allowed to participate in tender.

Figure 2 shows the monthly inflation rate in 2014 in both health and pharmaceutical sectors. The IFDA's price reduction policies resulted in a significant reduction in the

inflation rate of pharmaceutical sector so that the total inflation rate of this sector was 19% and 13% less than health sectors in 2014 and 2015 accordingly.

The more price reduction were conducted when the imported medicines were applied for basic health insurance coverage and/or extra financial protection.

In addition, advanced price setting methods including pay-back and risk-sharing agreement were imposed to control price ceiling in some cases.

Main achievements of the IFDA policies

Tendering and parallel import were two policies well-favored in attaining lower prices by price discovery mechanism. These policies make the IFDA capable of cutting prices through negotiation [9] with foreign manufacturing companies, eliminating monopoly, and increasing competition. Table 1 shows top 50 cases of price reduction in original brands in 2 years ending to 2015. As observed in this table, pharmaceutical market experienced up to 88% reduction in prices of some original brands so that these policies generated approximately 350 million US dollars national saving in 2014–2015 of which 225 million US dollars was due to direct reduction in the price of branded medicines.

Support of domestic production was another successful strategy providing more national self-sufficiency. By local production support and import limitation, the market growth rate of domestic products was approximately 26% from 2011 to 2015 (Fig. 3).

Fig. 2 Monthly inflation rate in health and pharmaceutical sectors in 2014–2015 (source: Iran Central Bank)

Increasing regulatory incentives, changing the definition of domestic manufacturing from secondary packaging to primary packaging and/or formulating and limiting original brand market share to 5–10% for products with domestically produced generics inclined the pharmaceutical originators to collaborate with Iranian companies to manufacture their medicines domestically. The most attractive incentive by the IFDA was increasing the allowed market cap up to 20% for original drugs whose primary packaging was conducted in Iran and waiving limitation for medicines completely formulated in the country.

This resulted in collaborations such as direct investment by a Danish company named Novo Nordisk, joint venture with Cipla, the Indian company, SBM, a Belgium-based company and Ipsen, the French company, licensing with Sanofi, the French company, as well as Roche and Novartis, the Swiss companies.

The next successful action with a considerable impact on managing shortage was proactive medicine inventory

program. In this program, a periodic review was used to control medicine stock through effective communication with supplying companies [20]. The medicines shortage declined approximately 90% during two years ending to 2014 so that it reached 30 medicines, which was maintained in next years (Fig. 4).

The MOU between the IFDA and insurance organizations expanding the level of pharmaceutical coverage for more vulnerable patients was the next favored program. This program increased the covered items from 189 to 304, decreased pharmaceutical out of pocket payments for these unaffordable medicines approximately 45% during 2013–2015, which is approximately 11% reduction in total pharmaceutical patients' payments including prescriptive and non-prescriptive medicines.

Discussion

Protection of society from negative effects of drug shortage and high patients' payments, managing importing problems and increasing national self-sufficiency always are the policymakers' concerns. Therefore, to tackle the crisis caused by sanctions some practical policies applied by IFDA to make medicines more accessible at the time of crisis. Price cut as the most frequently used policies in response to financial crisis in many European countries such as Cyprus and Greek [25–27] was one of these policies employed in Iran through two effective strategies, parallel import (PI) and tendering. PI, which is increasingly used by European countries in pharmaceutical

Table 1 Top 50 cases of price cut

Number of original brands subjected to price reduction	Price reduction (%)
7	80–88
13	70–79
20	60–69
10	54–58

Fig. 3 Market share of imported and domestically produced medicines (Source: IFDA Annual Statistics, 2015)

market, could be applicable in both emergent and non-emergent situations as an efficient policy for supplying medicines with more reasonable price when affordability is the main concern particularly in developing countries [28]. However, due to its negative impacts such as illegal import and counterfeit, reduction of investment on drug development, and pirated goods [9], we only recommend it for emergent conditions to avoid negative impacts of expensive branded medicines on patients' affordability. In addition, to secure quality, safety and efficacy of imported medicines through parallel import, the target medicines were procured from predetermined regulated markets approved by the IFDA according to the act of "emergency pharmaceuticals" [19].

Another problem of this strategy is lack of responsibility of non-agent companies regarding safety and quality of medicines. Accordingly, the best policy of the IFDA in this field in order to reduce these negative effects was negotiation with the exclusive representative of original

companies to decrease the brand prices to the discovered price through the PI so that the PI result shows that supply of almost 95% of imported medicines was held in official agents and only 5% of medicines were supplied through emergency companies. In addition, obtaining batch numbers' confirmation from manufacturer in cases of emergency imported medicine, sending samples to laboratory for quality testing, and setting strict punishments for companies violating the regulations were employed to secure safety and quality of imported medicines.

