

Rare Disease and Orphan Drug Situations in Turkey and around the World

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Abstract: Diseases with a prevalence less than 1/2000 are defined as "Rare Diseases". This group of diseases is a highly heterogeneous group that affects multiple systems. Approximately 80% of these are caused by genetic reasons, and the remaining 20% are caused by environmental factors or are idiopathic. Orphan drug is defined as a medicinal product designed for a life-threatening or chronically impairing rare disease but with a low possibility of obtaining a return on investment due to insufficient sales. In Turkey, where consanguineous marriage frequency is 25% on average, the probability of rare diseases is quite high. Lack of knowledge and specialist physicians, very expensive treatments, and lack of a designated regulation for rare diseases and orphan drugs are the main problems in our country. The research revealed that orphan drugs were imported to Turkey through the Turkish Pharmacists' Association (TEB) and not covered by Social Security, therefore making it hard for the patients with low income to reach these drugs.

Keywords: Rare; disease; orphan; drug

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1. Introduction

"Rare diseases" are occurred in a small number of people in comparison with the general population and basically the biggest problem of these diseases is they are thin on the ground. In Europe, diseases encountered in 1 person in 2000 are considered rare. A disease may be rare in an area while it may be frequent in another (<http://www.orpha.net> accessed 2016).

Rare diseases are highly heterogeneous group that affects any or multiple systems. Approximately 80% of these are caused by genetic reasons, and the remaining 20% are caused by environmental factors or are idiopathic. They progress with severe physical-mental impairments. These impairments negatively affect the quality of life and the life expectancy of the patients is quite low. Although rare diseases show

different epidemiological characteristics from country to country, they constitute an important public health problem for each country and lead to special diagnostic, treatment and follow-up difficulties. Therefore, these diseases require special approaches and applications, and they should be handled separately from common diseases (Dündar and Karabulut, 2010).

Rare diseases are medically important public health problems. These diseases can be described as “health orphans”, in other words, “Orphan Diseases”. “Orphan” is a Greek word. Calling these diseases which have been neglected for many years, have been hard and costly to research, diagnose, and treat “Orphan Diseases” is not a wrong analogy (Dündar and Karabulut, 2010).

The number of rare diseases also depends of the accuracy of the designation of the factors constituting the disease. Medical field designated “disease” as a change that occurs as a unique symptom pattern in the health status of an individual and that has a single treatment. Whether the pattern is unique or not is completely based on the accuracy of our analysis. This confusion is reflected in certain classifications of Orphanet (<http://www.orpha.net> accessed 2016).

2. Rare Diseases

Almost all genetic diseases are rare diseases; but not all rare diseases are genetic. For example, there are very rare infectious diseases, as well as autoimmune diseases and rare cancers. Today, the cause of many rare diseases is unknown. Rare diseases are severe, mostly chronic and progressive diseases. In many rare diseases, as in proximal spinal muscular atrophy, neurofibromatosis, brittle bone disease, chondrodysplasia or Rett syndrome, the symptoms may be observed at birth or in childhood. However, more than 50% of rare diseases (such as Huntington’s disease, Crohn’s disease, Charcot-Marie-Tooth disease, amyotrophic lateral sclerosis, Kaposi’s sarcoma, or thyroid cancer) manifest during adulthood (<http://www.orpha.net> accessed 2016).

In our country, where consanguineous marriage is common, the high number of rare diseases has grabbed the attention of genetic researchers. According to WHO data, 1:1000 people in every 100.000 people in European countries suffer from rare diseases. The prevalence of rare diseases is higher in Turkey due to consanguineous marriages. While the ratio of consanguineous marriages in the EU is 3-10 in a thousand, the ratio of consanguineous marriages in Turkey is 12-17 in a hundred. Therefore, it is expected that approximately 5-7 million people are affected by rare diseases in Turkey. Besides, our country also experiences the problems encountered throughout the world such as lack of knowledge about Rare Diseases and lack of specialist physicians in these areas, the high costs of the treatment of these diseases and the lack of a regulation that designates Rare Diseases and Orphan Drugs (Özbek U, 2014).

2.1. The Prevalence of Rare Diseases

In 2001, it was determined that the number of rare diseases was around 5000 and it constituted 10% of all human diseases. Today, this number is increasing day by day, and about 4-5 new diseases are

designated every month (Campos-Castell, 2001). There are between 5000 and 8000 rare diseases; most of them are of genetic origin and are noticed in childhood. They have high mortality and morbidity, and cause chronic debilitation in patients. It is thought that 6,5/10.000 people suffer from rare diseases in the United States (USA). Additionally, the Community Action Program between 1999 and 2003 showed that the prevalence was 5/10,000 in the European Union countries (Dear et al., 2006; Stolk et al., 2006; Taruscio and Cerbo, 1999).

