orphanet

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# Procedural document:
# Orphanet ICD-10 Coding Rules for Rare Diseases

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# I. Introduction

## 1. Purpose/objectives

Orphanet has developed and maintains the Orphanet nomenclature of rare diseases, a unique and multilingual standardised system aimed at providing a specific terminology dedicated to rare diseases. Each clinical entity is assigned a unique and time-stable ORPHAcode, around which the rest of the data present in the Orphanet database is structured. This clinical coding system provides a common language across healthcare and research systems for effective monitoring and reporting on rare diseases, thus improving their visibility.

The Orphanet nomenclature is aligned with other international terminologies and reference databases (including ICD-10, ICD-11, SNOMED-CT, OMIM, UMLS, MeSH, MedDRA, and GARD) in order to enable interoperability between different information systems.

As healthcare systems worldwide predominantly use ICD-10 for coding of diseases, and the parallel implementation of the Orphanet nomenclature in European, and global, healthcare systems is an ongoing process, enabling the interoperability between these two terminologies will standardise the coding of rare diseases in different healthcare systems, facilitate the identification of rare disease patients and allow for better epidemiological surveillance of rare diseases thanks to improved data retrieval and analysis.

The present document aims to define how rare diseases of the Orphanet nomenclature are aligned to, or attributed, a code in the World Heath Organization's *International Classification of Diseases*, 10th edition (ICD-10).

## 2. Disclaimer


- This publication is part of the project OrphaNetWork Direct Grant (831390) which has received funding from the European Union's Health Program (2014-2020).

- The content of this publication represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.
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## 3. Range of application

The ICD-10 coding of Orphanet diseases is managed by a dedicated information scientist at the Orphanet Coordinating team at INSERM-US14, under responsibility of the Scientific Director.

## 4. References

- ***Orphanet nomenclature and classification of rare diseases****:* describes the production, validation and update process of the Orphanet nomenclature, and outlines the maintenance and revision of the classification.
- ***Linearisation rules for Orphanet classifications****:* describes the rules of attribution of a preferential classification to each cinical entity of the Orphanet nomenclature. In contrast with the Orphanet classification of rare diseases, which follows a polyhierarchy principle, linearisation rules correspond to a monohierarchical view, in which a clinical entity belongs to one medical specialty only.
- ***International statistical classification of diseases and related health problems -10th revision***: searchable on the WHO online browser (link for the 2019 version in English).
- **List of Official ICD-10 Updates*:*** PDF files with the ICD-10 updates endorsed by the WHO over the years.
- ***ICD-O International Classification of Diseases for Oncology****:* A multi-axial classification of the site, morphology, behaviour, and grading of neoplasms, used by ICD-10.
- **ICD-10 instruction manual*:*** Volume 2 of ICD-10 that contains guidelines for recording and coding and describes practical aspects of the classification's use.
- ***Full ICD-10 training***: provides general information on ICD-10 and presents each chapter of the Tabular list.

## 5. Availability of data

Information on the Orphanet and ICD-10 alignement is available on the Orphanet website and in Orphadata :

| Platform | Section/access link | Purpose | Update frequency |
|---|---|---|---|
| Orphanet website | Rare diseases | Information by rare disease: nomenclature (including definitions), classification, **cross-referencing,** textual information and associated activities. | Daily |
| Orphadata | Rare diseases and cross-referencing | Computable file containing all diseases and their cross-referencing with external terminologies and databases. The alignments define if the concepts are perfectly equivalent (exact mapping) or not, thus giving precise information as to the comparability of terminologies. | Monthly |
| | Orphanet nomenclature files for coding (Nomenclature pack) | Computable files providing data for the implementation of ORPHAcodes in Health Information Systems. Includes alignement between ORPHA and ICD-10 codes. | Yearly |
| | Orphanet Rare Disease Ontology | Integrated and reusable OWL data files provided for computational analysis and integration of the Orphanet nomenclature into health and research information systems. | Twice/year |

**Table 1.** Availability of Orphanet alignements with other terminologies

## 6. Definitions

**ICD-10 terms and coding conventions:**

***ICD-10*** stands for International Statistical Classification of Diseases and Related Health Problems, 10th revision. The purpose of the ICD is to permit systematic recording, analysis, interpretation and comparison of mortality and morbidity data collected in different countries or areas and at different times. It has become the international standard diagnostic classification for all general epidemiological and many health-management purposes [1].

