EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PCWP/HCPWP COMP Feedback

2022 realisation highlights & 2023 workplan

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Selected Highlights

1. Birth of a new orphan ontology for Inherited Retinal Dystrophies

2. New Orphan Medicinal Products 2022

3. COMP 2023 Workplan

Birth of a new orphan ontology for Inherited Retinal Dystrophies

Problem statement

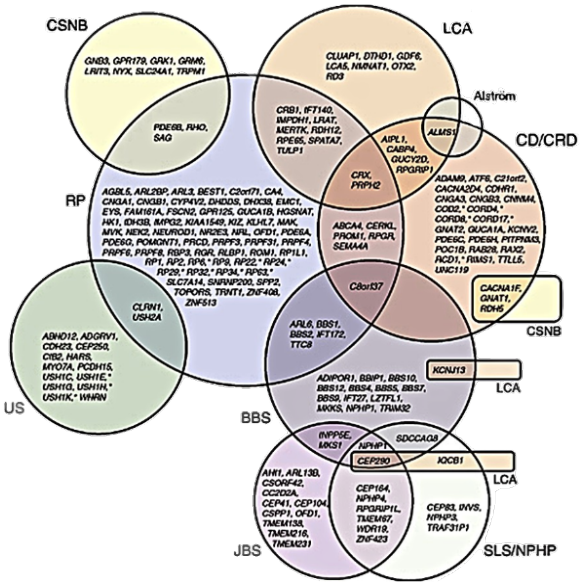
IRD = **spectrum** of heterogeneous inherited gene defects affecting the retinal structures

Classic classification = **phenotypically driven**

Genetic aetiology = **enormously complex**

340+ involved (known) genes

Phenotypical classification = **overlap pandemonium**



Problem statement

Traditional phenotypical orphan classification = **issues on a regulatory level**

Divide between **Orphan** Condition and **Therapeutic** Indication

Canary in coalmine = **Luxturna MA** (2018)

Need to align regulatory considerations of orphan ontology for IRD classification with clinical state of the art

Towards a solution

Initial recognition of need mid 2021

» First proposal of new ontology model

COMP workgroup start early 2022

» Proposal refinement

» **Clinical & Patient Expert Meeting** June 2022

Final proposal adopted by COMP and published January 2023

Towards a solution

- For therapies that are relatively broadly applicable in IRDs, terms (e.g. *Rod-dominant phenotype)* can be selected from table 1 for orphan designated conditions. If a particular broad therapy could target more than one group, multiple orphan designations may be needed.
- For targeted gene therapies, the OD condition can be constructed from the term "inherited retinal dystrophy due to dysfunction in the target-gene.
- Finally, for some IRDs which may not fit the table 1 scheme, an occasional singular orphan designation outside the table 1 structure may still be necessary for non-gene therapy product(s).

Table 1 Grouping for inherited retinal diseases for the purpose of orphan designation

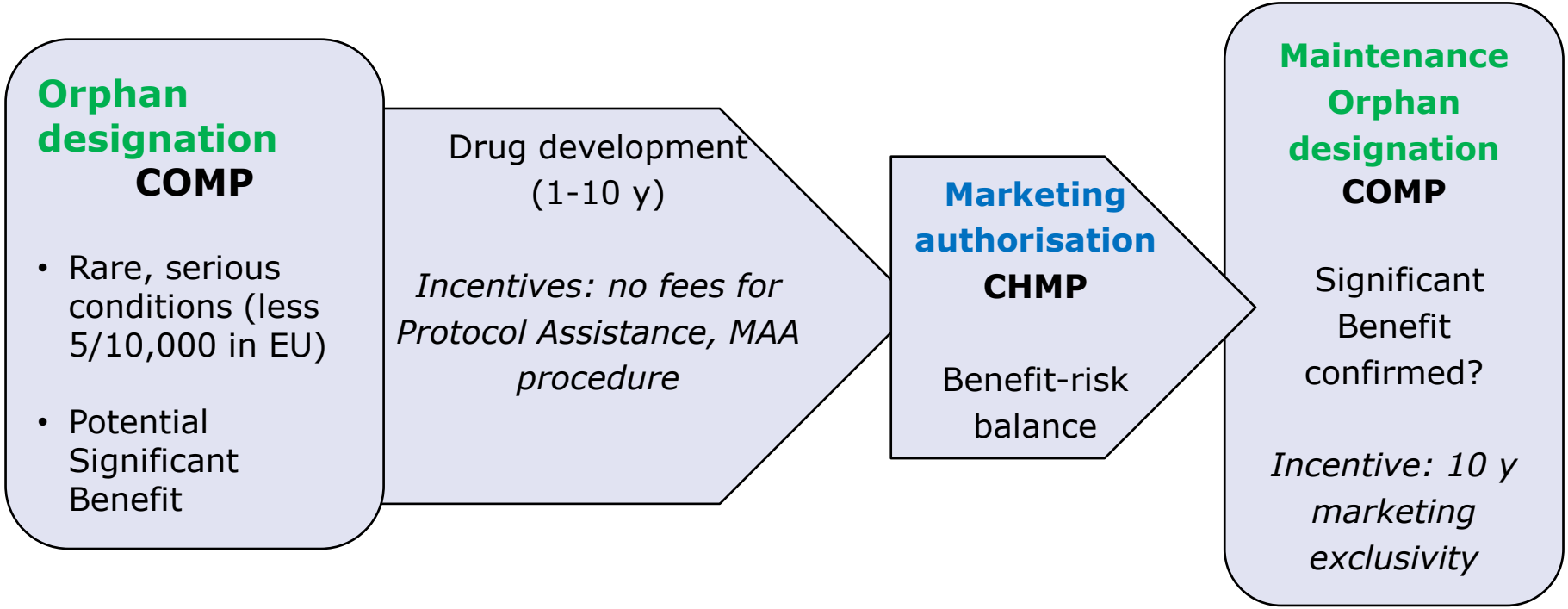
1. Non-syndromic IRD
    - *1.1. Cone-dominant phenotype**
    - *1.2. Rod-dominant phenotype*
    - *1.3. Macular dystrophy*
2. Syndromic IRD
    - *2.1. Cone-dominant phenotype*
    - *2.2. Rod-dominant phenotype*
    - *2.3. Macular dystrophy*
3. Inherited choroidal dystrophies
4. Hereditary vitreoretinopathies