Tendering, the second policy for decreasing price, being successfully followed in Iran during the crisis, had similar well-ending results in other countries such as Greek and Cyprus [26, 29].

Another well-established program helping the IFDA to forecast and manage shortage successfully was proactive inventory control, which is proposed to continue to monitor the market for avoiding any possible shortage.

Fig. 4 Average of drug shortage in 2012–2016 (Source: IFDA Annual Report, 2016)

As access to safe and efficient medicines is the first priority of the health system, supporting domestic pharmaceutical production was employed by Iran as an important protectionism strategy. This policy was used by some other countries around the world owing to its advantages including sustainable access and reasonable price, for example Russia allocated 4.1 billion US dollars to support and develop domestic pharmaceutical manufacture [30, 31]. In Iran, to follow this policy and maintain the IFDA achievements in this area, a permanent committee, named “economic resilience committee”, was established with stakeholders including domestic manufacturers and other experts.

Most of countries are also interested in designing policies to reduce patients’ payment and increase their financial protection through reimbursement policies [25–27]. As protecting households against financial risks is one of objectives of any health system, in the Iran’s Fourth Development Plan Act, reducing OOP by less than 30%, which it may be achieved by targeting or exempting individuals and health services is emphasized [32]. Thus, the MOU between the IFDA and insurance organizations was used for direct financial protection of vulnerable patients during the sanctions based on the scientific evidence such as burden of disease and impoverishment effect. Moreover, the IFDA intends to improve the list of targeted medicines in the MOU using cost-effective analysis and national essential medicine list (NEML).

Therefore, to manage future shortage more efficiently, developing the NEML and categorizing it as vital, essential and non-essential (VEN) is going to be conducted in Iran.

Conclusion

The sanctions imposed significant burden on the pharmaceutical sector in Iran; however, by employing the package of different policies, the IFDA was able to handle the crisis and reducing the negative impact of sanctions significantly.

The IFDA policies enhanced three dimensions of access including accessibility, availability, affordability, meanwhile increasing domestic manufacturing. This experience shows that the routine regulation and administrative processes which are effective in normal situation, may not be suitable in crisis. Access is the first priority in crisis and pharmaceutical system may compromise on its other goals such as customer satisfaction. In this line, some clinicians and patients were unsatisfied due to unavailability of original brand medicines and new expensive molecules.

In addition, pharmaceutical system may accept some uncertainty in licensing and procurement, which may lead to dissatisfaction of pharmaceutical companies and some other stakeholders.

In the same manner, expert in regulatory body may not be satisfied by their high work load for monitoring the market more frequently.

Although these temporary policies helped pharmaceutical market to maintain access in the short run, after crisis IFDA may need to rearrange the regulation for a normal market by more attention to quality, innovation, stakeholders’ satisfaction, and sustainability of financial resource. Based on this recent experience, two main gaps recommended to be considered in permanent policies.

Developing the national essential medicines list (NEML), providing clinical guidelines for rational prescribing, and employing cost-effectiveness evidence for pricing and reimbursement, developing integrated information system for monitoring the market []may help the IFDA toward more successful practice not only in the probable next crisis but also in the routine practice in normal context.

Finally, While the pharmaceutical system was shocked by the international sanctions, the IFDA policies and experiences focusing on the boost of domestic manufacturing, cost containment approaches, patient financial protection, and flexible Bureaucracy. is a successful example of economic resilience strategies in developing countries.

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Compliance with ethical standards

Conflicts of interest RD acted as the deputy minister and head of the IFDA, FP acted as the deputy for regulatory in IFDA, and HI acted as the head of planning department in IFDA during the policy implementation. Although NY, NM, and GGh acted as experts in IFDA for a while, they are not involved in IFDA practices during the mentioned crisis.

References

1. Cheraghali AM. Impacts of international sanctions on Iranian pharmaceutical market. *DARU J Pharm Sci*. 2013;21(1):1.
2. Setayesh S, Mackey TK. Addressing the impact of economic sanctions on Iranian drug shortages in the joint comprehensive plan of action: promoting access to medicines and health diplomacy. *Glob Health*. 2016;12(1):1–14.
3. America, C.o.t.U.S.o. *the Iran Threat Reduction and Syria Human Rights Act of 2012*. 2012; Available from: https://www.treasury.gov/resource-center/sanctions/Documents/hr_1905_pl_112_158.pdf. Accessed 20 Dec 2017.
4. Ghiasi G, et al. The impact of the sanctions made against Iran on availability to asthma medicines in Tehran. *Iran J Pharm Res*. 2016;15(3):567–71.
5. Mehralian G, et al. Intellectual capital and corporate performance in Iranian pharmaceutical industry. *J Intellect Cap*. 2012;13(1):138–58.