ICD-10 consists of 3 "Volumes":

1. The Tabular List: online version of ICD-10 that contains an alphanumeric listing of diseases in 22 chapters in which over 11400 3-digit codes are attributed to each entry, with a preceding letter that signifies to which chapter the disease belongs.
2. The Instruction Manual: contains an introduction to the classification, explains conventions of ICD, and gives instructions on coding.
3. The Alphabetical Index: book or CD format, a full alphabetical list of the diseases and conditions designed to enable to identify codes for further verification in the Tabular List.

[1] From ICD-10 Instruction manual https://icd.who.int/browse10/Content/statichtml/ICD10Volume2_en_2019.pdf

The ICD-10 defines three types of terms associated with ICD-10 codes in order to represent their range of application: *main terms, inclusion terms* and *index terms*.

A ***main term (=head of rubric, =diagnostic term)*** is the primary identification of an ICD-10 code. It is displayed in bold letters beside the code in the ICD-10 tabulated list. This is usually associated with ***specific code*** in Orphanet (see below).

An ***inclusion term*** is an instructional term associated with an ICD-10 code to define its range and use. This term does not have its own code. It is displayed in the ICD-10 tabulated list under the code and main term. It can be a synonym of the main name, different or borderline conditions destined to distinguish the boundary between one subcategory and another, or a specific disease subsumed under a code aiming to represent a group of diseases as a whole.

An ***index term*** has the same purpose than an inclusion term but is found only in the ICD-10 Alphabetic Index. It is not displayed in the ICD-10 tabulated list.

***Dagger and asterisk convention***: ICD-10 uses the symbols known as the dagger (†) and the asterisk (*) next to certain codes, or so-called dual coding system that provides information about an underlying generalised disease and its manifestation in a particular organ or site. The primary code identifies the underlying disease and is marked with a dagger (†), the primary code that must always be used for single condition coding. An optional code for the manifestation is marked with an asterisk (*), this code should never be used alone.

***Abbreviations NOS and NEC:*** NOS stands for ***Not Otherwise Specified*** ('unspecified' or 'unqualified'), indicates where a disease/injury belongs if there is no further information that allows a more specific code for a disease to be used. NEC stands for ***Not Elsewhere Classified***; it alerts a user to use the code only if there is no more specific code found elsewhere in the Index or in other chapters of the ICD (always check the inclusion and exclusion notes carefully).

## Orphanet terms and classification levels:

The **Orphanet nomenclature** is a multilingual, standardised, controlled medical terminology specific to rare diseases, that includes all clinical entities registered in the Orphanet database. Each clinical entity (Disorder, Group of disorders, or Subtype of disorder) is associated with a unique numerical identifier named ORPHAcode, as well as a preferred term, synonyms, and a definition.

An **ORPHAcode** is the unique and time-stable numerical identifier attributed randomly by the Orphanet database to each clinical entity upon its creation.

Three hierarchical levels determine the level of precision of each diagnosis included in the nomenclature:

- ***Group of disorders***: A collection of clinical entities sharing a set of common features
- ***Disorder:*** A clinical entity characterised by a set of homogeneous phenotypic abnormalities and evolution allowing a definitive clinical diagnosis [2]

[2] The Disorder level is designated as the main typological level for data sharing and statistical reporting across the

- ***Subtype of a disorder***: Subdivision of a disorder according to a positive criterion

**Orphanet alignement concepts:**

Orphanet uses the following annotation system to define the nature of the correspondance between an ORPHAcode and the associated ICD-10 code(s):

***Proximity relationships :***

- ***Exact***: The Orphanet entity and the ICD-10 code have the same range of application, they describe the same pathological entity
- ***BTNT*** (broader term to narrower term): The Orphanet entity has a broader range than the ICD-10 code used to represent it
- ***NTBT*** (narrower term to broader term): The Orphanet entity has a narrower range than the ICD-10 code used to represent it
- ***ND*** (not yet decided or unable to decide) is reserved for complex cases when the alignment cannot be qualified by any of the preceding labels