Although this may seem like a low number when considered individually, considering the high number of these diseases, the fact that it is a major public health problem with the sheer number of people affected in the European Countries such as Turkey and Italy, and the United States should not be forgotten. Therefore, it will be obvious that the number of the affected individuals is remarkably high. Different sources report that the number of people affected by rare diseases is 30 million in Europe and 25 million in North America (Wastfelt et al., 2006).

80% of the rare diseases are neuropathic diseases and the majority of these are diagnosed in childhood (Campos-Castell, 2001). There are neurological disorders in more than half of these, but there is no preventive or therapeutic approach. The prevalence evaluation of rare diseases is carried out by European Organization for Rare Diseases (Eurordis) and Orphanet with the support of the European Commission. The examples of these diseases include pulmonary arterial hypertension, Fabry disease, hereditary angioedema, chronic myeloid leukemia, idiopathic pulmonary fibrosis, cryopyrin-associated periodic syndrome (CAPS), gout, Familial Mediterranean Fever (FMF) (<http://www.orpha.net> accessed 2016).

2.2. What are the medical and social consequences of the rarity of these diseases?

There is a lack of medical and scientific knowledge in the rare diseases field. Physicians, researchers and political authorities have long been unaware of rare diseases and until recently. For most rare diseases, there is no total cure for the disease; however, appropriate treatment and medical care may improve the quality of life of patients and prolong their life expectancy. Striking advances in certain diseases indicate that we should continue to fight in the research and social solidarity areas (<http://www.orpha.net> accessed 2016).

All of those affected by such diseases face similar difficulties in accessing relevant information and qualified specialists in addition to the diagnostic process. Access to quality health care, general social and medical support, effective communication between hospitals and general practices, as well as professional and social integration and independence have emerged as equally specific problems (<http://www.orpha.net> accessed 2016).

Patients affected by rare diseases are also weaker in psychological, social, economic and cultural terms. These challenges can be overcome with appropriate policies. Most patients cannot be diagnosed due to the lack of adequate scientific and medical knowledge. The diseases of these patients are not designated. These are the people who have the greatest difficulty in getting the appropriate support (<http://www.orpha.net> accessed 2016).

2.3. Rare Diseases Designation Problem

Rare diseases are often designated late. This leads to significant problems in patients in terms of survival. For example, a questionnaire sent to 18,000 people composed of organizations and patients in 17 European countries regarding rare diseases including Crohn's Disease, Cystic Fibrosis, Duchenne Muscular Dystrophy, Ehlers-Danlos Syndrome, Marfan syndrome, Prader-Willi Syndrome, Tuberous Sclerosis, and Fragile X Syndrome revealed that 25% of the patients were diagnosed with correct diagnosis 5-30 years after the first symptom. Before definitive diagnosis, 40% of the patients were followed up with a misdiagnosis and 60% were not even diagnosed. Most of the misdiagnosed patients have been subjected to unnecessary medical interventions. 16% were operated unnecessarily, 33% received inappropriate medical treatment and 10% received psychological treatment with the assumption that the disease was psychosomatic. 25% of the patients went to another center to confirm the treatment and 2% applied to other centers abroad. One third of the patients did not find the communication methods established to make a diagnosis satisfactory. Therefore, this multi-centric and large scaled study showed that the knowledge and medical expertise required to diagnose rare diseases is insufficient. Therefore, the possibility of complications and late sequel is very high in these patients who have already been delayed more than enough. A prospective study conducted in Italy (between 1985 and 1997) shows that only 19,5% of 1935 infants born with metabolic disease can reach adult age (Dionisi-Vici C et al., 2002).

In order for the patients to access specialist care centers, the need to strengthen the links between reference centers should be a priority for many countries. The European Commission experts have proposed to improve the diagnostic tests of rare diseases and to reduce and prevent rare genetic diseases with early diagnosis with the universal neonates screening in European Union member countries. There are reference centers specialized in rare diseases, but most patients are not even aware of the existence of these centers (Dündar and Karabulut, 2010).

