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EUROPEAN REGULATION ON ORPHAN DRUGS

OUTCOMES OF THE UNIAMO - STAKEHOLDER WORKING TABLE

THE EFFEMERIDS OF UNIAMO 1/2022

ÜNIAMO
Federazione Italiana Malattie Rare

UNIAMO THE ITALIAN FEDERATION OF RARE DISEASES

European Regulation on Orphan Drugs
Multi-stakeholder discussion table
(9 and 30 September 2021 - 11 November 2021).

Version dated January 15, 2022

This notebook finalized on 15 January 2022 illustrates the results of the discussions, promoted by UNIAMO Italian Federation of Rare Diseases Onlus, within a multi-stakeholder working table with respect to the opportunities that the update of the European Regulation on Orphan Drugs offers for the community of people with rare diseases.

The opinions expressed by the participants are to be understood as personal and not representative of the official positions of the respective public or private bodies they belong to.

The document is a summary of what was discussed and aims to be a support tool for Italian policies in Europe, highlighting points of convergence and also what does not yet have a unanimous opinion among the subjects involved, but on which we can work to find agreement.

The Federation will continue to stimulate debate on these issues, involving all the actors involved and illustrating the positions of the community of people with rare diseases, collected through comparison processes internal and external to the Federation and in collaboration with Eurordis.

THIS DOCUMENT IS TRANSLATE WITH IA
Forgive any mistake!

Cite this document as follows:
Let's unite F.I.M.R. European regulation on orphan drugs - Multi-stakeholder discussion table (9 and 30 September, 11 November 2021), 2022.

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Federazione Italiana Malattie Rare

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Context analysis

People with rare diseases represent a particularly fragile segment of the population; they must, therefore, be monitored, protected and supported with greater attention during the SARS-CoV-2 pandemic.

In Europe, a disease is considered rare when it affects no more than 5 people per 10,000 inhabitants.
The first regulations relating to orphan drugs were introduced in the United States in 1983, with the enactment of the Orphan Drug Act, which for the first time raised awareness of the need to formulate a law on the matter. In 1999 the European Union adopted EC Regulation 141/2000 and subsequently EC Regulation 847/2000.
These Regulations have defined the criteria and procedure for the designation of orphan drugs, the assignment of this qualification by the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency - EMA, the attribution of incentives and, finally , the approval procedure.
Orphan drugs in the European Union must meet the following criteria:
1) must be indicated for a life-threatening or chronically debilitating disease;
2) they must be indicated for a rare clinical condition, defined by a prevalence of no more than 5 subjects per 10 thousand individuals, calculated at the European Union level;
3) no valid treatments must be available or, if treatments are already available, the new drug must represent a significant clinical benefit*.

To date, after 22 years, a revision of the Regulation has become necessary.
The European Commission has launched a public call for proposals, closed in July 2021.
At the same time, Eurordis has stimulated a public debate on the matter.
Uniamo, collecting the stimulus and contextualizing it to the Italian reality, promoted a specific working table which saw the participation of the major system stakeholders, with a view to harmonizing positions that were often very distant.

*source: AIFA

The evidence of MonitoRare*

- At the national level
-
- the total number of orphan drugs available in Italy at the end of 2020 was 75 (there were 71 at the end of 2019);
-
- in 2019, 9.7 million doses of orphan drugs were dispensed in Italy, i.e. 0.04% of total pharmaceutical consumption;
-
- spending on orphan drugs in Italy in 2019 amounted to €1,547 million with an impact of 6.6% on total pharmaceutical spending;
-
- the number of drugs for rare diseases included in the list of Law no. 648/1996 grew from 27 in 2012 to 35 in 2020;
-
- the number of people with rare diseases who have benefited from the AIFA fund (as per Law 326/2003, Art. 48) increases exponentially, going from 20 people in 2016 to 1,361 in 2020 (the number of beneficiaries rises to 2,298 also including rare tumors) with an approval rate of requests rising from 26.7% in 2016 to 82.9% in 2020.

*MonitoRare, VII Report on the condition of people with rare diseases, UNIAMO 2021

The evidence from Eurordis

- At European level:
- approximately 70% of patients with rare diseases have experienced treatments that were curative in only 5/6% of cases; in other cases, however, the treatments are mainly symptomatic and non-curative. A third of patients have never received any type of treatment;
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- the majority of authorizations for orphan drugs concern pathologies for which treatments are already available, in particular for "less rare" pathologies, with a strong inequity between pediatric and adult treatments. Furthermore, most of the authorizations concern drugs for the treatment of metabolic diseases and rare tumors.
-
-
- Eurordis search:
-
- 95% patients have no treatment options
- 98% of patients are affected by 11% of pathologies

Participants in the work of the Table

The participants at the tables were chosen for their expertise on the topics covered, trying to give a global representation of the main system stakeholders, from European to Italian institutions to the pharmaceutical industry.

