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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE

(CHMP)

CONCEPT PAPER ON THE NEED FOR REVISION OF THE CHMP NOTE FOR GUIDANCE ON THE CLINICAL DEVELOPMENT OF MEDICINAL PRODUCTS IN THE TREATMENT OF ASTHMA (CPMP/EWP/2922/01)

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1. INTRODUCTION

The CHMP note for guidance on the clinical investigation of medicinal products in the treatment of asthma came into operation in May 2003. Since then, it has been proven to be useful for both industry and regulators in the development and assessment of products aimed to treating asthma.

2. PROBLEM STATEMENT

Within the framework of the CHMP policy, it is proposed to revisit the document. Since it was first drafted, new international recommendations have been published as well as a number of initiatives to highlight the relevance of asthma as a chronic systemic inflammatory disease of high medical and social impact.

Importantly, children are a key target population for antiasthmatic drugs. Although current recommendations contemplate some aspects of the paediatric development of these drugs, a more detailed advice is needed.

3. DISCUSSION

EU regulatory recommendations on the clinical development of drugs for asthma are tailored according to the severity of the disease and the required background treatment. Pulmonary function parameters have been consistently considered as a solid basis for the demonstration of efficacy in patients with asthma.

Current clinical recommendations for the treatment of asthma indicate that treatment decisions should not only be guided by the assessment of severity, since, among other things, treatment itself is a key contributor to such classification. By contrast, clinical practice guidelines now put a greater emphasis on asthma control, which is in fact a composite of a number of clinical factors, including clinical symptoms, treatment requirements and spirometric measurements. The value of this holistic approach is recognised and its clinical meaningfulness in patient management is unquestionable. However, the applicability of the whole concept to drug development may need further discussion and proper validation. In a clinical setting where a stepwise approach is the basis of the therapeutic approach, the ascertainment of the contribution of a new substance to the overall treatment effect becomes a critical part of regulatory assessment. This acquires particular relevance in a clinical setting where background therapy is not assumed to be constant and is at the same time, not only a component of the main outcome, but also expected to have a critical impact on the clinical components of asthma control.

Taking into account the above-mentioned considerations, the CHMP opened a reflection process, including an ad hoc expert meeting held on 8 September 2009, where the major limitations of the current recommendations and critical aspects to be taken on board in an updated version of the guidelines were discussed.

4. RECOMMENDATION

In the light of the conclusions resulting from both internal discussions and experts' recommendations, the CHMP recommends starting a revision of the CHMP guidance document on asthma. The following critical aspects will need to be discussed in depth and covered as appropriate by the revised guideline:

1. Revision of the criteria used for the categorisation of patients with asthma according to updated clinical criteria.
2. Ensuring adequate representativeness of the population studied across the entire clinical development while keeping the necessary assay sensitivity of individual studies.
3. Discussing the value of "asthma control" as a tool for assessing drug efficacy. This should be based on a detailed evaluation of data supporting its use as a validated instrument for assessing drug efficacy in different clinical settings.
4. Value and limitations of lung-function parameters in drug development. Validity of lung function parameters other than FEV1 in the assessment of drug efficacy.

5. Need to reinforce the use of clinical measurements (symptoms) and patient-reported outcome measures) to complement lung function parameters and fully ascertain the true effect of individual drugs.
6. Reflection on an improved judgement of the contribution of individual drugs in the context of the stepwise therapeutic strategy in asthma.
7. Need for a dedicated chapter on children, particularly dealing with the following aspects:
    - Adequate definition of the paediatric populations (diagnostic criteria, age groups, asthma phenotype, atopic versus non-atopic, atopic co-morbidities).
    - Possible biasing events (e.g. start smoking in adolescents) to be recorded in the protocol
    - Need to study dose-relationship in children.
    - Discuss choice of endpoint for different age-groups.
    - Discuss choice of the device/ use of spacers.
    - Monitor correct use of the device.
    - Monitor treatment adherence.
    - Need for long-term follow-up to evaluate impact of MP on growth, development, maturation, bone, exacerbation, etc (in the context of risk management plan).
    - Long-term follow-up should include description of the natural course of asthma over years.

5. PROPOSED TIMETABLE

The draft revised guideline is expected for public release by end 2010.

6. RESOURCE REQUIREMENTS FOR PREPARATION

Involvement of PDCO will be requested. Additional discussion with external experts will be necessary.

7. IMPACT ASSESSMENT (ANTICIPATED)

The revised guideline is expected to better reflect the current scientific thinking with regard to clinical treatment of asthma and related developments. Depending on the outcome of the reflection on the aspects that need changes, the revision of the guideline could have a significant impact on the overall approach related to the drug development in asthma.

8. INTERESTED PARTIES

European Society of Pneumology.
European Respiratory Society.
European Academy of Allergology and Clinical Immunology.
European Federation of Allergy and Airways Diseases Patients Associations.
International Primary Care Respiratory Group.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

1. GINA Report, Global Strategy for Asthma Management and Prevention (2008 Update).
http://www.ginasthma.com/Guidelineitem.asp??l1=2&l2=1&intId=1561

2. NHLBI Guidelines for the Diagnosis and Management of Asthma.
http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm

3. CHMP Note for Guidance on the Clinical Development of Medicinal Products in the Treatment of Asthma (CPMP/EWP/2922/01).
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