A pan-European Paediatric Formulary

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INTRODUCTION

The European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and the European Pharmacopoeia Commission have launched an initiative to make available a formulary for extemporaneous formulations for paediatric medicines which is compiled of monographs for their preparation based on national or regional information. This activity is intended to help fill the gap until respective medicines, approved for the use in the paediatric population, are available.

The formulary is intended to provide clinicians and pharmacists with appropriate formulations as long as no respective licensed product is on the market; it is neither intended to be mandatory nor to replace or hinder the market entry of respective licensed products. Medicines which have been authorised for the use in the paediatric population by a regulatory authority and which are manufactured at an industrial scale are the ultimate goal.

Fig. 1: meeting of the European Pharmacopoeia Commission

Project set-up

A first group of experts has elaborated, under the auspices of the CD-P-PH, suitable criteria for evaluation of existing formulations for inclusion in the European Paediatric Formulary. A second working group under the auspices of the European Pharmacopoeia Commission will perform the practical selection and elaboration of the formulations. The EDQM provides the scientific secretariat and the publication platform.

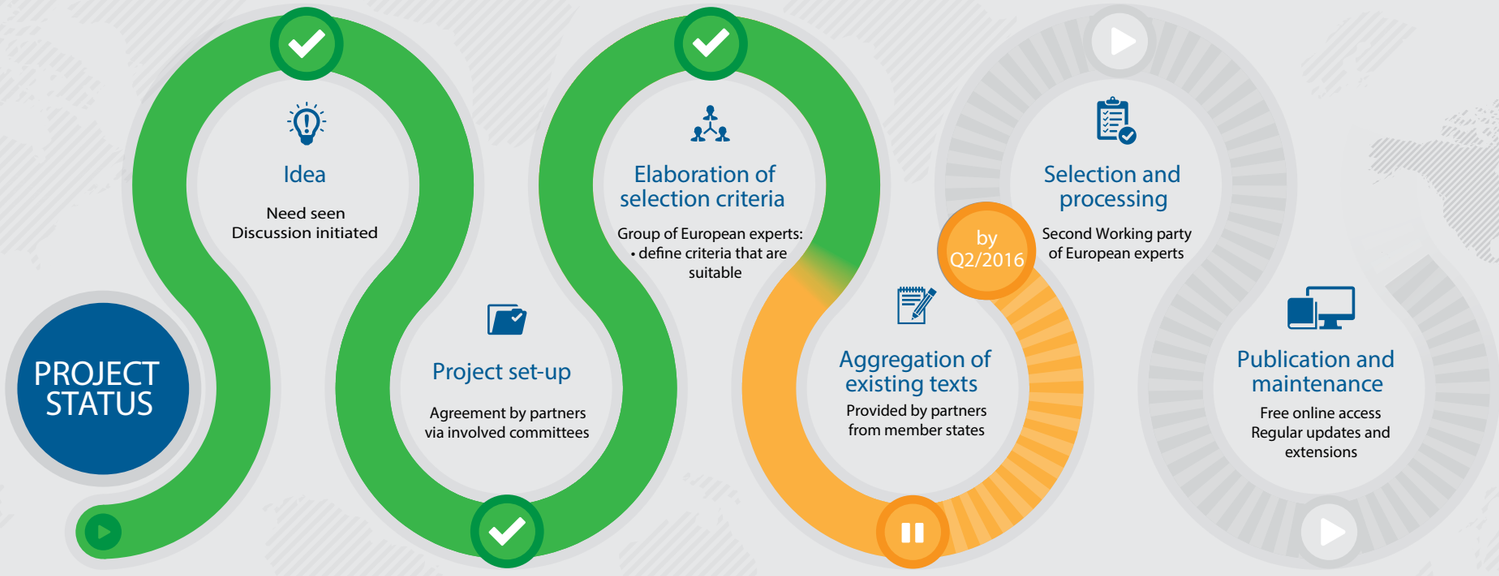

Fig.2: milestones of the PaedForm project

Criteria for selection and evaluation

The first group of experts has elaborated criteria which are to be used for the selection and evaluation of existing formulations to set an adequate quality standard. The decision to include an active substance and formulation in the European Paediatric Formulary requires careful consideration. Not only do quality criteria have to be taken into account for the evaluation, but also clinical criteria which are important.

