2014 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE

STATE OF THE ART OF RARE DISEASE ACTIVITIES IN TURKEY

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The European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

More information on the activities of the former European Union Committee of Experts on Rare Diseases and the EUCERD Joint Action can be found at www.eucerd.eu.

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ACRONYMS

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization

GENERAL INTRODUCTION

This document was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

The present report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2013. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the Commission Expert Group on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of the European Commission, its Agencies or national health authorities.

The report is split into six parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2013
Part III: European Commission activities in the field of rare diseases
Part IV: European Medicines Agency activities and other European activities in the field of rare diseases
Part V: Activities in EU Member States and other European countries in the field of rare diseases
Part VI: Activities at National level in each EU Member State and other European countries in the field of rare diseases

Parts I – V also include a description of the methodology, sources and validation process of the entire report, and a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning Turkey. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report.

Each year, there are around 15 000 downloads of the different sections of the report combined.

RARE DISEASE ACTIVITIES IN TURKEY

Definition of a rare disease

According to the National Draft Guideline for Orphan Medicines, the prevalence limit for the definition of a rare disease will be within the EU-defined limit of no more than 5 in 10'000 individuals. The Ministry of Health accepts pricing of human medicinal products to be considered under the 'orphan' approach when such a product is indicated for the treatment of diseases for which the aetiology is not clearly defined and those which affect no more than 1 in 100'000 individuals[1].

National plan/strategies for rare diseases and related actions

There is currently no national plan or strategy for rare diseases in Turkey: rare diseases are currently funded within the general health system budget[2].

In 2010, the Turkish Ministry of Health considered collaboration with Orphanet Turkey in specific projects for the establishment of a National Plan for Rare Diseases and a number of meetings have been organised amongst professionals in Turkey in the context of the Europlan project of which Turkey is a collaborating partner. The recognition of a national plan is mandatory for assigning priority actions for rare diseases. Under the "National Health Transformation Programme" the Ministry of Health has suggested developments in medicinal product use, medical and social care, surveillance and other relevant actions[3].

The 1st National Rare Disease Symposium took place on 27 November 2011 in Istanbul. Organised by the Orphanet Turkey team, this event brought together representatives from the Turkish Ministry of Health, Social Security authorities, patient organisations, scientists and industry. The symposium covered 3 main topics: rare disease and orphan medicinal products organisations and databases in EU; International and European Union and legislation on rare diseases and orphan medicinal products, and the current situation in Turkey; and problems and difficulties in the treatment and management of rare diseases in Turkey - how to overcome these obstacles. Participants discussed the current legislation at EU level in the field as well as the current situation in other countries such as Italy, France and Bulgaria. A second symposium was held in November 2013 is to discuss the areas to be considered in the scope of a national plan for rare diseases.

Centres of expertise

Though no centres of expertise for rare diseases currently exist, university hospitals and research centres are active in diagnosis and management of rare diseases, including centres at Hacettepe University Ankara) for metabolic and neuromuscular diseases, Istanbul University for neuromuscular diseases and Gazi University (Ankara) for metabolic diseases with the necessary infrastructure for specialised care (i.e. inpatient beds and outpatients clinics, pathology services, genetic counselling units, genetic testing facilities for post and prenatal diagnosis, biochemistry, physical therapy units, etc). These centres can accept referral patients from other centres/cities and state hospitals and are therefore described as 'reference centres'. For these centres, the Ministry of Health and the social security system covers the invoices of non-private patients.

Turkey is planning to establish national networks for the prevention, surveillance, diagnosis and treatment of rare diseases. Projects to establish national centres of reference for rare diseases are expected. These centres will be part of the overall planning of healthcare in the country. The Ministry of Health and the different regional healthcare authorities will have to coordinate their approach and harmonise regional network activities.

Registries

In order to identity the rare diseases currently prevalent in Turkey, there is a significant need to complete a comprehensive epidemiological survey at national level: this is currently being developed by stakeholders. Within the IT infrastructure of Hacettepe Hospitals a new registry program including clinical and laboratory

[1] Press release regarding the Pricing of Medicinal Products for Human Use (http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=225

[2] Notification regarding the Pricing of Medicinal Products for Human Use (http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=225)

[3] Turkey Health Transformation Program (http://www.saglik.gov.tr/EN/BelgeGoster.aspx?17A16AE30572D313AAF6AA849816B2EF1DACD7356F6C2568) http://www.orpha.net/actor/EuropaNews/2009/doc/TurkHealthPolicy.pdf

findings has been established for paediatric rare metabolic diseases. This registry is financed by Hacettepe Hospital and METVAK (Metabolic Diseases Foundation)

Turkey participates in the European registries EIMD, SCNIR, TREAT-NMD and EUROCARE CF.

