ÜNIAMO
Federazione Italiana Malattie Rare

ANNO 2024

# MonitoRare

Decimo Rapporto sulla condizione delle persone con malattia rara in Italia

## Executive Summary

## Con il patrocinio di

Senato della Repubblica

ISTITVTO SVPERIORE DI SANITÀ

agena.s. AGENZIA NAZIONALE PER I SERVIZI SANITARI REGIONALI

agenzia industrie difesa

Forum Terzo Settore

orphanet

MR MONITORARE


***David***
*Williams syndrome*

# EXECUTIVE SUMMARY

This year too there are numerous points for reflection that emerge from reading the "MonitoRare" report and, as usual, they offer a subsequent and more detailed in-depth analysis. In these first pages we undertake the arduous task of trying to effectively summarize the photograph of this tenth edition of the report with the sole intention of offering for the reflection of all stakeholders in the rare diseases sector some elements that , more than others, assume, at this moment, a strategic role for the future of assistance to people with rare diseases (PcMR) and their families at an international, national and local level.

Some examples of the strengths of the rare disease system in Italy that the tenth edition of MonitoRare confirms are:

**- the accessibility of the drug**

- in 2022, 11.4 million doses of orphan medicinal products were dispensed (3 million more than the previous year), i.e. just 0.04% of total pharmaceutical consumption;

- **spending on orphan medicinal products in 2022 amounted to €1,982 million with an impact of 6.0% on total pharmaceutical spending;**

- **the number of medicines for rare diseases included in the list of Law no. 648/1996 grew from 31 in 2018 to 57 in 2023 (there were just 13 in 2012);**

- **the number of people with rare diseases who have benefited from the AIFA fund (as per Law 326/2003, Art. 48) continues the decline started in 2021, reaching 149 in 2023, after having witnessed an exponential increase in previous years, going from 20 people in 2016 to 1,361 in 2020;**

- as many as 8 of the 18 Advanced Therapy Medicinal Products (ATMPs) with European approval (data updated in August 2023) are currently reimbursed in Italy, 9 ATMPs are being evaluated and 4 have not obtained reimbursement;

**- access to information**

- there are 15 Regions/PPAAs that have an institutional information system specifically dedicated to rare diseases: over 9,000 PLWRD with whom they came into contact in 2023, to which must be added the over 2,200 PLWRD who came into contact with the Rare Disease Helpline from the National Center for Rare Diseases of the National Institute of Health -Istituto Superiore di Sanità (CNMR-ISS);

- training

- the number of ECM courses dedicated to rare diseases will stand at 84 in 2023, (of which 23, 30%, with the presence of a Uniamo representative among the speakers), a continuously increasing trend (there were 49 in 2021); a return to in-person training has been positively recorded;

- diagnosis, neonatal screening and clinical laboratories

- at the end of 2023 the extended neonatal screening program is fully active in all Regions/Autonomous Provinces and the homogenization of hereditary metabolic diseases included in screening panels at regional level pursuant to Law 167/2016 can be considered achieved. Furthermore, more than half of the Regions/PPAAs have expanded, often in the context of experimental projects, the panel of diseases considered to also include some other pathologies;

- the Prime Ministerial Decree of 12 January 2017 "Definition and updating of essential levels of assistance" in art. 38 guarantees all newborns the services necessary for the early diagnosis of congenital deafness and congenital cataracts. At the end of 2023, neonatal audiological screening will be active throughout the national territory. Similarly, neonatal ophthalmological screening is active throughout the country with the sole exception of two regions where it is being implemented;

- **constant growth in the last five years in the number of rare diseases tested in the Italian clinical laboratories considered in the Orphanet database which, given the substantial stability of the number of laboratories (n=278), increased by almost 450 units in the space of 5 years: from 2,282 in 2018 to 2,723 in 2023;**

- the experience of the various programs implemented for undiagnosed diseases is consolidated;

- It should also be remembered that the 2024 budget law provided for a) the establishment of a Fund for Next-Generation Sequencing tests, with an allocation of 1 million euros for 2024, for the strengthening of genomic profiling tests ) and b) the refinancing, with 1 million euros for the year 2024, of the Fund established with the 2022 budget to allow the strengthening and access to Next-Generation Sequencing tests for genomic profiling of tumors for which prescription drugs are available with significant levels of evidence and appropriateness;

- the quality and coverage of surveillance systems

- the coverage of the regional registers of rare diseases (RRRD) increases: the estimated prevalence of the population of people included in the RRMR as of 31.12.2022 rises to 0.83% (0.87% in children under 18 years) from 0.30% of the first edition of the MonitoRare Report in 2015;

