Paediatric medicine: Special considerations

Introduction

Special measures and considerations are necessary when developing paediatric medicines in order to protect children from any undue harm during the medicines development process. The following article covers some of these special considerations, especially regarding the formulation of medicines for children and the optimisation of paediatric clinical trial design. The ethical implications of paediatric studies are also discussed below.

Questions for consideration

A number of questions should be considered by the sponsor early in development in order to evaluate the suitability of developing a medicine in the paediatric population.

- Is there any presence of a serious or life-threatening disease for which the product represents a potentially important advance in therapy?
- Is paediatric development relevant – that is, do the intended indications (conditions the candidate medicine aims to treat) exist in children?
- How likely is the use in different age ranges of patients (paediatric subsets defined by ICH) and how often or in what way does the disease occur in children?
- How serious is the condition?
- Is there an unmet medical need in children? What is the significant therapeutic benefit? (Considering the availability and suitability of alternative treatments.)
- Are there unique paediatric indications for the

medicine?

- Is the medicine novel (new), or does it have a known component (an active substance that has previously been used for treating adults)?
- Could the active substance have potential in other therapeutic areas?
- Are there any unique safety concerns? What is the known safety profile of the medicine (including non-clinical findings)?
- Is there a potential need for age-specific paediatric formulation development? Would this be possible to develop (considering the availability of appropriate ingredients)?
- Is it feasible to conduct clinical trials in a paediatric population?

Formulating medicines for children

Clinical trials are only part of what is needed. Age-specific formulations are also essential in order to resolve:

- The difficulties swallowing tablets if a syrup is not available;
- Serious calculation errors when using adult formulations to obtain paediatric dosage; **or**
- The use or amount of excipients (inactive ingredients) that would be inappropriate in children

Additionally, alternative delivery systems will need to be considered, such as:

- Flavours and colours
- Liquids, suspensions, and chewable tablets
- Taste masking may be required
- May differ for each age group
- One size does not fit all

European Paediatric Formulation Initiative (EuPFI)

The European Paediatric Formulation Initiative (EuPFI)[1] was founded in 2007 by a group representing pharmaceutical industries, hospitals, and academics – stakeholders who all have an interest in research in children's medicines to create better medicines for children.

The main objective of EuPFI was to resolve scientific, regulatory, and technological issues linked with paediatric formulation development by:

- Identifying the challenges associated with the development of paediatric formulations
- Raising awareness and improving medicines and their dosage forms for children
- Identifying potential gaps in knowledge relating to paediatric formulation development
- Promoting early pharmaceutical consideration for the development of paediatric medicines
- Improving the availability of information for paediatric formulations

Optimising paediatric clinical trial design

In March 2012, the Food and Drug Administration (FDA) Advisory Committee for Pharmaceutical Science and Clinical Pharmacology met to discuss how to improve paediatric clinical trial design and dosing. This committee recommended the use of modelling and simulation to predict what will happen in a paediatric clinical trial when a particular dose of a medicine is given.

Also at this meeting, the majority of the committee (12 out of 13 doctors) agreed that doses for the adolescent (>12 years)

population can be derived using adult data without the need for a dedicated pharmacokinetic (PK) study; however, some committee members recommended that this approach should be considered on a drug-specific basis. Further information is available from the FDA website.[2]

Ethical issues in paediatric studies

Children are a vulnerable sub-group, and special measures are required to shield them from undue risk. Working with ethics committees familiar with paediatric populations is important to ensure that:

- Recruitment does not involve inappropriate incentives;
- Consent is given in the form of a signed informed consent form by parents or a legal guardian. Older children may also need to sign an informed consent form, or give their assent;
- Participants are fully informed using language they are able to understand;
- Studies minimise risk;
- Studies minimise distress – study staff should know how to deal with children; and
- The study protocol is designed specifically for the population.

Resources

- Rose, K., & Van den Anker, J. (Eds.). (2007). *Guide to paediatric clinical research*. Basel: Karger.
- Rose, K., & Van den Anker, J. (Eds.). (2010). *Guide to paediatric drug development and clinical research*. Basel: Karger.

References

1. More information on EuPFI is available from their website: http://www.eupfi.org/ (Retrieved 24 August, 2015).
2. Food and Drug Administration (2012). *Summary minutes of the advisory committee for pharmaceutical science and clinical pharmacology March 14, 2012*. Retrieved 11 July, 2021 from https://web.archive.org/web/20161023224355/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AdvisoryCommitteeforPharmaceuticalScienceandClinicalPharmacology/UCM306989.pdf