Neonatal screening policy

The Ministry of Health is responsible for neonatal screening of phenylketonuria and congenital hyperthyroidism since 2007 and bitonidase deficiency since 2009. Data in 2011 shows that over 95% of the population is covered by these screening policies. Neonatal screening is coordinated by the Newborn Screening Coordination Centre based at the Refik Saydam Disease Prevention and Control Centre in Ankara. A free national screening and counselling program for thalassemia is also available through Thalassemia Counselling Centres organised by Turkish Ministry of Health.

Genetic testing

Genetic testing is carried out mainly at University laboratories. There are no national guidelines concerning genetic testing, but two information documents have been prepared by Hacettepe Medical School on ethical principles of genetic testing and counselling through the National Commission for UNESCO Bioethics Committee web site (in Turkish). Tests are reimbursed through the Social Security System and private insurance schemes. Testing abroad is possible.

Diagnostic tests are registered as available in Turkey for 111 genes and an estimated 164 diseases in the Orphanet database[4].

National alliances of patient organisations and patient representations

The Turkish Rare Diseases Platform[5] is a new Platform bringing together yet a few rare disease patient organisations in Turkey. Established on 28 February 2013, it aims to motivate rare disease patient communities to come together and share their know-how to bring more service to rare diseases patients, family members and caretakers. It aims to be the platform to voice the issues of rare diseases patient associations and rare diseases patients and caretakers. Some private foundations (such as the Foundation for Metabolic Disorders – METVAK) are active in counselling, creating public awareness and networking for patients and families.

Sources of information on rare diseases and national help lines

Orphanet activity in Turkey

There is no official, rare disease specific information centre on rare diseases in Turkey other than Orphanet. Since 2006 there is a dedicated Orphanet team for Turkey currently hosted by the Istanbul University Experimental Medical Research Institute Department of Genetics. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. The team also maintains the national Orphanet Turkey website[6] in the Turkish language. The team organised the 6th Eastern European Rare Disease Conference in Istanbul on 24-26 November 2011 and the 1st National Rare Disease Symposium in Istanbul on 27 November 2011: a second National Symposium took place in November, 2013.

Official information centre for rare diseases

There is currently no official information centre for rare diseases in Turkey, although information is provided by the Ministry of Health's Mother and Child Health Directorate in Ankara.

Help line

There is currently no official help line for rare diseases in Turkey.

Other sources of information on rare diseases

No specific activity reported.

Guidelines

Treatment guidelines have been issued by the Ministry of Health for the following rare diseases: Gaucher type I and III; LSD type I, II and VI; Fabry; Niemann Pick; Pompe; and Wolman diseases.

[4] Information extracted from the Orphanet database (January 2014).
[5] http://www.enderhastaliklar.org/
[6] http://www.orpha.net/national/TR-TR/index/orphanet-t%C3%BCrkiye/

Training and education initiatives
A bylaw has been accepted for fellowship training program paediatric metabolic diseases.

National rare disease events in 2013
Some rare diseases have an annual designated day (e.g. phenylketonuria day, 1 June) to raise awareness of these diseases. A second symposium on rare diseases was held in November 2013 is to discuss the areas to be considered in the scope of a national plan for rare diseases.

Hosted rare disease events in 2013
No specific reported activities.

Research activities and E-Rare partnership
National research activities
TUBITAK (The Scientific and Technological Research Council of Turkey) has in the past supported research on rare diseases in Turkey.

Participation in European research projects
Teams from Turkey participate/participated in 16 FP7 rare disease related projects.

E-Rare
Turkey, represented by TÜBİTAK, has been a member of the E-Rare and E-Rare-2 projects. TÜBİTAK participated in all Joint Transnational Calls (JTC) of the E-Rare-1 and E-Rare-2 projects. In the 1st Joint Transnational Call, Turkey was represented in 2 of the 13 consortia/projects selected for funding of €700'000. In the 2nd Joint Transnational Call E-Rare, Turkey was represented in 4 of the 16 consortia/projects selected for funding, with a total of around €400,000 funding. In the 3rd Joint Transnational Call, TÜBİTAK supported 3 Turkish research teams within 13 selected consortia. Turkey also participated in the 4th Joint Transnational Call in 2012, however teams from Turkey are not involved in the selected consortia. The fifth E-Rare joint transnational call (JTC 2013) for funding multilateral research projects on rare diseases have been decided to open on December 7, 2013 by 17 European organisations including TÜBİTAK. The Turkish funding commitment was 0,6 M€ for the fifth call Launched in 2013, however Turkish teams were not amongst those participating in the selected projects.

