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SCIENCE MEDICINES HEALTH

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When is it relevant to include a bodyweight limit in the wording of a paediatric indication?

As a general principle, the target paediatric population should be defined with a lower age limit in section 4.1 of the SmPC and section 4.2 of the SmPC should make recommendations on the posology for this population taking relevant factors such as age and/or bodyweight into account, as well as advising on the formulation/strength/pharmaceutical forms when necessary. Posology recommendations in 4.2 should not be included for population not covered in the target population defined in 4.1.

When posology (dose) recommendations depend on weight, it may be considered in some situations if the most appropriate lower limit of the paediatric population in section 4.1 should be best defined in terms of age, weight or both, e.g.:

- when the age group covered by the claimed indication commonly includes subjects with a weight below that of the study population supporting the posology recommendations, and if extrapolation based on PK modelling is not feasible or appropriate.
- when a suitable formulation/strength is missing for delivering appropriate weight-based dosages in a relevant percentage of target age group.

In such cases, the wording of the indication may need to be adjusted:

- If the age-defined target population with an established positive benefit risk is consistent with the weight range supporting dose recommendations, and, dose recommendations can be covered with the proposed formulation(s)/strength(s), the target population in 4.1 will be defined by age only.
- If the age-defined target population with an established positive benefit risk is consistent with the weight range supporting dose recommendations, but a suitable formulation/strength is missing for delivering the appropriate dosage in a relevant percentage of subjects with the lowest weights, it may be adequate to include a weight cut off value in 4.1.

  For example, if an indication (4.1) is proposed in children aged ≥ 6 years and section 4.2 only recommends a posology for subjects weighing ≥ 25 kg because of lack of suitable pharmaceutical form, the wording of the indication may be revised to specify "children aged ≥ 6 years weighing ≥ 25 kg" to address the discrepancy between age and weight (since the median percentile for children aged 6 years is 20 kg and ≥ 25 kg covers only the upper 10 percent of 6-year old children).

  However, if the gap between the proposed lower age and the weight cut off is very large (e.g. ≥ 6 years of age and weighing more than 50 kg), it may be more appropriate to delete the lower age cut off and only have a weight cut off or have a higher age cut off (that better matches the weight limit).
- If the age-defined target population with an established positive benefit risk is not consistent with the weight range stated in 4.2, it may be relevant to include a weight cut-off in 4.1 to reach consistency with 4.2.

  For example, an indication (4.1) could be restricted to adults and adolescent 12 years and older and weighing at least 40 kg, when no posology recommendation can be made in patients weighing less than 40 kg (which is approximately the 50th percentile for 12 year-old children).

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