Giacomo Baruchello, Blueprint Medicines
Simona Bellagambi, EURORDIS - UNIAMO
Simone Boselli, EURORDIS
Federico Bressa, Biogen Italia
Maria Elena Congiu, Ministry of Health
Enrico Costa, COMP EMA, AIFA
Michela Gabaldo, Fondazione Telethon
Yllka Kodra, Ministry of Health
Armando Magrelli, COMP EMA
Immacolata Pagano, AIFA
Nicola Panzeri, Roche Pharma Italy
Sandra Petraglia, AIFA
Annalisa Scopinaro, UNIAMO President
Luisa Strani, Alexion AstraZeneca Rare Disease

Points for reflection

The points of convergence

- the European Regulation n. 141/2000 has given good results in the years it has been in force. Therefore the system on which it is based must be updated but not substantially modified. It was underlined that we must act precisely on the parts that have proven to be less efficient, but not dismantle the general system.
-
- It is therefore important not to go to "zero sum": efforts must be intensified in weaker areas without cutting back on what has given a good result to date. Greater investments and not redistribution of resources.
-
- Role of the COMP (the European Medicines Agency committee responsible for "orphan drug designation") in the orphan drug designation process. The COMP does not always have an important role throughout the lifecycle of the medicine; intervenes only if there are specific needs linked mainly to the evaluation or confirmation of the orphan drug designation, unlike what happens for advanced therapies where the CAT (Committee for Advanced Therapies) supports, from a scientific point of view, the CHMP (Committee for the evaluation of medicinal products for human use) the review of the registration dossiers. The proposal is to provide, in the revision of the European regulation, support and synergy between COMP and CHMP throughout the entire life cycle of the medicine.
-
- Early dialogue was considered by all to be a fundamental tool; it must concern both the European and national levels and start from the early stages of the process and also continue into the monitoring and possible revision phase.

It was unanimously underlined that the involvement of patients and patient representatives is fundamental in the regulatory decision-making process, from registration to HTA evaluations.

The Italian experience on early access and forms of treatment reimbursement has some points of innovation compared to other states. It would therefore be appropriate for our Government to be highly proactive at a European level, trying to raise the bar compared to what is already being done.

None of those present questioned the maintenance of market exclusivity.

Points of reflection on which there was no unanimity / or are not currently achievable but which should be explored further:

- At the moment, many of the therapies developed impact a small minority of pathologies. There is therefore a felt need, especially among patients, to broaden the range of pathologies that can hope for treatment.
-
- The proposal from the patients' representatives would therefore be to combine the already existing incentives with further incentives that could divert part of the attention to pathologies that currently lack any treatment.
-
- How to choose the pathology prioritization criteria, which therefore define the audience for which the incentives are applied? At the moment the prevalence criterion is clear and predictable.
- Someone has underlined how replacing it with other criteria could make a long-term effect unevaluable, also considering the fact that some criteria could be complicated to evaluate or difficult to track.
- Others have instead underlined how it would be appropriate to also take into account other indices of complexity, including subjective indices of quality of life.
- A final observation was made underlining that, even where treatments already exist, it is not certain that these are decisive, therefore the progressive improvement in the quality of life also involves continuing studies until the real cure is found.
-
- There was also discussion about the phase from which it could be possible to take advantage of incentives: if these were granted even in the early stages of development, publication of the data could be guaranteed (even with negative results) for the benefit of the community studying the same pathologies.

- With respect to ultra-rare pathologies and the need for equal access in all countries, the proposal from a few years ago by Nordic countries was explored (see http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2016/12/WC500218602.pdf) with respect to the possibility of activating European funds which, once the registration procedure is closed, immediately make the new drugs available to all European patients at an established and fixed price, then leaving the individual national HTAs a year/two to close the price/reimbursement process to guarantee fair access to therapy. This proposal has received various consensus, despite the difficulty in actually putting it into practice.
-
- Again with respect to ultra-rare diseases and closely linked to the above, a further hypothesis was to leverage the application of cross-border law, to therefore move patients to the center or few centers of excellence truly capable of administering the therapy. If there are no doctors capable of providing the treatment, a contract for all 27 states could be redundant.
-
- At the same time, however, some points must be kept in mind that need to be evaluated: the patient's condition, which does not always allow for movement; costs associated with travel, especially if there are no refunds in the country of origin; the travel commitment, often borne by the caregivers.
-
- The COVID experience has shown that some procedures can be optimized and accelerated, in emergency conditions (which could be true for many rare diseases). Using tools such as rolling review, rapid scientific advice as well as the creation of objective task forces could guarantee a faster registration and access process.

