14 November 2024
EMA/501950/2024 (CHMP/EWP/517497/2007/Rev 1)
Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the need for revision of the addendum on weight control in children to the guideline on clinical evaluation of medicinal products used in weight control

Agreed by Cardiovascular Working Party	6 June 2024
Adopted by PDCO	14 Nov 2024
Adopted by CHMP for release for consultation	14 Nov 2024
Start of public consultation	2 December 2024
End of consultation (deadline for comments)	28 February 2025

The proposed guideline will replace Guideline on clinical evaluation of medicinal products used in weight control - Addendum on weight control in children (EMEA/CHMP/EWP/517497/2007).

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	Overweight, obesity, weight control, guidance, treatment

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1. Introduction

Childhood obesity (CO) has become a major health problem worldwide and its incidence is steadily increasing. This concept paper (CP) refers to the need for revision of the Addendum on weight control in children to the guideline on clinical evaluation of medicinal products used in weight control (EMEA/CHMP/EWP/517497/2007).

2. Problem statement

The current Addendum on weight control in children to the guideline on clinical evaluation of medicinal products used in weight control was adopted by the CHMP in July 2008 and came into effect on February 1st, 2009 (1). Meanwhile, the Guideline on clinical evaluation of medicinal products used in weight management (EMA/CHMP/311805/2014) was revised in 2016 (2). Changes to the Addendum are proposed with the aim to align the Addendum with the Guideline for adults (where appropriate) and to reflect recent developments in this rapidly evolving field with respect to approval of new medicinal products for weight management as well as clinical practice guidelines (3).

3. Discussion (on the problem statement)

The following areas of the Addendum have been identified for considerations of revisions:

- **Introduction**: The section needs updating to reflect current scientific knowledge and development.
- **Definition of overweight/obesity in children**: Currently, Body Mass Index (BMI)-related metrics are proposed for the definition of overweight and obesity in children (3, 4). In children and adolescents, BMI should be adjusted according to age and sex. In addition, BMI metrics may not be ideal as they do not directly reflect adiposity nor the consequences of excess adiposity in an individualized way. Therefore, other staging tools may help to better characterize the target population for pharmacological treatment (5).
- **Trial Design**:
    - **Run-in period**: Currently, a run-in period of at least 3 months is required, which may discourage people from inclusion in clinical trials. Therefore, the need for a run-in period and its length will be considered.
    - **Inclusion and exclusion criteria** will be considered in light of the intended target population.
    - **Primary and secondary endpoints**: The currently recommended primary endpoint is change in BMI Standard Deviation score (SDS) or BMI (%) from baseline. Appropriate primary and secondary endpoints will be considered, also attempting to capture the medical, mental and functional outcomes.
    - **Comparator**: The use of placebo in placebo-controlled trials leads to drop-out. Therefore, ways to avoid drop-out of clinical trials will be considered.
    - **Follow-up after discontinuation:** Currently, an observation phase of at least 6 months is recommended after stopping drug therapy. Stopping therapy may however have its drawbacks and may not add a lot of information. Therefore, the need for a follow-up after discontinuation and its length will be considered.

4. Recommendation

The CVS Working Party (CVSWP) at the EMA, the PDCO and the CHMP recommend revising the Addendum on weight control in children to the guideline on clinical evaluation of medicinal products used in weight control. Points that will be addressed are listed in section 3 of this CP.

5. Proposed timetable

This CP will be released for a 3-month public consultation. Following this, it is planned to release the draft Guideline within 6 months after completion of the public consultation on the CP. The draft Guideline will be released for a 6-month public consultation and, following the receipt of comments, it will be finalised within approximately 6 months.

6. Resource requirements for preparation

The drafting process will be done internally by the Drafting Group created for the revision including experts from the CVS WP and PDCO. Contribution from the Scientific Advice Working Party, Methodology Working Party at the EMA and the COMP will be requested if needed.

7. Impact assessment (anticipated)

The document is intended to update methodological aspects when performing trials to develop medicinal products for weight management in children. It should also provide a clear basis for the CHMP when assessing safety and efficacy of medicinal products developed in this indication and when providing Scientific Advice in this field.

8. Interested parties

The interested parties in the guideline include the industry (PhARMA, EFPIA and others), Academia, the European Society of Cardiology, the European Association for the Study of Diabetes, European Association for the Study of Obesity (EASO), in particular the Childhood Obesity Working group (COWG), clinical trialists involved in development weight control medicinal products in children and other Regulatory Agencies.

9. References to literature, guidelines, etc.

1. EMA. Guideline on clinical evaluation of medicinal products used in weight control (CPMP/EWP/281/96 Rev.1) Addendum on weight control in children. 2008.

2. EMA. Guideline on clinical evaluation of medicinal products used in weight management. 2016.

3. Kelly AS, Bahlke M, Baker JL, de Beaufort C, Belin RM, Fonseca H, et al. Considerations for the design and conduct of pediatric obesity pharmacotherapy clinical trials: Proceedings of expert roundtable meetings. Pediatr Obes. 2024;19(11):e13161.

4. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320(7244):1240-3.

5. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-94.

6. Hadjiyannakis S, Ibrahim Q, Li J, Ball GDC, Buchholz A, Hamilton JK, et al. Obesity class versus the Edmonton Obesity Staging System for Pediatrics to define health risk in childhood obesity: results from the CANPWR cross-sectional study. Lancet Child Adolesc Health. 2019;3(6):398-407.