***Specificity relationships :***

- ***Specific code:*** Indicates that the Orphanet entity is matched by an ICD main term that has its own code in ICD-10
- ***Inclusion term:*** Indicates that the Orphanet entity is matched by an ICD term that does not have its own code, but is rather displayed in the ICD-10 tabulated list under the code and main term.
- ***Index term:*** Indicates that the Orphanet entity is matched by an ICD term that does not have its own code and that is only displayed in the Alphabetical Index.
- ***Attributed code:*** Indicates that the Orphanet entity has no matching term at all in ICD-10 and the ICD-10 code of its closest corresponding entity according to Orphanet's rules is used.

***Validation status:*** Indication that the curation is carried out according to Orphanet procedures and is scientifically valid.

- ***Not yet validated*** means that the coding is provisional and has been checked by only one medical expert within Orphanet.
- ***Validated*** means that the coding has been double-checked and is regarded as sure**.**

## 7. Filing and updates

The present ICD-10 coding rules document is updated annually by the data manager in charge of the attribution of the ICD-10 codes in the Orphanet database. The most up-to-date version is available on the Orphanet website:
http://www.orpha.net/orphacom/cahiers/docs/GB/Orphanet_ICD10_coding_rules.pdf

European Union. It is used to establish the total number of rare diseases that exist.

# II. Orphanet/ICD-10 coding rules

These ICD-10 coding rules for Orphanet rare diseases apply to all Orphanet clinical entities (groups of disorders, disorders and subtypes of disorders), and specifically aims at covering the totality of entities at the ***Disorder*** classification level, which is recommended to be used as the definitive clinical diagnosis and for statistical reporting. Subtypes of disorders are aligned with an ICD-10 code when an exact match exists, otherwise they inherit the ICD-10 code attributed to the disorder. Groups of disorders are only aligned with ICD-10 code when an exact match exists.

Codes can be considered as heritable by default throughout Orphanet classifications. This means that if a disease is mentioned in ICD-10, its coding will be inherited by all its subtypes, unless the ICD-10 explicitly tells otherwise.

E.g. *ORPHA685 Hereditary spastic paraplegia* is coded *G11.4 Hereditary spastic paraplegia*. The code G11.4 is also used for the subentities:

- *ORPHA102012 Pure hereditary spastic paraplegia*
    - *ORPHA100980 Autosomal dominant pure spastic paraplegia*
    - *ORPHA100982 Autosomal recessive pure spastic paraplegia*
    - *ORPHA320332 X-linked pure spastic paraplegia*
- *ORPHA102013 Complex hereditary spastic paraplegia*
    - *ORPHA98888 X-linked complex spastic paraplegia*
    - *ORPHA100979 Autosomal dominant complex spastic paraplegia*
    - *ORPHA100981 Autosomal recessive complex spastic paraplegia*
    - *ORPHA320360 Maternally-inherited spastic paraplegia*
- *ORPHA320335 Pure or complex hereditary spastic paraplegia*
    - *ORPHA320342 Pure or complex autosomal dominant spastic paraplegia*
    - *ORPHA320346 Pure or complex autosomal recessive spastic paraplegia*
    - *ORPHA320350 Pure or complex X-linked spastic paraplegia*

and all subtypes of hereditary spastic paraplegia identified by numbers, further down in the hierarchy.

By extension, if a group of diseases can be coded with a precise ICD-10 code (e.g. *ORPHA98473 Muscular dystrophy* exactly matches *G71.0 Muscular dystrophy*), all subordinate entities can be presumed to be coded the same way (with NTBT relationships). This rule must however be mitigated by the fact that many rare disease entities are actually classified under several parents. It is then necessary to choose which parent in the Orphanet classification has priority: this is done according to the Orphanet linearisation.

## 1. ICD-10 reference version

The alignment of Orphanet rare diseases with ICD-10 codes is based on the 2019 online version of the ICD-10.

