Orphanet Report Series
Rare Diseases collection

JANUARY 2021

List of rare diseases and synonyms in alphabetical order

Methodology

www.orpha.net www.orphadata.org

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Methodology

Orphanet provides a comprehensive list of all rare diseases registered in the Orphanet database, published annually.

In Orphanet, rare diseases are defined using the following approach:

- Every entity is defined by its clinical homogeneity, regardless of its aetiology or the number of causal genes identified;
- The rarity is defined according to the European legislation defining a prevalence threshold of less than 5 affected persons per 10,000 in the European population (*Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products*, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32000R0141&from=EN).

In order to be registered in Orphanet, a disease must be described in at least two independent individuals in international scientific literature (peer-reviewed articles), confirming that it is not an incidental association of clinical signs.

Each disease is registered with one preferred term and as many synonyms as necessary. A unique numerical identifier, the ORPHAcode, is randomly attributed by the database to each disease. This code is never re-used for a different entity, so it is stable in time.

The Orphanet nomenclature is organised in a multi-hierarchical and polyparental classification system around the major medical specialties and based on clinical criteria according to diagnostic and therapeutic relevance.

A level of precision, named **classification level,** is attributed to each entity registered in the nomenclature: **Group of disorders**, **Disorder**, or **Subtype of disorder**. These three levels organise the relational structure of the Orphanet classification.

Some ORPHAcodes created in the past may be absent from the current list of rare diseases. This is due to the removal of some diseases from the Orphanet nomenclature in 3 possible situations:

- **Obsolescence**: the entity has no reason to exist in Orphanet, due to one of the following reasons: exact duplicate of another active disease; unclear entity that cannot be precisely characterised; disease with only one published case; or category no longer in use.
- **Deprecation**: the disease was initially described as an independent diagnosis, but is now considered as part of another existing disease as a result of the evolution of knowledge. In this case, information related to the deprecated disease is reassigned and users are redirected towards the target active disease.
- **Non rare:** the disease does not meet the European definition of a rare disease in light of current epidemiological knowledge.

Data collection

As new scientific knowledge arises, the Orphanet nomenclature of rare diseases is updated via the regular addition of new diseases or the modification of existing diseases. The nomenclature production and update process rely on two non-exclusive sources: documented sources (peer-reviewed literature) and expert advice.

The scientific knowledge is monitored through:

- A bi-monthly analysis of a defined set of international peer-reviewed scientific journals covering the diversity of medical specialities represented in Orphanet;
- A monthly Medline search algorithm: (nosology[Title] OR classification[Title] OR nomenclature[Title] OR terminology[Title]) AND (rare disease* OR syndrome* OR disorder*);
- Specific Medline queries according to requests from experts, users of the database or needs arising from services newly registered in

Orphanet (e.g. diagnostic test, expert centre, patient organisation).

- Decisions related to the update of the nomenclature of rare diseases are assessed monthly by a medical and scientific committee within Orphanet and further validated with consulted experts.

The Orphanet rare disease nomenclature is produced in English and is translated into the languages of translation of the Orphanet database (French, German, Italian, Spanish, Portuguese, Polish, Czech and Dutch). A medical validation of the translations is carried out.

For more information on the production and update process of the Orphanet nomenclature and classification, please consult our related procedure.

Data presentation

Preferred names and synonyms of all diseases present in the Orphanet nomenclature (active diseases) are listed in alphabetical order with their respective ORPHAcodes in a spreadsheet available at the following link (right click to access file): **http://www.orpha.net/orphacom/cahiers/docs/GB/List_of_rare_diseases_in_alphabetical_order.xlsx**

These include all three levels of classification present in Orphanet (*disorder*, *subtype of disorder* and *group of disorders*). An asterisk (*) is added to indicate active entities/ORPHAcodes that are specifically present at the *disorder* and *subtype of disorder* levels of classification, **since these are the levels that must be used for the coding of confirmed diagnoses in health records**.

Additionally, the complete list of deprecated diseases, which are no longer part of the Orphanet nomenclature, is provided by alphabetical order in the second tab of the spreadsheet, to indicate the target active disease (and corresponding ORPHAcode) that must be used instead of each deprecated disease.

Obsolete entries are not listed in this file. In the case of duplicates, the nomenclature of the obsolete entry is usually reassigned to the active rare disease listed in the nomenclature file.

The Orphanet nomenclature is available in other formats:

- computable XML datasets derived from the Orphanet database, enabling massive data analysis. These include the Orphanet nomenclature files for coding (Nomenclature pack), specifically designed for the implementation of ORPHAcodes in health information systems.
- the Orphanet Rare Disease Ontology (ORDO), a structured and machine-readable vocabulary useful for the computational analysis of rare diseases.

These resources can be accessed and downloaded on the Orphadata platform.

- Nomenclature information (including definitions) is also available by rare disease on the Orphanet website.

For any questions or comments, please contact us: contact.orphanet@inserm.fr

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