Pharmaceutical Regulatory Affairs: Open Access

Mallkuçi, Pharm Regul Aff 2017, 6:1
DOI: 10.4172/2167-7689.1000190

Review Article OMICS International

Regulatory Framework of Orphan Medicines in Albania

Ilda Mallkuçi*

Marketing Authorization and Regulatory Affairs Department, National Agency for Medicines and Medical Devices, Tirana, Albania

***Corresponding author:** Ilda Mallkuçi, Marketing Authorization and Regulatory Affairs Department, National Agency for Medicines and Medical Devices, Tirana, 1001, Albania, Tel: 00355673016217; E-mail: ildushka81@hotmail.com

Received date: June 09, 2017; **Accepted date:** June 19, 2017; **Published date:** June 26, 2017

Abstract

There are no legal basis for the orphan medicines mentioned in Law No. 105/2014, 31.07.2014 "On drugs and pharmaceutical service", amended. They are regulated by this low as the other medicines authorized in Albania according to the centralized procedure. This procedure is applied for the medicines authorized from EMA and FDA. The main document for this procedure is the Certificate of the Pharmaceutical Product from EMA or FDA. Specific requirements for the centralized procedure are detailed in Decision of the Council of Ministers No. 299, 08.04.2015. Actually in Albania are authorized for marketing 14 orphan medicines; they are designed for the treatment of rare diseases as mucopolysaccharidosis II and VI, Fabry disease, Cystic Fibrosis, Acromegaly Pituitary ACTH Hypersecretion, Idiopathic Pulmonary Fibrosis, Multiple myeloma etc. These medicines are authorized in Albania since 2008 until 2017 (although the lack of specified legal basis), most of them several months to 4 years from the first authorization by EMA. To qualify for orphan designation, a medicine must meet these criteria: it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; the prevalence of the condition in the EU must not be more than 5 in 10,000; no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. 60% of designated orphan medicines are intended for paediatric use. Because rare diseases are a global issue, the Agencies work closely with its international partners on the designation and assessment of orphan medicines. Recommendations: Approaching the Albanian legislation with EU legislation regarding orphan medicines and creating a data base on the extension of use of Orphan medicines in Albania.

Keywords: Orphan drug; Marketing authorization; Centralized procedure; EMA; FDA; Fabry disease; Cystic fibrosis; Rare disease

Introduction

About 30 million people living in the European Union (EU) suffer from a rare disease. The European Medicines Agency (EMA) plays a central role in facilitating the development and authorisation of medicines for rare diseases, which are termed 'orphan medicines' in the medical world [1].

By definition an orphan medicine is a medicine for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10,000 people in the European Union) or where the medicine is unlikely to generate sufficient profit to justify research and development costs [1].

By definition an orphan disease is defined as a condition that affects fewer than 200,000 people nationwide. This includes diseases as familiar as cystic fibrosis, Lou Gehrig's disease, and Tourette's syndrome, and as unfamiliar as Hamburger disease, Job syndrome, and acromegaly, or "gigantism" [1].

The US was the first nation to introduce orphan drug legislation and, in the intervening years, a number of other countries have followed suit, for example Japan (1993), Singapore (1997), Australia (1998) and the EU (2000). Other countries, such as Canada, recognize the importance of orphan drug legislation and consider applications for rare diseases on a case-by-case basis, but have yet to issue regulations [2].

Legal Basis for Orphan Medicines in Albania

Actually there is no specific legal basis for the orphan medicines in Albania. They are regulated by the Law No. 105/2014, 31.07.2014 "On drugs and pharmaceutical service", amended and by the Decision of the Council of Ministers No. 299, 08.04.2015, amended, as some other medicines authorized in Albania according to the centralized procedure. This procedure is applied for the medicines authorized from EMA and FDA. The main document for this procedure is the Certificate of the Pharmaceutical Product from EMA or FDA. There are no financial incentives for this category of medicines. The total fee, paid by the pharmaceutical company that has the exclusivity of the orphan medicines for Albania is 800€ (100€ prepayment prior to application) and (700€ final payment), after it was released the Order of Minister [3].

According to the Decision of the Council of Ministers No. 299, 08.04.2015 "On the regulation for issuing the marketing authorization for drugs and their classification in the Republic of Albania" the requirements for issuing the marketing authorization for an orphan medicine in Albania are as follows:

- Certificate of the Pharmaceutical Product (CPP), according WHO (original document);
- Good Manufacturing Practice Certificate (legalized copy);
- Marketing authorization certificate/decision from FDA or EMA, or in two countries of European Community (notarized copy and translated into English in the reference country);
- Modules 1-5 in CTD format (All these documentations are revised in the moment of the application for MA from the Agency) [4].