2.4. International Organizations

Rare Diseases cover a highly heterogeneous group, both prevalently and medically. Knowledge about these diseases, diagnostic methods and treatment options are also heterogeneous. Low prevalence, geographic distribution of patients and researchers cause a lack of infrastructure related to these diseases. This has revealed the need for the establishment of various funds. France, Germany, Italy and Spain are conducting a research program that supports the interdisciplinary in which the resources related to rare diseases are insufficient and international information network (Wetterauer and Schuster, 2008).

For the last 25 years, various authorities have noticed that the medical processes, which are diagnosis, prevention and treatment alternatives, are quite backward compared to normal diseases. Additionally, the pharmaceutical industry has not been willing to support drug development projects related to these diseases. With the increase in national awareness, support organizations related to this situation were also established abroad. "The National Organization of Rare Disorders (NORD)" founded in 1983 is an example from the United States (Dündar and Karabulut, 2010).

“Eurodis” is an organization established in Europe in 1997 taking NORD as a model to improve the quality of life of people affected by rare diseases. It has also been a driving force for the adoption of the European Regulation on Orphan Drugs. Therefore, the organizations supporting these diseases, in particular NORD, pressured the US authorities in 1983 and the Orphan Drug Act, which was later adopted by other countries, was enacted. Thus, in 1983, the US-The Orphan Drug Act, in 1993 Japan, and in 2006, the European Union enacted various laws related to the treatment and prevention of these diseases (Haffner, 2008).

The International Classification of Diseases (ICD) coding system used by many countries is not suitable for rare diseases. Lack of an international coding system for these diseases leads to the lack of a common knowledge bank, and a language for the prevention of these diseases, protection methods and treatments for both patients and researchers of these diseases. This is an extra problem for these diseases, which are already in the second place because of the small number of them and because their treatment significantly affects the country’s economy. To this end, national and international organizations have been established for some rare diseases. Although these organizations vary from country to country, they are usually established under the leadership of researchers, patients, public institutions and pharmaceutical companies (Dündar and Karabulut, 2010).

3. Orphan Drug and Related Designations

According to the WHO definition, “Drug is the substance or product that is used/intended to be used to change the physiological systems in favor of the pathological conditions field”. Before a drug is introduced, it is subjected to extensive research and strict controls, and it is made available only after it is approved by the authorities and licensed (Akıcı and Ulupınar, 2013).

There are other features that distinguish a drug from other products. The facts that drugs are included into life with a very dynamic and detailed knowledge and they are produced and consumed, they are subject to comprehensive legislation, they have rigorous pre-clinical and clinical research process before licensing, licensing process, after-license research, review and surveillance processes, pricing, reimbursement processes, and equivalents, the patent period, the struggles to stay in the market among competitors, and management of crisis in health and non-health related issues are examples of this privileged position of drugs (Republic of Turkey Social Security Institution Book, 2013).

While new drugs based on a patented molecule and does not have any similar are considered as “original drugs”, and the products that are proven by the scientific studies that they have the same properties with the original drugs and provide the same treatment, but that can only be launched after the expiration of the patent periods of the original drugs are called “generic (equivalent) drugs” (Çalışkan, 2008).

“Orphan” drugs are drugs that the sponsors are reluctant to develop under normal marketing conditions since the small market-size of the drugs that are meant to treat but address to really rare diseases will not allow the sponsors to pay off the capital they invest in the research and development of the product (<http://www.orpha.net> accessed 2016).

Patients affected by rare diseases cannot be excluded from treatment options and developments in science; they have equal rights with other patients in terms of treatment. Public authorities have introduced incentive measures for the health and biotechnology industry to trigger research and development activities in the orphan drug sector (<http://www.orpha.net> accessed 2016).

These practices started with the enactment of the Orphan Drug Act in the United States in 1983, followed by the practices in Japan and Australia in 1993 and 1997; and the practices started in Europe in 1999 when Member States adopted the orphan medicine policy (<http://www.orpha.net> accessed 2016).

The special care and attention required for these drugs which the pharmaceutical industry is reluctant to develop introduced the “orphan drug” concept. A drug is called an orphan drug only when there is a scientific justification suitable for its use during any stage of the use of this drug (Blankart et al., 2011).

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Access to orphan drugs is important to reduce the morbidity and mortality of rare diseases. For example, until pirfenidone was introduced, lung transplantation was the only treatment option for patients with idiopathic pulmonary fibrosis and survival was 3 years with 50% chance (Aagaard and Kristensen, 2014). Although the suitability and availability of orphan drugs are important and necessary, there are challenges in the treatment of these diseases. Such that only one out of 10 patients with rare disease receives special treatment. The development of orphan drugs requires high costs and original investments, given the small patient population per rare disease (Blankart et al., 2011).