## 2. Default rules:

### a. Priority to any ICD-10 mention

Any explicit mention from the ICD-10 has priority over internal decisions, even if the ICD-10 dispositions are deemed to be inaccurate.

E.g. *Progeria* is an inclusion term of *E34.8 Other specified endocrine disorders*. Therefore, *ORPHA:740 Hutchinson-Gilford progeria syndrome* must be coded E34.8, even if it is not correct to describe it as an endocrine disease.

### b. Use a single four-character ICD-10 code

The general rule is to represent diseases by a single four-character ICD-10 code, which correspond to the WHO-recommended level that should be used as the definitive clinical diagnosis and for statistical reporting, whether the published ICD-10 mentions the disease or not.

In particular, when the ICD-10 does not mention the disease and therefore needs to be interpreted, the most significant involvement is selected, meaning the one:

- corresponding to the most severely affected body system;
- most determining for the prognosis;
- whose specialist is most likely to be relied on for disease management.

The selection of the most significant involvement should generally be consistent with the *Orphanet linearisation for rare diseases* procedure (see References).

There are nevertheless a number of exceptions to the single four-character ICD-10 code rule that are described below.

#### i. Exception: Entities representable by a three-character code

The use of a three-character code is possible when there is no further subdivision in ICD-10. E.g. *ORPHA:924 Acanthosis nigricans* represented by *L83 Acanthosis nigricans*, because there are no four-character codes for this disease.

#### ii. Exception: Entities representable by a set of four-character ICD-10 codes

It may be that the ICD-10 provides several contextual codes when Orphanet only has a general entity. This is not infrequent especially with infectious diseases, which have for historical and practical reasons very detailed ICD-10 codes, whereas they are less detailed in Orphanet. Coding such diseases properly requires additional information compared with the range of Orphanet entries. In such cases, it is useful to provide the whole set of codes that represent the disease more accurately.

**Set of ICD-10 codes that belong to the same classification branch**

Some entities have a good match with a three-character code, with specific manifestations further represented in ICD-10 by subdivision into four-character codes.

For instance, ORPHA:49 Cystic fibrosis matches *E84 Cystic fibrosis*, which is further subdivided

as follows:
*E84 Cystic fibrosis (Incl.: mucoviscidosis)*

- E84.0 Cystic fibrosis with pulmonary manifestations
- E84.1 Cystic fibrosis with intestinal manifestations
    - Distal intestinal obstruction syndrome
    - Meconium ileus in cystic fibrosis+ (P75*)
    - Excl.: meconium obstruction in cases where cystic fibrosis is known not to be present (P76.0)
- E84.8 Cystic fibrosis with other manifestations
    - Cystic fibrosis with combined manifestations
- E84.9 Cystic fibrosis, unspecified

In such instances, the entity is to be coded in the Orphanet database by the whole set of possible four-character codes, rather than by the single three-character code. The rationale for this choice is to direct coders using Orphanet as a reference towards one of the four-character codes that they must actually use.

E.g. *ORPHA:31202 Melioidosis* is represented by the following ICD-10 codes:

- *A24.1 Acute and fulminating melioidosis*
- *A24.2 Subacute and chronic melioidosis*
- *A24.3 Other melioidosis*
- *A24.4 Melioidosis, unspecified*

Coding with *A24.4 Melioidosis, unspecified* only would exclude all cases that in practice are specified. By contrast, associating the *A24.1, A24.2, A24.3* and *A24.4* codes will allow users to retrieve effectively cases of melioidosis as a whole from medical records.

## Set of ICD-10 codes that belong to different classification branches

Orphanet entities for tumours present systematic challenges for ICD-10 coding. Definitions used by Orphanet are primarily based on morphology, while ICD-10 defines criterias based mainly on tumoural behaviour (malignant, benign, uncertain or unknown), then on topography, and finally uses the additional *ICD-O* (see References) to represent the morphology of tumours.

If the tumour is usually benign, with only rare cases of malignant transformation, the code for the benign tumour can be used alone. If the tumour has a high potential for malignant transformation, the code for the malignant tumour can be used alone.