PaedForm

CLINICAL

THERAPEUTIC RELEVANCE AND CLINICAL JUSTIFICATION

Active Substance

Positive assessment for its use including
- ✓ **No safety signals** from pharmacovigilance systems
- ✓ **Not withdrawn** from market because found to be unsafe or ineffective
  – exceptions if important for particular groups (e.g. codeine, chloral hydrate)
- ✓ Is **of therapeutic benefit** and relevant to current practice
- ✓ Availability of **authorised products for other age groups** whose formulation is not appropriate

Excipients

- ✓ **Not harmful**

Formulation

- ✓ **Age-appropriate dosage form**
- ✓ **Excluded if authorised formulation is available**

QUALITY

Production

- ✓ **Preparation process described**
- ✓ **Reproducible**

Formulation

- ✓ All raw materials **comply with Ph. Eur. or national pharmacopoeial requirements**
- ✓ All **excipients** necessary, **suitable** for their function and compatible
- ✓ Qualitative and quantitative **composition stated**

Tests

- ✓ **Suitable tests for process controls** or **additional analytical tests on final product**

Storage

- ✓ **Evidence on** chemical, physical and microbiological **stability** available
- ✓ **Shelf life** stated together **with container system**
- ✓ Container of pharmacopoeial quality used

Criteria for maintenance

A **periodical re-evaluation** will keep the whole formulary up-to-date but needs to be balanced with what is feasible.

The following points will be considered:

- **Review** at the latest **after 5 years**
- Active monitoring of
  - ✓ **Recommendations from PRAC**
  - ✓ **Approval of age-appropriate medicines after EU approval** (PUMA or centralised procedure)
- **Follow-up and evaluation of information received** about e.g.
  - ✓ Other safety signals
  - ✓ Quality issues
  - ✓ New drugs for first-line treatment
  - ✓ Marketing of age-appropriate dosage forms in individual countries
  - ✓ New formulations, qualities or clinical use

Critical points

The project relies heavily on the available information from national formularies and on other well-established formulations. Access to and availability of background data to check the quality will be crucial. A substantial effort has to be made to get appropriate input.
The quality of the European Paediatric Formulary depends largely on information received from the stakeholders. All interested parties are actively invited to send both their data and comments during a public consultation period, for all new and revised formulations within the Formulary. All future feedback will be essential.
In addition, some concerns have been voiced that this project might undermine the efforts of recent EU and international legislation designed to improve the availability of appropriate paediatric medicines. However, for many older active substances in regular use, appropriate licensed medicines for children are not, and may never be, available. Clearly it takes many years for authorised medicines to meet all the needs. The purpose of the formulary is a contribution to fill this gap.

Conclusion and Perspective

The European Paediatric Formulary will be a platform to collect and to make available appropriate formulations for paediatric use which allow the preparation of unlicensed medicines of acceptable quality. Easy and free access is a prerequisite to help users and to promote the health of children who are in need of such medicines. As long as no adequate authorised medicines are available, the European Paediatric Formulary can help to reach this aim.
The project is still in its early stages and the above-mentioned selection criteria have been fixed. After the final agreement on the criteria the second working party starts its task of evaluating existing formulations and drafting future monographs. These will be made available on an online platform which will be updated regularly after a period of public consultation. Input from all interested external parties is highly welcome and needed for success.

Acknowledgement

The work on this project on a European level would not be possible without the support of the member states and the work of the nominated experts. For the first group of experts which is defining the inclusion criteria, special thanks go to its chair Patricia Scognamiglio, Switzerland, as well as to all the other experts of the group experienced in compounding, regulatory or clinical aspects, including two observers from the EMA PDCO. I would also like to acknowledge Prof. Jörg Breitkreutz, Germany, who chairs the second working group which will be in charge of preparing the final monographs.

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