The development of orphan drugs often follows the same legislative pathways as other drugs because of the pharmacokinetic, pharmacodynamic, dosing, stability, safety and efficacy tests required to be performed. However, certain statistical responsibilities have been reduced in their development. For example, orphan drug regulations agree that phase III clinical trials cannot be performed on 1000 patients in the development of drugs. The market area of the drugs with limited application can be quite small, so it is not considered profitable for companies. Health Authorities carry out motivating activities in this sense (Hadjivasiliou, 2014). Governments may have interventions in various areas of drug development:

- Tax deduction
- Improved patent protection and marketing rights
- Providing financial assistance for clinical trials
- Providing a government-sponsored initiative for research and development

Orphan drug manufacturers also benefit from a small customer base to reduce costs on the clinical side, as they have smaller trials. According to the FDA, the approval period for orphan drugs for clinical trials is 10 months while this period is 13 months for normal drugs. This allows the orphan drugs to be introduced to the market as soon as possible. A 2011 study revealed that orphan drug trials between 2004 and 2010

were smaller and with higher probability for less random selection compared to non-orphan drugs, but still had a higher FDA approval rate, and 15 orphan cancer drug was approved while this number was 12 for non-orphan cancer drugs (Kesselheim et al., 2011).

The 2014 orphan drug report shows that the orphan drug designations continue to increase rapidly. It is expected that the prescribed orphan drugs sold until 2020 will be \$176 billion. Although the orphan populations are small, the cost of spending per patient is quite high. The same report emphasized that orphan drug economy mirrored the entire pharmaceutical market but there were some big differences (Hadjivasiliou, 2014).

Although the European Medicines Agency (EMA) allows access to all member states, in practice, each Member State enters into the market with the drugs which will be paid by its own national health system. For example, 35 orphan drugs were introduced to market in Belgium, 44 drugs in the Netherlands, 28 drugs in Sweden in 2008, 35 drugs in France and 23 drugs in Italy in 2007 (Denis et al, 2010).

The fact that a drug has been authorized for marketing in Europe or America does not mean that this drug is available in all countries. The marketing authority holder must decide in advance on the commercialization in each country; the drug then undergoes the necessary procedures in each country to determine the conditions of reimbursement and the price. The approach differences between the countries in spite of the joint efforts further complicate patients' access to orphan drugs (European Medicines Agency, <https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview> (accessed 15 October 2016).

3.1. Orphan Drug Development in the USA

In the United States of America, pressure and lobbying activities were carried out by the National Rare Disorders Organization to have a specific law that would encourage pharmaceutical companies to develop orphan drugs. Within this context, in 1979, the FDA established a Task Force on orphan diseases: "When a drug is designated as a potentially life-saver or otherwise providing unique great benefit to a patient, the search and the introduction of this drug by the government is the obligation of the community represented." Thus, in January 1983, the Orphan Drug Act was adopted in the USA. The purpose of the FDA Office of Orphan Products Development is to evaluate and develop the products (drugs, biological products, devices or medical foods) intended for the diagnosis and treatment of rare diseases or conditions. In carrying out this task, the FDA evaluates all the scientific and clinical data obtained from companies in order to design and designate the promised products for rare diseases and to further the scientific development of promising medicinal products (Pedro, 2013).

The Office of Orphan Products Development provides incentives for companies to develop orphan drugs. Since 1983, this program has successfully enabled the development and introduction of more than 575 biological products and drugs for rare diseases. However, less than 10 products supported by the industry were introduced to the market between 1973-1983. There are also other programs that deal with orphan medicines in the USA. The Orphan Drug Designation program provides orphan status to drugs and biological origin designed for safe and effective treatment, diagnosis or prevention of rare