The Centralized procedure: The Agency confirms the validity of the submitted application and assesses the submitted documentation on the medicinal product, in line with the provisions of the Law and of this Regulation, within 15 days. The date of the beginning of the procedure for granting marketing authorization is considered the date of confirmation of the pre-payment fee. The Agency evaluates the documentation for marketing authorization, within 20 working days after the beginning of the procedure and passes it to the Permanent Commission of Medicinal Products (KPB) for further examination. The Permanent Commission of Medicinal Products (KPB) examines the respective file, within 5 working days:

- In case, the documentation is complete, it issues the recommendation for granting a marketing authorization;
- The documentation is not complete, the KPB send an official answer with supported arguments for this action to the Agency which then notifies the interested company [4].

Authorized Orphan Drugs in Albania

There are 14 medicines authorized for marketing in Albania designed for rare diseases, from different marketing authorization holders.

S. No.	Trade name & INN	Dosage form	MAH	MA
1	ELAPRASE (Idursullfase) status E	Concentrate for solution for infusion × 2 mg/ml	Shire Human Genetic Therapies AB-Sweden	05.10.2015 (MA from EMA: 08.01.2007)
2	VPRIV (Velaglucerase alfa)	Powder for solution for infusion × 400 U	Shire Pharmaceuticals Ireland Limited-Ireland	05.10.2015 (MA from EMA: 26.08.2010)
3	REPLAGAL (Agalsidase alfa)	Concentrate for solution for infusion × I mg/ml	Shire Human Genetic Therapies AB-Sweden	27.01.2017 (MA from EMA: 03.08.2001)
4	NAGLAZYME (Galsuffase) status E	Concentrate for solution for infusion × 1 mg/ml	Biomarin Europe Limited-UK	18.10.2016 (MA from EMA: 24.01.2006)
5	CERDELGA (Eliglustat (as tartrate))	Hard capsules × 84.4 mg	Genzyme Europe B.V.-Netherlands	20.10.2015 (MA from EMA: 19.01.2015)
6	ELELYSO (Taliglucerase alfa)	Powder for solution for intravenous infusion × 200 units	Pfizer Inc., USA	18.07.2014 (MA from EMA: 25.10.2012)
7	ESBRIET (Pirfenidone)	Hard capsules × 267 mg	Roche Registration Limited-UK	01.07.2016 (MA from EMA: 28.02.2011)
8	FARYDAK (Panobinostat as Panobinostat lactate anhydrous)	Hard capsules × 10 mg Hard capsules × 15 mg Hard capsules × 20 mg	Novartis Pharma AG-Switzerland	18.10.2016 (MA from EMA: 28.08.2015)
9	SIGNIFOR LAR (Pasireatide as Pasireotide parnoate)	Powder and solvent for suspension for injection × 20 mg Powder and solvent for suspension for injection × 40 mg Powder and solvent for suspension for injection × 60 mg	Novartis Pharma AG-Switzerland	18.10.2016 (MA from EMA: 24.04.2012)
10	TOBI PODHALER (Tobramycin)	Inhalation powder Hard capsules × 28 mg	Novartis Europharm Limited-UK	28.05.2015 (MA from EMA: 20.07.2011)
11	TASIGNA (Nilotinib)	Capsules × 200 mg Hard capsules × 150 mg	Novartis Pharma Schweiz AG-Switzerland	08.04.2016 for 150 mg and RMA 20.11.2013 for 200 mg (MA from EMA: 19.11.2007)
12	NEXAVAR (Sorafenib as Sorafenib tosylate)	Film-coated tablets × 200 mg	Bayer Pharma AG-Germany	RMA 03.09.2013 (MA from EMA: 19.07.2006)
13	IMBRUVICA (Ibrutinib)	Hard capsules × 140 mg	Janssen-Cilag International NV-Belgium	04.08.2015 (MA from EMA: 21.10.2014)
14	FABRAZYM E (agalsidase beta)	Powder for concentrate for solution for infusion x 35 mg	Genzyme Europe B-The Netherlands	24.10.2016 (MA from EMA: 03.08.2001)

Table 1: Authorized orphan drugs in Albania.

In Table 1 are three medicines (Elaprase, Replagal and Naglazyme) which are designed for rare diseases, but they don't have an orphan status according to EMA. They status is Under Exceptional Circumstances.

