Reviewer 1: Simple opinion about orphan medicines

Access to and affordability of medicines for rare diseases

The problems encountered with ODs are[1]:

- Problem with the positioning of ODs in clinical practice (lack of knowledge about natural course of the disease, lack of methodology to study them…)
- Lack of knowledge and training of health professionals (not aware to diagnose and to treat adequately)
- Deficient diagnosis system, in the major situations lack of genetic or the molecular diagnostics facilities leads to only clinical diagnosis with consequent problems of validity, reproducibility, coding...
- High prices varying significantly between diseases ($ 10,000 per year, whereas in the case of enzyme replacement therapies over $150,000 per year). The mean cost of treatment with ODs in E.C is € 2,000 to 300,000 [2]. Affordability of ODs has become a major issue for payers particularly in emerging countries.
- Problem related to a public health approach is the crisis in the discovery and development of new antibiotics (by this way all drugs become orphan in the future, not because of rareness of the disease, but because other factors hinder sufficient investment in drug discovery and development, assort of "neglected – rare diseases combination").

General discussion

ODs there are by definition, not of interest for the majority of health needs of the population and often little evidence are available at the time or approval by the E.M.L. Committee. The question of whether to include these medicines will virtually always be "symbolic" one, because we are aware that historically EML have been a symbolic function in promoting new concepts in selecting et promoting drugs related to real need.

Some proposed selection criteria for ODs

1. Prevalence of rare disease
2. No alternative on EML
3. Diagnosis of the disease is technically possible in most countries
4. Expertise infrastructure : knowledge and training to diagnose and to treat are available
5. Effectiveness
6. Safety
7. Availability of the product

What kind of propositions?

The solutions to include ODs in EML are two sorts:

1. To rephrase the definition of the complementary list according to the criteria for selection of ODs and to keep the essential medicines committee unchanged.
   The proposed complementary list presents the two categories of medicines:
   a) Essential medicines for the priority diseases for which specialized diagnostic or monitoring facilities, and /or specialist medical care, and/or specialist training are needed.

b) Essential medicines for the rare diseases, those with no alternatives on EML and with the diagnosis technically possible in most countries, the knowledge and the training are available, and the medicines are known to be effective, safe and available.

2. To establish a new special Expert Committee with expert opinion on the effective therapies for rare diseases that provides guidance for rational programs as earlier past of EML in 1977.

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[1]: Mainly from a discussion paper of Pieter Stolk, Marjolein Willemen, Hubert G. Leufkens. Utrecht Institut for Pharmaceutical Sciences, the Netherlands, 2005

[2]: La Revue Prescrire 2006; 277:780 – 787.