diseases/disorders affecting more than 200,000 people in the USA. However, it is not expected to provide for the development and marketing costs of the drugs that can provide treatment. The Rare Pediatric Disease Priority Review Voucher Program states that a sponsor that was granted approval for a drug or biological product for a “rare pediatric disease” may be eligible to receive a certificate that can be used to have a future marketing application examined with priority. Humanitarian Device Exemption (HDE) Program states a device that intends to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 new people in the United States each year. With the increase in national awareness about rare diseases and orphan drugs in the USA, support organizations have started to be established. For example, there are international organizations in the USA, such as the National Organization for Rare Disorders (NORD) founded in 1983. These groups are focused on improving the treatment of rare diseases. Patients often participate in these organizations to trigger and create a pressure on prescribers, regulatory agencies and political bodies in relation to the availability of orphan drugs. There are patient advocacy groups for easier access to orphan drugs and their treatment, and these groups lobby for third party taxpayers or governments that finance health care, to ensure full reimbursement of orphan drugs, regardless of their higher prices. In addition to the authorities, some universities leap forward on the subject. For example; the Orphan Drug Research Center at the Pharmaceutical University of Minnesota helps small-scaled companies with insufficient expertise and resources in drug synthesis, formulation, pharmacometry and bio-analysis. The Center for Rare Disease Therapies at the Keck Institute in Claremont, California, supports existing projects to stimulate the inactive potential orphan drugs by identifying barriers to commercialization, such as formulation and problems with biological processing (Developing Products for Rare Diseases & Conditions. U.S. Department of Health and Human Service <http://www.fda.gov/orphan/oda.htm>; accessed 7 February 2010).

In 1989, the Good Therapeutic Act was amended to include certain articles that would encourage Australian pharmaceutical companies to develop orphan drugs. However, the full orphan drug policy was established in 1997 (Gammie et al, 2015).

3.2. Orphan Drug Development in the European Union

The European Union defines a rare disease as a condition that threatens life or chronically weakens maximum 5 people in 10,000 people (Pedro, 2013).

A decision adopted by the EU Council of Ministers on November 30, 1995 requested the European Commission to investigate rare diseases and consider certain legislation on orphan drugs. The Orphan Medical Products Regulation (EC) N° 141/2000 was adopted by the European Parliament and the European Council on December 16, 1999. Additionally, the European Commission defined “similar medicinal products” and “clinical superiority” terms and introduced application provisions on orphan drugs and adopted the Regulation (EC) N° 847/2000 on April 27, 2000. Pursuant to the European regulation n ° 141/2000, only human drugs can be called “orphan drugs”. Therefore, this definition does not cover veterinary medicines, medical devices, nutritional supplements and dietary products (<http://www.orpha.net> accessed 2016).

Additionally, with this Regulation, the European Commission adopted a new Regulation (847/2000) stipulating the provisions for the application of the criteria which are important in the designation of orphan drugs, the definition of similar medicinal products and the clinical superiority. The aforementioned regulations are the regulatory key framework for orphan drug provisions in the EU (Pedro, 2013).

The European Union has a central procedure for orphan drug designation and approval of marketing among its member countries. Cross-border regulations are of paramount importance since patients cannot be treated due to inadequate access to orphan drugs and the lack of specialized investigators and facilities. The 2011/24/EC Directive clarifies patient rights in cross-border health care. This directive enables the patients with rare diseases in the Member States to get health care services throughout the European Union in case the national health system cannot provide the necessary treatment within a reasonable period of time. However, due to differences in national pricing and reimbursement policies among Member States of the European Union, the patients still suffer from different access to orphan drugs (Aagaard and Kristensen, 2014).

Patients often participate in certain organizations to trigger and create a pressure on prescribers, regulatory agencies and political bodies in relation to the availability of orphan drugs. In Europe, for example, the Rare Diseases Europe (EURORDIS) was established focused on improving the treatment of rare diseases. Patient advocacy groups can establish partnerships with regulatory bodies such as EMA and EURODIS (Gammie et al, 2015).

4. Orphan Drug Status in Turkey

In our country, where consanguineous marriage is common, the high number of rare diseases has grabbed the attention of genetic researchers. According to the World Health Organization data, 8,000 people in every 100,000 people in European countries suffer from rare diseases. The prevalence of rare diseases is higher in Turkey due to consanguineous marriages (Dündar and Karabulut, 2010).

A study carried out on 55,175 marriages between the years 1970 to 1987 revealed that consanguineous marriage rate in Turkey was 21.21%, and that most of them was the first-degree cousin marriages. While consanguineous marriage rate is 3-10 per thousand in European Union countries, this rate is higher in Turkey. The rate of consanguineous marriages in different regions varies between 20-25%. The incidence of autosomal recessive diseases in the children born to these marriages is found to be above the average of Turkey. Therefore, it is expected that approximately 5.7 million people are affected by rare diseases in Turkey. The rate of consanguineous marriages differs according to race, social characteristics, religion and moral rules. A study investigated the effects of consanguineous marriages on miscarriages, stillbirths, congenital malformations and neonatal mortality rates, it was revealed that miscarriage, stillbirth, mental-motor retardation and infant mortality rates of 0-2 years were found to be higher in these marriages. Post-neonatal, infant and under-5 mortality rates were found to be higher in first-degree cousin marriages than in non-relatives. The problems faced throughout the world regarding rare diseases are also experienced in our country. These are the lack of knowledge and specialist physicians and the high cost of treatment and lack of a regulation in our country up to this day to designate rare diseases and orphan drugs. Therefore,