In the last column it is stated the first MA in Albania and the first MA in EMA. For example Nexavar is authorized in EMA in 2006 and in 2008 it was issued the first MA in Albania and then the renewal in 2013. This medicine is authorized and present in the Albanian market for at least 10 years. Cerdelga is authorized for marketing entering 9 months from the first MA in EMA. Most of these orphan medicines are authorized in Albania from several months to 4 years from the date of the first MA in EMA, despite the lack of legislation, financial and administrative incentives from the Albanian Authorities. It is very important to state that the MA fees in Albania are very low, compared with the fees in other EU and Balkan countries. From a financial point of view it is impossible from the authorities to reduce furthermore the MA fees for this category of medicines. The only categories that have a financial incentive are antitumorales (Table 2) [4].

Orphan Drugs	Therapeutic Indication
ELAPRASE (Idursulfase) status E	Mucopolysacharidosis II
VPRIV (Velaglucerase alfa)	Gaucher disease
REPLAGAL (Agalsidase alfa)	Fabry disease
NAGLAZYME (Galsulfase) status E	Mucopolysacchridosis VI
CERDELGA (Eliglustat (as tartrate))	Gaucher disease
ELELYSO (Taliglucerase alfa)	Gaucher disease
ESBRIET (Pirfenidone)	Idiopathic pulmonary fibrosis
FARYDAK (Panobinostat as Panobinostat Lactate Anhydrous)	Multiple myeloma
SIGNIFOR LAR (Pasireotide as Pasireotide pamoate)	Acromegaly, Pituitary ACTH Hypersecretion
TOBI PODHALER (Tobramycin)	Cystic Fibrosis, Respiratory Tract Infections
TASIGNIA (Nilotinib)	Leukemia, Myelogenous, Chronic, BCR-ABL Positive
NEXAVAR (sorafenib as Sorafenib tosylate)	Carcinoma, Hepatocellular Carcinoma, Renal Cell
IMBRUVICA (Ibrutinib)	Leukemia, Lymphocytic, Chronic, B-Cell Lymphoma, Mantle-Cell
FABRAZYME (Agalsidase beta)	Fabry disease

Table 2: Orphan drugs and their therapeutic indications.

Orphan Designation in EU

Considering that this category of medicines is authorized for marketing in Albania with the certificate of the pharmaceutical product from EMA or FDA, the administrative and technical documentations are revised from the Albanian Authority in only 20 days, because of the fact that this documentation is revised mainly by EMA and FDA.

The European Agency of Medicines is responsible for reviewing applications from sponsors for orphan designation. To qualify for orphan designation, a medicine must meet a number of criteria: it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; the prevalence of the condition in the EU must not be more than 5 in 10,000 or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition [1].

After EU Designation

Developing medicines intended for small numbers of patients has little commercial incentive under normal market conditions. Therefore, the EU offers a range of incentives to encourage the development of designated orphan medicines.

Sponsors who obtain orphan designation benefit from protocol assistance, a type of scientific advice specific for designated orphan medicines, and market exclusivity once the medicine is on the market. Fee reductions are also available depending on the status of the sponsor and the type of service required. When planning the development of their medicinal product, sponsors should consult the relevant scientific guidelines. Sponsors must submit an annual report to the Agency summarizing the status of development of the medicine. 60% of designated orphan medicines are intended for paediatric use. Medicines authorized across the EU with the results of studies from a paediatric investigation plan included in the product information are eligible for an extension of their supplementary protection certificate. For designated orphan medicines, the incentive is an additional two years of market exclusivity [1].

Global Dimension

Because rare diseases are a global issue, the Agency works closely with its international partners on the designation and assessment of orphan medicines, in particular: the United States Food and Drug Administration, sharing information on orphan medicines under their confidentiality arrangement. The two authorities have also developed common procedures for applying for orphan designation and for submitting annual reports on the status of development of designated orphan medicines. The Japanese Ministry for Health, Labour and Welfare on issues related to orphan medicines.

Recommendations

- Approaching the Albanian legislation with EU legislation and with the legislation of region countries regarding orphan medicine;
- Creating a data base on the extension of use of orphan medicines in Albania;
- Creating new cooperation bridges with the relevant Agencies of other countries to share the experiences in the field of orphan medicines.

References

1. http://www.ema.europa.eu/ema/
2. Hall AK, Carlson MR (2014) The current status of orphan drug development in Europe and the US. Intractable Rare Dis Res 3: 1-7.
3. National Agency for Medicines and Medical devices (2015) On drugs and pharmaceutical service. Law No. 105/2014, 31.07.2014.
4. National Agency for Medicines and Medical devices (2015) Decision of the Council of Ministers No. 299, 08.04.2015.