E.g. *ORPHA:99867 Thymoma* is represented by the following ICD-10 codes:

- *D15.0 Benign neoplasm of other and unspecified intrathoracic organs*: *Thymus*
- *C37 Malignant neoplasm of thymus*

In this instance, using two codes allows to represent malignant and benign possible behaviours.

E.g. *ORPHA:2965 Prolactinoma* is represented by the following ICD-10 codes:

- *D35.2 Benign neoplasm: Pituitary gland*
- *E22.1 Hyperprolactinaemia*.

This is an example of secreting tumours that should be coded both as a tumour and as the endocrine disorder caused by their secretion.

**Double coding by the dagger-and-asterisk system**

The system of a main code with a dagger associated to a secondary code with an asterisk has been introduced in ICD-9 and maintained in ICD-10 to represent several cases when two approaches are useful. The ICD-10 user manual lists the following uses of this system:

- local manifestation of a generalised disease, especially infections;
- functional activity (and consequences) of endocrine tumours;
- the organic cause of a mental or behavioural disorder;
- a toxic or pharmacologic cause of disease;
- a traumatic cause of disease.

Such double codes are allowed only when the possibility is explicitly afforded by the ICD-10. A secondary asterisk code can be used only in association with a primary dagger code.
The dagger-and-asterisk system is used when relevant to code Orphanet entities.

E.g. *ORPHA:137586 Herpes simplex virus keratitis* is coded by the association of:

- *B00.5+ Herpesviral ocular disease*
- *H19.1* Herpesviral keratitis and keratoconjunctivitis*

### c. Default rule: do not use « unspecified » codes

Orphanet entities always refer to specified clinical entities, therefore the xy.a or xy.b « […], unspecified » codes should never be used. The xy.c « other specified […] » codes should be used instead when no explicit representation of the disease is available in the ICD-10.

E.g. *ORPHA:1986 Gollop-Wolfgang complex*, a rare congenital limb malformation, is not mentioned in the ICD-10, and was therefore attributed the code *Q74.8 Other specified congenital malformations of limb(s)*.

**Exception: Tumours**

Neoplasms are classified according to their behavior, then to their anatomical location. Therefore the "unspecified" term generally refers here to the tumour site, not to the disease. Depending on the disease definition, a rare neoplasm could therefore be coded using as many localisation-specific codes as deemed appropriate, with or without an "unspecified" one.

E.g. *ORPHA:213610 Carcinosarcoma of the corpus uteri* is a rare, malignant, mixed epithelial and mesenchymal tumor of the uterine body composed of high-grade carcinomatous and sarcomatous elements, and is therefore coded with *Malignant neoplasm of corpus uteri > C54.9 Corpus uteri, unspecified*.

### d. Default rule for entities not mentioned in ICD-10: priority to the clinical presentation

Many rare diseases are not mentioned at all in ICD-10, even as an index term. The coder must therefore interpret the ICD-10 to find the most appropriate representation.

When several ICD-10 coding rules apply to the same Orphanet entity, the code representing the predominant clinical manifestation takes priority over the other relevant codes. As a guide, two criteria can most often be followed:

- the position of the entity within the Orphanet classifications of rare diseases;
- the linearisation selected for the entity.