although there are many expert researchers working on rare diseases, the number of researchers who reach clear results is quite low. When proper working conditions are provided, when necessary arrangements are made for both researchers and patients regarding rare diseases, the diagnosis, prevention and, if possible, treatment practices can be done more properly (Dündar and Karabulut, 2010).

The Orphan Drug Study Group was founded in October 2008 with the participation of 39 companies that are members of Turkish Researcher Pharmaceutical Companies Association. The purpose of this study group is to gather the stakeholders of Rare Diseases and Orphan Drugs and to realize long-term projects, increase public awareness and contribute to national health policies. The orphan drug numbers in Turkey by numbers as determined by AIFD are detailed in the figures below (Balik, 2014).

Figure 1. Available percent of the orphan drugs licensed in the European Union in Turkey (Balik, 2014)

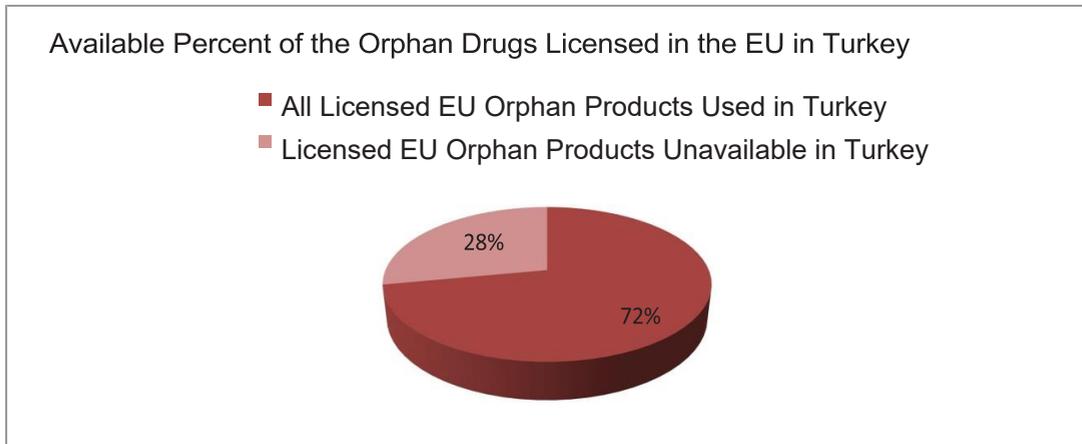


Figure 2. The percentage of the orphan medicinal products licensed in the EU used in Turkey through various access processes (Balik, 2014)

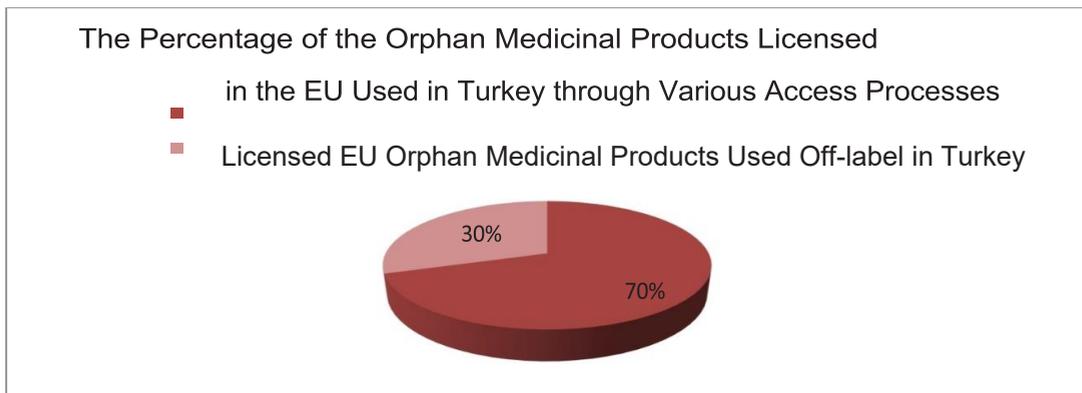


Figure 3. Therapeutic field distribution of the EU orphan products licensed in EU and used in Turkey (Balık, 2014)