- the data contained in the RRRDs relate to all the rare diseases referred to in Annex 7 of the Prime Ministerial Decree of 12.01.2017: based on the over 468,000 PLWRD registered in the RRRDs at the end of 2022 (+43,000 units compared to the previous year). The most present group is that of "Diseases of the central and peripheral nervous system" with 15.8%, followed by the group "Congenital malformations, chromosomopathies and genetic syndromes" with 15.3% and by the group "Diseases of the blood and hematopoietic organs" with 12.4%. All the other groups of pathologies have a percentage weight of less than 10% of the total;

- **the differences by age are very significant: in children/young people, 39% of rare diseases are attributable to the group of "Congenital malformations, chromosomopathies and genetic syndromes", its percentage weight is reduced to just over 10% in adults for whom the the modal class appears, however, to be the group of "Diseases of the central and peripheral nervous system" (just under 18%);**

- **just below 1 person with a rare disease in 6 of those included in the RRRDs is over 18 years old while approximately 1 in 3 is over 60 years old;**

- **the phenomenon of healthcare mobility is significant: the estimate of mobility between Regions based on RRRDs data is equal to 20% in the overall population and reaches 29% in minors;**

- based on the data currently included in the RRRDs, the number of people with rare diseases with cost exemption in our country should exceed 585,000 units;

- according to the most recent studies, the prevalence of rare diseases would be between 3.5% and 5.9% of the population worldwide: the overall number of people with rare diseases in Italy would consequently be between 2.0 and the 3.5 million people, a figure far higher than that of the exempt PLWRDs alone;

- research

- **after the slight increase recorded in 2021, the weight of authorized clinical studies on rare diseases on the total clinical trials is stable (30.6%). The authorized clinical trials on rare diseases in 2023 stand at 187 after the increase in the previous two years (they were 260 in 2021 and 230 in 2022);**

- in 2022, clinical trials on rare diseases in Phase I and II will well exceed the threshold of 50% of the total (56.1%);

- in relation to clinical trials on rare diseases, chemical active ingredients remain prevalent (5.5% of the total), in line with the previous year (56.5% in 2022);

- ATMPs (Advanced Therapy Medicinal Products) are more widespread in clinical trials on rare diseases (9.8%) compared to the overall average (5.3%);

- the number of research projects on rare diseases is growing in absolute value with the presence of Italian research groups - which went from 900 in 2018 to 1,131 in 2023 - but, in percentage terms, the data confirms the decreasing trend of the five years precedents;

- the reference centers

- there are 260 reference centers for rare diseases identified by the Regions/PPAA (4.4 per 1 million inhabitants), an increase compared to the 235 in 2022, probably due to the implementation of the CSR Agreement no. 121 of 24 May 2023 on the document "Reorganization of the National Rare Diseases Network"; 80 of these centers are part of at least one ERN (there were 66 until the end of 2021);

- as regards cross-border healthcare, Italy is characterized by a decidedly higher level of active mobility - a figure which is confirmed to be increasing also in 2022 with 19,737 incoming patients (+35% compared to 2021) - compared to mobility passive (outgoing patients, 118 in 2022);

- during 2023, a further 33 Diagnostic Therapeutic Assistance Pathways (PDTA) were approved by the Regions/PPAA (there were 12 in 2022), bringing the overall number to over 320 PDTA defined at the end of 2023;

**- the active participation of people with rare diseases and their association representatives**

- **the number of Italian associations of people with rare diseases is 718 (1.2 per 100,000 inhabitants);**

- **16 Regions/PPAAs declare that they foresee for the presence of representatives of associations of people with rare diseases in regional participation bodies on rare diseases;**

- 3 representatives of people with rare diseases are members of the "Coordination Center for newborn screening" provided for by art. 3 of Law no. 167 of 19 August 2016 "Provisions regarding mandatory neonatal diagnostic tests for the prevention and treatment of hereditary metabolic diseases";

- **a representative of people with rare diseases is a member of the national coordination center of territorial ethics committees provided for by Law 11 January 2018, n. 3 "Delegation to the Government regarding clinical trials of medicines as well as provisions for the reorganization of the health professions and for the health management of the Ministry of Health";**

- **a representative of people with rare diseases was identified among the members of the SNE Working Group;**

- **two representatives of people with rare diseases were identified among the members of the National Rare Diseases Committee;**

- **UNIAMO has also been included, since July 2023, among the permanent guests of the National Observatory on the condition of people with disabilities. Lastly, in autumn 2023, a representative of UNIAMO was called to be part of the "Technical table for the analysis and definition of useful elements for a state law on family caregivers" which was established on 17 January 2024;**

Also on the positive side

is the fact that, at the end of 2023, there are 17 Regions/PPAAs that have included the topic of rare diseases within the general health planning tools (in force or in the process of being approved in 2023) or that have defined a Regional Plan for Rare Diseases.

