EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO contribution to consultation topic n. 3

This contribution was discussed by a subgroup and adopted by the Paediatric Committee in November 2012.

The Paediatric Committee sees a great need to obtain an indication gained after proper assessment of data and providing information to prescribers, offering appropriate paediatric formulations and forms for all the medicines that are currently used off-label in children through extemporaneous preparations of insufficient quality.

The PDCO is in agreement with the European Commission that in terms of output, the PUMA concept has been disappointing.

Funding of studies into off-patent medicinal products has been provided for 15 projects (also aiming at PUMAs) that have been financed through the 7th Framework Programme, but that have not yet resulted in PUMA applications. Around 30 paediatric investigation plans aimed at future PUMA applications have been agreed by the PDCO, but so far only 2 applications for PUMAs have been received by the EMA (with a third to be submitted in January 2013) after 6 years.

The PDCO therefore agrees with the Commission that the incentives of data exclusivity and market protection, and fee reductions have not worked sufficiently for off-patent medicinal products to outweigh the inherent costs and economic risks of pharmaceutical development, in particular that of paediatric forms. This has been confirmed by the marketing authorisation holder of the only PUMA, and from feedback received from academics trying to set up consortia to answer FP7 calls. Pharmaceutical companies do not seem to be willing to invest in PUMAs, where substitution with generic adult pharmaceutical forms is the rule, and where this type of innovation is not (sufficiently) rewarded by payers. In addition, academics may not be willing to invest in research on old medicines because they are for most of them sufficiently convinced that most of the off label use relies on sufficient data.

The national incentives that are currently available do not seem to have been more successful.

The PDCO therefore considers that novel approaches are needed, to reach the broader objective of stimulating the regulatory approval of paediatric indications and pharmaceutical forms for much needed off-patent medicinal products. This may require legislative measures to be efficient. The PDCO discussed the following proposals, which could be included in the review of the legislation after 10 years.

- While the PDCO is aware that market exclusivity (instead of data exclusivity/market protection) has been suggested by some stakeholders, this will not solve many of the issues listed above, and generics may already be authorised when a PUMA is granted.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

- Additional or alternative incentive for an unrelated but commercially more attractive product. For example, a company obtaining a PUMA might get additional protection (patent or other) for another, unrelated product. The protection extension could be variable, and shorter than that for completion of a PIP for a new product.
- Possibility for orphan medicinal products to obtain the two-year extension of the market exclusivity even when not covered by a patent or SPC. In other words, allowing "voluntary PIPs" to be rewarded for off-patent orphan medicinal products.
- Tax incentives at national level. Fixed monetary incentive. This could take the form of reimbursement/funding of part of the pharmaceutical or clinical development costs for products that obtain a PUMA.
- Change in scope of PIPs for PUMAs. Currently, there is a single definition and scope for a PIP. The PIP needs to cover all paediatric subsets regardless of the situation (art. 7, 8 or 30). However, this is problematic for prospective PUMA developments, particularly those aimed at neonates' use only, an area of particularly high unmet medical need. The need to provide data and perform studies in other age groups without the same needs greatly increases burden and costs and creates a disincentive for applicants.
- Legislation to discourage extemporaneous preparations where there are authorised paediatric forms and formulations, reducing the off-label use of other pharmaceutical forms or products not authorised for children. This measure is intended to prevent medication errors (dose), major modifications of pharmacokinetics (difference in bioavailability of crushed tablets for example), and use of excipients that are unsafe for children.
- Legislation to allow NCA/EMA to set up databases, assess and complete on own motion (art 29) the information.