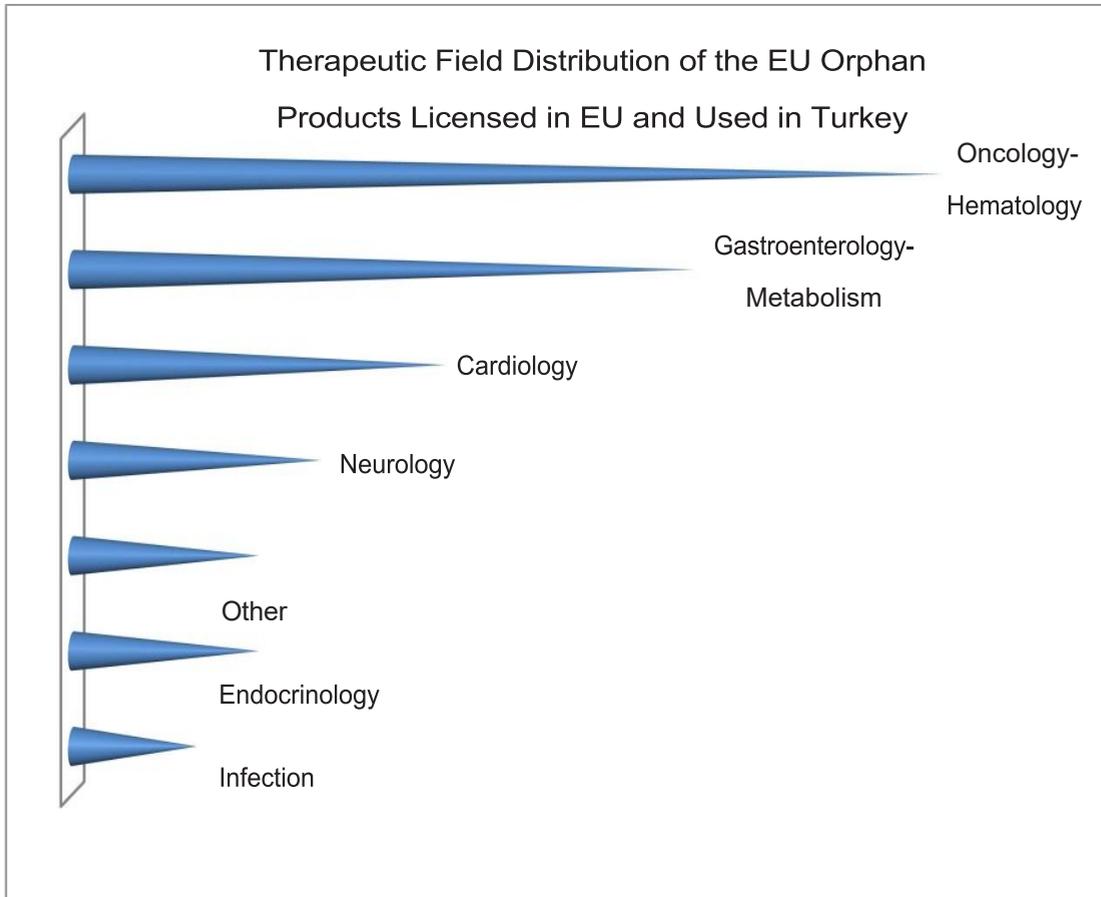
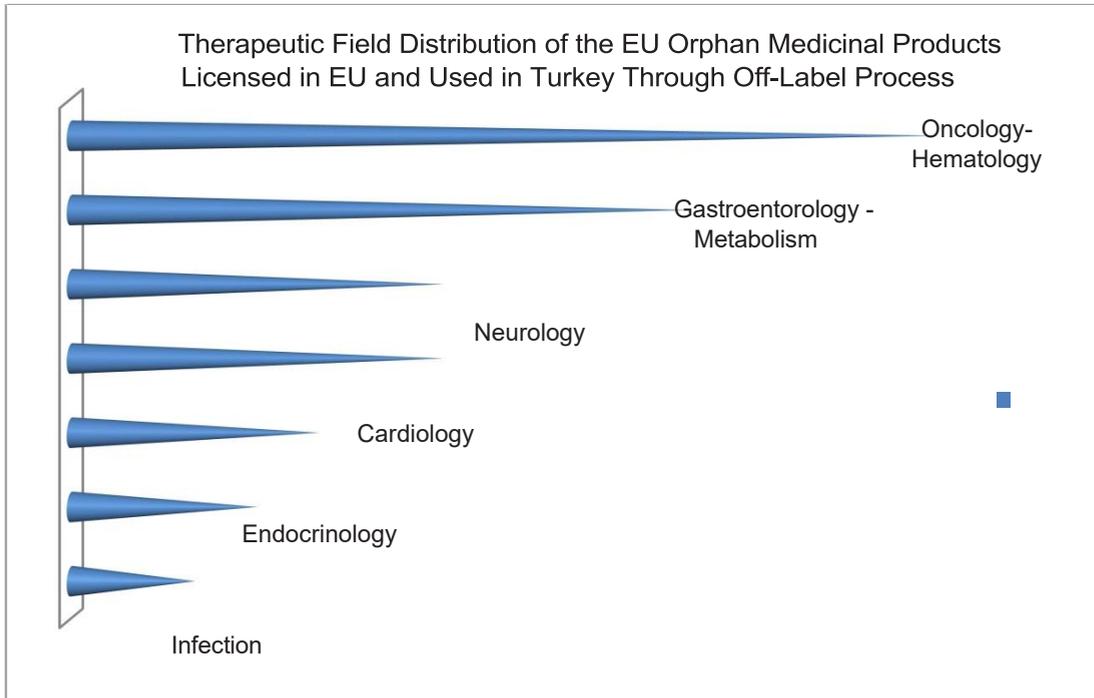