- Compassionate use, currently limited to some states with very different legislation, could be managed at the EMA advice level, promoting early access to the drug before actual centralized registration.
-
- It is necessary to outline precise areas of collaboration between countries, aiming at the simplification and de-bureaucratization of existing processes and the benefit of which is the prerogative of all European countries. The proposal of adaptive licensing is brought to the table, a new, already tested approach to drug approval, in order to speed up times and adapt current rules to make effective drugs more quickly available to patients who can benefit from them. Adaptive licensing consists of the early authorization of a medicine in a limited patient population and continues with a series of phases of gathering real-world evidence and adapting the marketing authorization to broaden access to the medicine to larger patient populations.
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- We also discuss the possibility of introducing additional financial incentives (European common fund) to finance national structures that collect data in the post-authorization phase; it would represent an important added value especially for ultra-rare diseases.
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- The issue of incentives for research, development and marketing of orphan medicinal products emerged clearly with a connotation of importance, especially for ultra-rare diseases and in all phases of research. The example was given of reagents that discount VAT at 22%, without concessions. They should also be at national level, not just European.
-
- The example of the Joint Procurement Agreement experimented during the Covid-19 pandemic for vaccines and monoclonal antibodies was given. Some have highlighted that it could easily be applied to drugs for rare and ultra-rare diseases. On the other hand, it was observed that if the idea of structuring a centralized HTA were to come to fruition, it would be superfluous.

Points of intersection with other topics:

- Use and access to the AIFA 5% fund: it was highlighted that there are some critical issues related to the transparency of its use and management of nominal requests, aspects which AIFA is already monitoring with a view to greater clarity and simplification.
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- Need for better harmonization and in some cases revision, at Italian level, of early access methods: 5% Fund, Law 648/96, compassionate use and open label extension studies. It is underlined that some obstacles are of a bureaucratic nature.
-
- It would be important to strengthen the monitoring conducted by AIFA with horizon scanning, thus anticipating the structural needs that will become essential once the therapy is approved or to identify the most promising drugs that can gain early access. We need data collection systems, specialized personnel and equitable distribution across the territory. Adequate planning is required.
-
- In order to guarantee the homogeneous accessibility of the drug to all people with rare diseases on the national territory, it is necessary to monitor so that the times of inclusion in the regional handbooks after AIFA approval are as homogeneous as possible.
-
- During the discussion, the topic of infrastructures serving the trials and administration of therapies was also raised. The issue of infrastructural needs, despite being more of a domestic concern than a community one, is nevertheless an important issue, in light of the constant budget limitations on the current expenditure front. In fact, there are important items in the state budget intended for healthcare construction and technological updating which should be allocated with respect to the needs of transformation of the patient's diagnostic-therapeutic and healthcare path, especially if as a consequence of "paradigm changes" deriving from advancement of therapies and diagnostic techniques.

The presentation in the final event on November 11th

In order to present the fruit of the reflections of the two work meetings, a final public event was organized at the American Studies Center in Rome.
Under the expert direction of Annamaria Baccarelli, European and Italian parliamentarians, representatives of patients, of the pharmaceutical industry through the two trade associations (Assobiotec and Farmindustria), of European and Italian regulatory authorities, and experts in bioethics took turns on stage. and in HTA assessments.

The event had the media partnership of Rai per il Sociale, StartMag and Edra and was broadcast live on the channels of the Centro Studi Americani, on the StartMag page and on the Uniamo Facebook page. Furthermore, it was translated by LIS interpreters to make it accessible to the signing community.

Registration of the event is available at this link.
(https://www.youtube.com/watch?v=zabI_aTgHXM&ab_channel=EdraLSWR).

Below is the presentation poster of the event.

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SPEAKERS

L'impegno di UNIAMO a tutela del paziente raro

Annalisa Scopinaro, Presidente Federazione Italiana Malattie Rare, UNIAMO

SALUTI ISTITUZIONALI

Beatrice Lorenzin, Coordinatrice Health&Science Bridge
Annamaria Parente, Presidente XII Commissione Igiene e Sanità, Senato
Paola Binetti, Senatrice, Presidente Intergruppo parlamentare Malattie Rare
Fabiola Bologna, Segretario XII Commissione Affari Sociali, Camera dei Deputati
Lisa Noja, Membro XII Commissione Affari Sociali, Camera dei Deputati
Fabio Massimo Castaldo, Vicepresidente del Parlamento Europeo
Brando Benifei, Membro del Parlamento Europeo, Vicepresidente dell'Intergruppo parlamentare sulle disabilità
Gianmarco Medusei, Presidente del Consiglio regionale della Liguria, Delegato per il Coordinamento della Commissione salute, Conferenza dei Presidenti delle Assemblee legislative delle Regioni e delle Province autonome