IRDiRC
With a Memorandum of Understanding (MoU) documenting, the commitment of the indicated E-Rare group of funders, who agree on making every reasonable effort to fulfil the intents expressed in their participation in IRDiRC, has been signed between each Party including TÜBİTAK. EC responded positively to this demand that the group of E-Rare funders join IRDiRC in 2012.

Orphan medicinal products
At the end of 2011, the Directorate General of Pharmaceuticals and Pharmacy (IEGM), attached to the Turkish Ministry of Health, transformed into the independent national competent authority, The Turkish Medicines and Medical Devices Agency (TİTCK). In Turkey, licencing applications for all human medicinal products are submitted, by accredited licence holders, to TİTCK, in line with the "Regulation on Licensing for Medicinal Products for Human Use".

In 2010, the Orphan Drug Study Group (ODSG) was formed from officers working at the Directorate-General of Pharmaceuticals and Pharmacy (IEGM), TİTCK from here on. The main purpose of ODSG was to prepare the national Guideline for Orphan Medicines. In the course of activities, ODSG compiled information relating to orphan medicinal products and rare diseases in the European Union (EU), studied Regulations 141/2000/EC and 847/2000/EC, and developed a national approach for orphan medicinal product policies in Turkey. The National Draft Guideline for Orphan Medicines was formed in the first quarter of 2011. The Draft Guideline was open for consultation by the pharmaceutical sector, and responses received by the second half of 2011.

Orphan medicinal product committee
The Draft Guideline for Orphan Medicines includes the establishment of a "Scientific Commission for Orphan Medicines".

Orphan medicinal product incentives

Data exclusivity is applied in terms to original products for which no generic registration application has been submitted in Turkey since 1 January 2005 among the original products which have been registered for the first time in one of the countries within the Customs Union Area after 1 January 2001, and original products which shall be registered for the first time in one of the countries within the Customs Union Area after 1 January 2005. The data exclusivity period consists of 6 years to commence as of the first registration date of these products in the Customs Union Area. With regard to those products which benefit from patent protection in Turkey, the implementation of the data exclusivity period of 6 years is limited to this patent period[7].

The Orphan Drug Study Group (ODSG), formed in 2010 by the Ministry of Health (MOH) have proposed a draft National Draft Guideline for Orphan Medicines, including incentives for the development and registration of orphan drugs, which has been publicly available since 2011. The Ministry of Health updated the draft guideline in 2013 but did not share information on proposed changes. The updated version is waiting for approval by the head of the regulatory agency TITCK. Publication of the final National Guideline is not expected before the end of 2014.

Today however, no regulations or guidelines are in place for rare diseases and/or orphan drugs. Only 30% of drugs for rare diseases have marketing authorisation in Turkey, with another 30% imported into Turkey via Turkish Pharmacists' Association (TEB), subject to approval by the Ministry of Health on a case-by-case basis. The remaining 40% of these drugs are not available in Turkey[8].

Drugs for the treatment of rare diseases are exempted from the reference pricing policy that is applicable to normal medicinal products. The Ministry of Health accepts pricing of human medicinal products to be considered under the 'orphan' approach when such a product is indicated for the treatment of diseases for which the etiology is not clearly defined and diseases which affect no more than 1 in 100'000 individuals. (A recent draft guideline proposes to change this to no more than 1 in 10'000 individuals).

Incentives related to orphan drug status in Turkey (as expected for the near future) are Waivers from MAA.

Orphan medicinal product market availability situation

At present, the Turkish Ministry of Health (MOH) has not yet developed a national policy with reference to "rare diseases" and "orphan medicinal products", as commonly defined inside the European Union (EU). Therefore, patients suffering from known rare diseases in Turkey access treatment with nationally licenced or non-licenced human medicinal products that have been granted marketing authorisation by other competent authorities under "orphan designation" and/or indicated for the treatment of specific rare diseases.

In 2013, 53 (of the 67 designated and centrally authorised medicines under the EU orphan medicinal products legislation) are accessible in Turkey. Of these orphan medicinal products, 21 are licenced in Turkey and 32 are procured by pre-licencing procedures.

Around half of the EU authorised orphan medicinal products accessible in Turkey are oncology-haematology products whereas nearly one quarter is gastroenterology-metabolism products, coming in first and second place, respectively. Oncology-haematology and gastroenterology-metabolism products also dominate the list of EU-authorised orphan medicinal products procured through pre-licencing procedures in Turkey.