Another important positive signal for the world of rare diseases comes from the implementation process of the National Recovery and Resilience Plan which not only led to the launch of the reform aimed at the reorganization of the network of Scientific Hospitalization and Treatment Institutes (IRCCS ), but also promoted the strengthening of research activities on rare diseases through the creation of two competitive research calls which led to the funding of n. 126 projects (74 on rare diseases and 52 on rare tumors) with a contribution of 100 million euros.

The other side of the coin is represented by the critical issues that persist, such as the long implementation time of measures relating to people with rare diseases. In this regard it is sufficient to remember the following:

- the panel of pathologies subject to neonatal screening has not yet been updated, effectively rendering Law no. 30 December 2018 still "ineffective". 145 which envisaged the expansion of neonatal screening to include neuromuscular diseases of genetic origin, severe congenital immunodeficiencies and lysosomal storage diseases;

- to date, most of the implementation measures of the specific measures provided for by Law no. 175/2021 - support for research on rare diseases and the development of orphan medicinal products and the solidarity fund to support the care and assistance work of people suffering from rare diseases - has not yet been approved;

- the entry into force of the new rates for specialist outpatient care provided for by the Decree of the Ministry of Health of 23 June 2023 - which has finally implemented the update of the Essential Level of Care LEAs still foreseen by the Prime Ministerial Decree of 2017 - has been deferred to 1 April 2024 and then, lastly, further postponed to 1 January 2025.

**Furthermore, there still remain significant territorial inhomogeneities in access to health, socio-health and social services of which the following are an example:**

- **the heterogeneity in the geographical distribution of Italian hospitals participating in the ERN: 7 Regions/PPAA do not have any reference center participating in the ERN and 2/3 of the hospitals participating in at least one ERN are located in the northern regions. This is a not irrelevant aspect also in light of the reorganization document of the National Rare Diseases Network and the potential role, within it, of the so-called. "centres of excellence" (the reference centers that participate in the ERNs);**

- the difficulty in accessing care as demonstrated by the data on healthcare mobility, especially for minors with rare diseases exempt from the RRRDs

- **the differences found in the territorial distribution of healthcare facilities authorized to administer ATMPs (0.7 centers per 1 million inhabitants in the Southern Regions vs. 1.4 in the North);**

- the failure to define the Diagnostic-Therapeutic Care Paths for people with rare diseases in some territories and the diversity of the models adopted for the definition;

- **the still partial coverage of the entire population of people with rare diseases exempt from some of the Regional Rare Disease Registries.**

Added to these aspects is another element of concern linked to the economic stability of the system with particular reference to the economic sustainability of ATMPs which seriously puts at risk, for people with rare and ultra-rare pathologies, access to treatments that have given evidence of enormous clinical benefit.

The approval of the National Plan for Rare Diseases 2023 - 2026 on 24 May 2023 represents, on the one hand, an important milestone (also due to the attention dedicated much more extensively than in the previous plan to the topic of pharmacological and non), long awaited by the PLWRD community, but at the same time represents a new starting point for other, important, objectives - 77 - to be achieved through the implementation of the planned actions (n=115).

To date, all the Regions/PPAA, with only one exception, have taken steps to implement the "National Rare Diseases Plan 2023 - 2026" and the document for the "Reorganization of the national network of rare diseases" with their own formal act.

However, only 16 Regions have already identified a regional coordination centre, reference centers and centers of excellence for rare diseases, generally by the deadline of 31 January 2024, in accordance with the contents of the reorganization document. of the national rare disease network.

Finally, to date, only 6 (out of 16, as the Regions with Special Statute and the Autonomous Provinces are excluded from the allocation with the sole exception of Sicily) are the Regions that have already taken steps to formally commit the resources allocated for the year 2023 for the implementation of the "National rare disease plan 2023-2026" and the document "Reorganization of the national rare disease network". To date, therefore, just over 1/4 of the resources - 25 million euros - made available overall for the year 2023 have already been formally committed to support the implementation of the NPRD 2023-2026; not only from the examination of the first relevant measures can we already highlight some signs of critical issues linked to the limits of the fragmentation observed in the distribution of resources and the dispersion of resources across multiple objectives.

One year after its approval, the NPRD 2023-2026 appears, in fact, to still be at the starting line but the actions undertaken to implement the NPRD and identify the centers by the Regions/PPAA are, in fact, prodromal to its full implementation: now everyone's commitment is needed to put the numerous and detailed provisions contained in the Plan into practice.

***Elisabetta***
*Kleefstra syndrome*

MONITORARE

ÜNIAMO
Federazione Italiana Malattie Rare

Via Nomentana, 133
00161 Roma
www.uniamo.org
segreteria@uniamo.org

**Dona il 5x1000**
C.F. 92067090495
IT53M0306909606100000010339