6. Davari M, Walley T, Haycox A. Pharmaceutical policy and market in Iran: past experiences and future challenges. *J Pharm Health Serv Res.* 2011;2(1):47–52.
7. Kebriaeezadeh A, et al. Trend analysis of the pharmaceutical market in Iran; 1997–2010; policy implications for developing countries. *Daru J Pharm Sci.* 2013;21:52.
8. Cheraghali AM. Iran pharmaceutical market. *Iran J Pharm Res.* 2010;1–7.
9. Peiravian F. Parallel import: is it worth? *Iran J Pharm Res.* 2014;13(4):1111–4.
10. Fox, E.R., B.V. Sweet, and V. Jensen. *Drug shortages: a complex health care crisis.* In *Mayo Clinic Proceedings.* 2014. Elsevier.
11. Moher D, Stewart L, Shekelle P. All in the family: systematic reviews, rapid reviews, scoping reviews, realist reviews, and more. *Syst Rev.* 2015;4(1):183.
12. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol.* 2005;8(1):19–32.
13. Peterson J, et al. Understanding scoping reviews: definition, purpose, and process. *J Am Assoc Nurse Pract.* 2017;29(1):12–16.
14. Hosseini, S.A., Impact of sanctions on procurement of medicine and medical devices in Iran; a technical response. *Arch Iran Med.* 2013;16(12).
15. Nakanishi H. The construction of the sanctions regime against Iran: political dimensions of unilateralism. In: Marossi AZ, Bassett MR, editors. *Economic Sanctions under International Law: Unilateralism, Multilateralism, Legitimacy, and Consequences.* The Hague: T.M.C. Asser Press; 2015. p. 23–41.
16. World Health Organization. Where are we now? 2010; Available from: www.who.int/whr/2010/10_chap01_en.pdf. Accessed 6 Oct 2017.
17. Ventola CL. The drug shortage crisis in the United States: causes, impact, and management strategies. *Pharmacol Therapeut.* 2011;36(11):740–57.
18. Kheirandish M, et al. A review of pharmaceutical policies in response to economic crises and sanctions. *J Res Pharm Pract.* 2015;4(3):115.
19. Zaboli P, et al. Pharmaceutical laws and regulations in Iran: an overview. *J Res Pharm Pract.* 2016;5(3):155–61.
20. Rachmania IN, Basri MH. Pharmaceutical inventory management issues in hospital supply chains. *Management.* 2013;3(1):1–5.
21. Kheirandish M, Rashidian A, Bigdeli M. A news media analysis of economic sanction effects on access to medicine in Iran. *Iran J Pharm Res.* 2015;4:199–205.
22. Lee JL, et al. A systematic review of reference pricing: implications for US prescription drug spending. *Am J Manag Care.* 2012;18(11):e429–37.
23. Carone, G., C. Schwierz, and A. Xavier, Cost-containment policies in public pharmaceutical spending in the EU. *Economic and Financial Affairs,* 2012.
24. Brekke KR, Holmås TH, Straume OR. Price regulation and parallel imports of pharmaceuticals. *J Public Econ.* 2015;129:92–105.
25. Vogler S, Zimmermann N, Wirtz VJ. Policies beyond the crisis: lesson learned. *Journal of Pharmaceutical Policy And Practice.* 2015;8(1):E2.
26. Vondoros S, Stargardt T. Reforms in the Greek pharmaceutical market during the financial crisis. *Health Policy.* 2013;109(1):1–6.
27. Petrou P, Vondoros S. Cyprus in crisis: recent changes in the pharmaceutical market and options for further reforms without sacrificing access to or quality of treatment. *Health Policy.* 2015;119(5):563–8.
28. Maskus, K.E., Final Report to World Intellectual Property Organization. 2001.
29. Kanavos, P., E. Seeley, and S. Vondoros, Tender systems for outpatient pharmaceuticals in the European Union: evidence from the Netherlands, Germany and Belgium. 2010: Enterprise and Industry, European Commission.
30. Federation, A.C.f.t.S.B.H.i.t.R., Russian Pharmaceutical Market. Current review and future outlook until 2020. Opportunities for Swiss companies. 2012.
31. Alexander Bykov, Healthcare in Russia: trends and prospects: import substitution and innovative development of Russian pharmaceutical industry. 2009.
32. Organization, W.H., Health financing for universal coverage.

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