## 3. Decisions for specific groups of diseases

| ORPHA entities | Subtypes or predominant features (when applicable) | ICD-10 code to use | Examples |
|---|---|---|---|
| **Tumours:** coding depends first on behavior, then on topography | If **usually benign** (only rare cases of malignant transformation) | Code for the **benign tumour** alone | *ORPHA:180267 Giant adenofibroma of the breast* aligns with *D24 Benign neoplasm of breast* |
| | If high potential for **malignant transformation** | Code for the **malignant tumour** alone | *ORPHA: 168811 Malignant peritoneal mesothelioma* is coded *C45.1 Mesothelioma of peritoneum* |
| | If **multiple possible behaviours** (malignant, benign, uncertain or unknown) | **2 or 3 codes** that fully represent the disease | *ORPHA:99867 Thymoma* aligns with both:<br>• *D15.0 Benign neoplasm* (*Thymoma (benign)* as index term)<br>• *C37 Malignant neoplasm of thymus (Thymoma – malignant* as Index term) |
| **Secreting tumours** | | Code of the **tumour +** Code of the **endocrine disorder** caused by their secretion, with the mapping typed ND | *ORPHA:2965 Prolactinoma* aligns with both:<br>• *D35.2 Benign neoplasm: Pituitary gland*<br>• *E22.1 Hyperprolactinaemia* |
| **Cancer-predisposing syndromes:** | No explicit representation is available in the ICD-10. | Code of the **relevant cancer**, with the mapping typed ND | *ORPHA:893 WAGR syndrome* aligns with *C64 Malignant neoplasm of kidney, except renal pelvis.*<br>WAGR syndrome is associated with an increased risk of developing Wilms tumor, that is an index term of C34.<br>*ORPHA:524 Li-Fraumeni syndrome* aligns with *C97 Malignant neoplasms of independent (primary) multiple sites*<br>*ORPHA:357027 Hereditary retinoblastoma* aligns with *C69.2 Malignant neoplasm: Retina* |

| ORPHA entities | Subtypes or predominant features (when applicable) | ICD-10 code to use | Examples |
|---|---|---|---|
| **Susceptibility to infections**: to be coded as immunodeficiencies not as infections | | *D84.8 Other specified immunodeficiencies* | *ORPHA:319589 Autosomal dominant mendelian susceptibility to mycobacterial diseases due to partial IFNgammaR2 deficiency* |
| **Rare Diabetes** | | *E13 Other specified diabetes mellitus* | *ORPHA:1667 Wolcott-Rallison syndrome* |
| **Glycogen storage disease** | Irrespective of their phenotype | *E74.0 Glycogen storage disease* | *ORPHA:2088 Fanconi-Bickel syndrome* |
| **Leukodystrophies** | Sphingolipidosis | *E75.2 Other sphingolipidosis,* along with an inclusion term *Metachromatic leukodystrophy* as closest entity | *ORPHA:99027 Adult-onset autosomal dominant leukodystrophy* |
| | Demyelinating leukodystrophy | *G37.8 Other specified demyelinating diseases of central nervous system* | *ORPHA:99027 Adult-onset autosomal dominant leukodystrophy* |
| | Otherwise | *G93.8 Other specified disorders of brain* | *ORPHA:527497 NKX6-2-related autosomal recessive hypomyelinating leukodystrophy* |
| **Congenital disorders of glycosylation** | | *E77.8 Other disorders of glycoprotein metabolism* | *ORPHA:79327 ALG1-CDG* |
| **Periodic fevers** | | *E85.0 Non-neuropathic heredofamilial amyloidosis,* along with an inclusion term *Familial Mediterranean fever* as closest entity | *ORPHA:342 Familial Mediterranean fever*<br>*ORPHA:32960 Tumor necrosis factor receptor 1 associated periodic syndrome* |
| **Intellectual disability syndrome**: no specific ICD code exists for intellectual disability | Syndromic intellectual disability | Coded according to the other malformation present | *ORPHA:352587 Focal epilepsy-intellectual disability-cerebro-cerebellar malformation* aligns with *Q04.8 Other specified congenital malformations of brain*<br>*ORPHA:284282 Autosomal recessive cerebellar ataxia-epilepsy-intellectual* |