Orphan medicinal product pricing policy

Normally, all drugs in Turkey are subject to a reference pricing policy. However, orphan medicinal products are exempted from this. Orphan products are priced up to the reference price laid down in official documents of the products where these products were imported and manufactured in its country of origin. Price of these products shall be revised making calculation on amounts of sales price every year. The Ministry of Health accepts pricing of human medicinal products to be considered under the 'orphan' approach when such a product is indicated for the treatment of diseases for which the aetiology is not clearly defined and those which affect no more than 1 in 100'000 individuals[9].

Orphan medicinal product reimbursement policy

All orphan medicinal products entering the market are 100% reimbursed.

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[7] Regulation on Licensing of Medicinal Products for Human Use
http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=226

[8] Source: Ceren Akdere, AIFD Orphan Drugs Working Group, February 2013

[9] Press release regarding the Pricing of Medicinal Products for Human Use
(http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=225)

Other initiatives to improve access to orphan medicinal products

Orphan medicinal products are procured in Turkey by TİTCK through 3 means. A medicine may be:

1. Licenced and already on the market for purchase;
2. Currently non-licenced in Turkey, however procured on grounds that it is approved in USA or the EU, or on a case-by-case basis in return for prescription ratification if its efficacy and safety is proven and a clinical trial protocol is running;
3. Approved under the scope of the compassionate use programme, to be clinically administered to patients.

Orphan devices

No specific activity reported.

Other therapies for rare diseases

No specific activity reported.

Specialised social services

Some therapeutic recreational programmes and services aimed at the integration of patients in daily life are provided by patient organisations and private foundations with the aid of private donations. Disability benefits can be obtained from the government towards special education classes.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2013 IN TURKEY

National plan/strategies for rare diseases and related actions

A second symposium was held in November 2013 is to discuss the areas to be considered in the scope of a national plan for rare diseases.

National alliances of patient organisations and patient representations

The Turkish Rare Diseases Platform[10] is a new Platform bringing together yet a few rare disease patient organisations in Turkey. Established on 28 February 2013, it aims to motivate rare disease patient communities to come together and share their know-how to bring more service to rare diseases patients, family members and caretakers. It aims to be the platform to voice the issues of rare diseases patient associations and rare diseases patients and caretakers.

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Research activities and E-Rare partnership

E-Rare

Turkey, represented by TÜBİTAK, has been a member of the E-Rare and E-Rare-2 projects. The Turkish funding commitment was 0,6 M€ for the fifth call Launched in 2013, however Turkish teams were not amongst those participating in the selected projects.

Orphan medicinal products

Orphan medicinal product incentives

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[10] http://www.enderhastaliklar.org/

in 2013 but did not share information on proposed changes. The updated version is waiting for approval by the head of the regulatory agency TITCK. Publication of the final National Guideline is not expected before the end of 2014.

LIST OF CONTRIBUTIONS[11]

Contributions in 2010
Ugur Ozbek, Fatma Atalar and Tufan Acuner *(Orphanet Turkey, Istanbul University)*
Meral Ozguc *(Hacettepe School of Medicine, Ankara)*
Pelin Kilic *(Turkish Ministry of Health)*

Contributions in 2011
Ugur Ozbek, Fatma Atalar and Tufan Acuner *(Orphanet Turkey, Istanbul University)*
Meral Ozguc *(Hacettepe School of Medicine, Ankara)*
Pelin Kilic *(Turkish Ministry of Health)*

Contributions in 2012
Pelin Kilic *(Orphan Drugs Study Group Coordinator - TİTCK)*
Ömer Yemşen *(Orphan Drugs Study Group, Chief of Unit - TİTCK)*
Fikriye Handan Öztunca *(Orphan Drugs Study Group Member - TİTCK)*
Ugur Ozbek, Fatmahan Atalar *(Orphanet Turkey, Istanbul University)*

Contributions in 2013
Ugur Ozbek, Fatma Atalar *(Orphanet Turkey, Istanbul University, Istanbul)*
Meral Ozguc *(Hacettepe School of Medicine, Ankara)*
Pelin Aksungur *(Turkish Ministry of Health, Ankara)*
Nihan Eryilmaz *(Turkish Scientific Research Council-TUBITAK, Ankara)*

Contributions in 2014
Pelin Aksungur *(Turkish Ministry of Health, Ankara)*
Engin Doğan *(Turkish Ministry of Health, Ankara)*

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- Orphanet Turkey national website
  http://www.orpha.net/national/TR-TR/index/orphanet-t%C3%BCrkiye/

[11] The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.
[12] All websites and documents were last accessed in May 2014.