Figure 4. Therapeutic field distribution of the EU orphan medicinal products licensed in EU and used in Turkey through off-label process (Balık, 2014)



4.1. Licensing, Pricing and Reimbursement Legislations

Since orphan drug is not designated under the Licensing Regulation and there is no specified licensing criteria for such drugs, there is no products produced in Turkey and licensed as orphan drugs. The guideline that was started in 2011 has not been completed yet (Balık, 2014).

Pursuant to Article 7 of the Communiqué on Pricing, orphan products can be priced up to 100% of the reference price, or even up to 5% more. Additionally, the pricing can be determined according to the cost card for the orphan products produced in our country. In this case, however, the price requested on the cost card cannot exceed 20% of the reference product price. Claims of above 20% are evaluated by the Commission (Balık, 2014). However, since there is no product licensed as an orphan drug, there is no product that can use this article. There is no regulation specific to orphan drugs in the reimbursement legislation (Balık, 2014). So what are the expectations of the pharmaceutical sector on orphan drugs in Turkey? (Balık, 2014).

For licensing;

- For the Orphan Drug designation criteria to be the same as the EU, and in this context, accepting the incidence rate of the disease as 5 out of 10.000,
- Defining licensing processes that will allow easier and quicker licensing, enabling assessment priority,

- Release of GMP Audit before the application for license,
- Waiver of license application fees, analysis fees, license fees, GMP audit fees, revenue office fees, variation application fees, clinical research application fees and import application fees (Balık, 2014).

For pricing;

- Being able to determine the price of the orphan drug 5% higher than the reference price as specified in the repealed old Pricing Communiqué,
- Application of the current exchange rate on these products (Balık, 2014).

For reimbursement;

- Priority assessment of reimbursement applications for orphan drugs,
- Shortening the assessment period,
- Reduction of public discount rates considering the effect on the budget (Balık, 2014).

Conclusion

It is important to be aware that every family can catch a rare disease at any time. There has been an increase in public awareness of rare diseases in recent years but the knowledge on the development of treatment for these diseases is still quite insufficient. Therefore, regional and financial services supporting patients such as day care services, recreation centers, emergency units, socialization and rehabilitation centers, summer camps and training should be developed.

It is known that patient with rare diseases and their families are more proactive than normal patients who have other common diseases, they also have much more knowledgeable about their problems than the health professionals who are trying to relieve their suffering, because of the result of rare diseases. Therefore, the social dimension and consequences of rare diseases should be considered.

Beyond the variety of these diseases, patients suffering from rare diseases and their families face many difficulties directly caused by the rarity of these pathologies; failure to reach the correct diagnosis, lack of knowledge, social outcomes, deficiencies in health care services, high cost, limited medication, and care options.

Patients suffering from rare diseases are defined as the ones undiagnosed and untreated by the healthcare system. In this general framework of difficulties, it should be emphasized that there is always a way to use this limited but increasing information and tools available.

Conflict of Interests

Author declares no conflict of interests.

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