* Phenotypes include inherited pathological dysfunction as well as inherited progressive degenerations

Source

Marketing authorisation orphan medicinal products 2022

Process flow Orphan Designation



New orphan products; approved in 2022

24 in total

First-time indications (no satisfactory alternative treatments available):

- Kimmtrak (tebentafusp): **uveal melanoma**
- Zokinvy (Lonafarnib): **Progeria**
- Filsuvez (birch bark extract): **epidermolysis bullosa**
- Nulibry (Fosdenopterin): **molybdenum cofactor deficiency type A**
- Upstaza: aromatic L-amino acid decarboxylase: **(AADC) deficiency**
- Livmarli (Maralixibat): **Alagille Syndrome**
- Ebvallo (Tabelecleucel): **post-transplant lymphoproliferative disorder** (EBV+)

New products: orphan designation not maintained at MA

- 6 new products lost orphan status at Marketing Authorisation in 2022
- Positive B-R balance; but no Significant Benefit versus other products as required for 10 y Marketing Exclusivity

- Haemato-oncology: Crowded area

  Breyanzi (lisocabtagene maraleucel): lymphoma; Zynlonta (lloncastuximab tesirine): DLBCL ; Pepaxti (melphalan): Multiple Myeloma

- ERT in Pompe Disease: modifications of existing enzyme therapies, failed to show superiority in direct comparison versus old product

  Nexviadyme (avalglucosidase alfa) & Pombiliti (cipaglucosidase alfa) : Pompe's Disease

COMP 2023 Workplan (Draft)

Key Objectives, Vertical

- **Optimise the quality of initial orphan designation applications** and maintenance in order to reduce failed orphan designations & orphan status maintenances.
- Ensure **consistency**, transparency, quality and detail of the **COMP grounds of opinions and orphan maintenance assessment reports**.
- **Explore cases and process options for real world evidence (RWE)** in orphan designation decision making.

Key Objectives, Horizontal

- To further develop **early interaction process between the CHMP and COMP** in view of opinion consistency, exchange of expertise/information.

- Revision of **guideline on small clinical trials** including **indirect comparisons.**

- **Support EC activities on review of the orphan regulation** + ensure that the experience and consolidated proposals of the COMP are captured

Any questions?

Planned Activities, Horizontal

- COMP/CHMP members to liaise in case of rapporteurship or co-rapporteurship
- Evaluation of CHMP-COMP interaction process based on 2020-2022 experience
- Review of indirect comparison methodology for demonstrating significant benefit in preparation of the revision of the GL on trials in small populations
- Provide expertise and recommendation to EC on the new orphan regulation as needed
- Work with the EC on implementing the legislation

Planned Activities, Vertical

- Define requirements for major contribution to patient care at OD and maintenance time
- Implement revised and optimised process for assessment at time of maintenance (6-month pilot)
- Review of public-facing information on EMA website
- Work towards flexibility in the definition of orphan conditions to be more in line with innovative scientific development
- Refine COMP critical decisions repository
- Continue pilot of RWE studies to support COMP decision-making (including HMA/EMA Big Data Steering Group recommendations)
- Review the data on medical plausibility for advanced/innovative therapies