VENTI ANNI DI REGOLAMENTO EUROPEO: BENEFICI E NECESSITA' DI REVISIONE

Armando Magrelli, Vice Chair Committee for Orphan Medicinal Products
Maurizio De Cicco, Vice Presidente Farmindustria
Annalisa Scopinaro, Presidente UNIAMO

TERAPIE INNOVATIVE: DALLE SPERIMENTAZIONI AI PAZIENTI

Sandra Petraglia, Area pre-autorizzazione AIFA
Riccardo Palmisano, Presidente Assobiotec-Federchimica
Simona Bellagambi, Delegato Europeo UNIAMO

SPERIMENTAZIONI CLINICHE & HTA: IL RUOLO DEL PAZIENTE

Carlo Maria Petrini, Presidente Centro di coordinamento nazionale dei comitati etici territoriali per le sperimentazioni cliniche sui medicinali per uso umano e sui dispositivi medici
Francesco Saverio Mennini, Professore di Economia Sanitaria e Economia Politica e Direttore del CEIS – EEHTA (Economic Evaluation and HTA) presso l'Università degli Studi di Roma Tor Vergata, Presidente della SiHTA
Annalisa Scopinaro, Presidente UNIAMO

COORDINA

Annamaria Baccarelli, Caporedattore Redazione Istituzionale, Rai Parlamento

UNIAMO Italian Federation of Rare Diseases

UNIAMO Italian Federation of Rare Diseases is the body representing the community of people with rare diseases.

It has been operating since 1999 for the protection and defense of the rights of people with rare diseases and their families, and has over 160 affiliated associations which are constantly growing.

Develop a constant dialogue with representatives of the institutions (Ministries, AIFA, Istituto Superiore di Sanità, Agenas, Regions, clinical reference centres, ERN network, GPs and PLS, scientific societies, etc.), researchers, private players representing the requests of people with rare disease and possible solutions.

It gives a voice to all the people who find themselves affected by a rare or ultra-rare disease, as well as those who are still looking for a diagnosis.

The sense of disorientation, uncertainty, loneliness, the pain felt when receiving a diagnosis of a rare disease are alleviated by the awareness that the Federation, together with all the Associations, makes every possible effort to improve the quality of life of the person and their his family members and caregivers.

Concrete support is given with the SAIO service (listening, information and orientation service) - aimed at individuals and associations -, with other support projects and with awareness-raising, promotion and protection of rights, advocacy in all the sectors, from research to bioethics, from health approaches to social supports.

You can support our action in many ways:
- making your professionalism available
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The Ephemèrides of UNIAMO

The idea of a Uniamo editorial series is not new. However, a series of conditions had to be met for it to become reality.
In the search for a name that would characterize our publications we came across "effemèride".
The Treccani dictionary reports the following definition:

effemèride (or efemèride) s. f. [from lat. ephemĕris -ĭdis, gr. ἐφημερίς -ίδος «diary», comp. of ἐπί «above» and ἡμέρα «day»]. –
1. a. Anticam., the books in which the king's actions were recorded were called ephemerides, first day by day (hence the name), then according to a broader chronological scheme. b. In full, diary, daily chronicle of events: but what more do I spend in giving you an e. of my life? (D. Bartoli).
2. In more recent times, the term has been used as the title of periodical publications, especially of a literary or scientific nature (never of political newspapers); for example, the literary Ephemerides, which were printed in Rome from 1772 to 1795 and contained reviews of new books; the scientific and literary Ephemerides for Sicily, which were published from 1832 to 1840.
3. Table or group of numerical tables, called e. astronomical (or even nautical, as they mainly serve the needs of navigation), which provide the coordinates of the stars (or other astronomical data variable over time) at pre-established and equal intervals, for example. from day to day or from hour to hour. By extension, also the books, generally published annually, which contain such collections.

Each of the three definitions contains an element that we felt close to us: the daily recording of documents, which reminds us of an ideal journey into pathology; the periodic publication, which responds to our wishes; the table that provides the coordinates, our aspiration and intent in the publication of these brochures.

The relative rarity of the use of this term, its feminine connotation, its originality given that the last person who used it dates back to 1840 for literary or scientific publications, further convinced us that we were made for each other for the other: Federation and effemèride, community of people with rare diseases and periodic publication that recounts a journey and tries to guide its route.

Here is therefore the beginning of a series that will follow the federation's activity by giving an account of the meetings and working groups set up on specific themes, and the fruit of their work.

Most of the time, always.

ÜNIAMO
Rari, mai soli

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