| ORPHA entities | Subtypes or predominant features (when applicable) | ICD-10 code to use | Examples |
|---|---|---|---|
| | | | *disability syndrome due to WWOX deficiency* aligns with *G11.1 Early-onset cerebellar ataxia* |
| | isolated/non-syndromic intellectual disability | *F70-78 Mental retardation* (depending on the severity) | ORPHA:101685 Rare non-syndromic intellectual disability is coded *F70 mild mental retardation + F71 moderate mental retardation + F72 severe mental retardation + F73 profound mental retardation* |
| **Mitochondrial diseases:** | If mentioned as an inclusion or index term | Code to which the inclusion or index term is ascribed | *ORPHA:506 Leigh syndrome* corresponds to an inclusion term under the code *G31.8 Other specified degenerative diseases of nervous system*, *ORPHA:480 Kearns-Sayre syndrome* corresponds to an inclusion term under *H49.8 Other paralytic strabismus* |
| | All mitochondrial myopathies not explicitly mentioned in ICD-10 | *G71.3 Mitochondrial myopathy, not elsewhere classified (by default)* | *ORPHA:352470 DNA2-related mitochondrial DNA deletion syndrome* |
| | Irrespective of the predominant involvement | *E88.8 Other specified metabolic disorders* | *ORPHA:324535 Combined oxidative phosphorylation defect type 11* *ORPHA:24 Fumaric aciduria* |
| **Spinocerebellar ataxias** | Nonprogressive form | *G11.0 Congenital nonprogressive ataxia* | *ORPHA:314647 Non-progressive cerebellar ataxia with intellectual disability* |
| | Age of onset < 20 | *G11.1 Early-onset cerebellar ataxia* | *ORPHA:96 Ataxia with vitamin E deficiency* |
| | Age of onset > 20 | *G11.2 Late-onset cerebellar ataxia* | *ORPHA:284289 Adult-onset autosomal recessive cerebellar ataxia* |
| **Neurodegenerative or progressive encephalopathy** | | *G31.8 Other specified degenerative diseases of nervous system.* | *ORPHA:726 Alpers-Huttenlocher syndrome* corresponds to an inclusion term under *G31.8* |

| ORPHA entities | Subtypes or predominant features (when applicable) | ICD-10 code to use | Examples |
|---|---|---|---|
| **Early-onset epileptic encephalopathy syndromes** | | Are coded according to the **main type of seizures** | *ORPHA:166299 Benign partial epilepsy of infancy with complex partial seizures* is coded by *G40.2 Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures* |
| | If not applicable | *G40.4 Other generalized epilepsy and epileptic syndrome* | *ORPHA:33069 Dravet syndrome*<br>*ORPHA:1935 Early myoclonic encephalopathy* cooresponds to an inclusion term under *G40.4* |
| **Hereditary sensory and autonomic neuropathies** | | *G60.8 Other hereditary and idiopathic neuropathies* | *ORPHA:88642 Channelopathy-associated congenital insensitivity to pain* |
| **Congenital bile acid synthesis defects** | | *K76.8 Other specified diseases of liver* | *ORPHA:276066 Bile acid CoA ligase deficiency and defective amidation* |
| **Joubert syndrome** | All forms, with or without other involvement | *Q04.3 Other reduction deformities of brain* | *ORPHA:1454 Joubert syndrome with hepatic defect* |
| **Cerebellar malformations** | Not mentioned in the ICD-10 | *Q04.8 Other specified congenital malformations of brain* (however incorrect it is to refer to the cerebellum as "brain") | *ORPHA:65285 Lhermitte-Duclos disease* |
| **Distal arthrogryposes** | | *Q68.8 Other specified congenital musculoskeletal deformities* because "arthrogryposis (congenital)" is an Index term under this code | *ORPHA:115 Congenital contractural arachnodactyly* |
| **Ectodermal dysplasias** | Anhidrotic/hypohidrotic | *Q82.4 Ectodermal dysplasia (anhidrotic)* | *ORPHA:181 X-linked hypohidrotic ectodermal dysplasia* |
| | Normohidrotic/hyperhidrotic | *Q82.8 Other specified congenital malformations of skin* | *ORPHA:247827 Ectodermal dysplasia-cutaneous syndactyly syndrome* |

| ORPHA entities | Subtypes or predominant features (when applicable) | ICD-10 code to use | Examples |
|---|---|---|---|
| **Polymalformation syndromes** | Syndromes where multiple systems are affected without a clear clinical predominance of a single system | *Q87.8 Other specified congenital malformation syndromes, not elsewhere classified* | *ORPHA:210144 Lethal polymalformative syndrome, Boissel type* |
| **Chromosomal microdeletions and microduplications** | Microduplications | *Q92.3 Minor partial trisomy* | *ORPHA:261229 14q11.2 microduplication syndrome* |
| | Microdeletions | *Q93.5 Other deletions of part of a chromosome* | *ORPHA:94064 Deafness-infertility syndrome* |

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

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