European Medicines Agency

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

RECOMMENDATION OF REVISION OF THE NOTE FOR GUIDANCE ON CLINCAL INVESTIGATION OF MEDICINAL PRODUCTS IN TREATMENT OF EPILEPTIC DISORDERS (CPMP/EWP/566/98 Rev. 1)

AGREED BY THE EFFICACY WORKING PARTY	September 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	18 October 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 January 2008

Comments should be provided to EWPSecretariat@emea.europa.eu

KEYWORDS	Epilepsy, concept paper, anti-epileptic, guidance

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1. INTRODUCTION

Epilepsy is a neurological disorder with seizures as the most dominant feature. Epilepsy, once diagnosed, is a life-long condition with a major physical, psychological and social impact on the patients. The prevalence is estimated 5-8 per 1000 subjects.

The current Note for Guidance (NfG) came into operation in May 2001 and hence the need for a revision warrants discussion.

2. PROBLEM STATEMENT

The current epilepsy guidance largely reflects the most common seen clinical development plan for anti-epileptic agents and is in accordance to the current state of art, although some details may be refined.

Currently the design of clinical trials in monotherapy is under discussion i.e. superiority trials *versus* inferiority trials and the role of placebo. Hence the study design of monotherapy studies at least needs some discussion. Further as in de add-on setting more and more agents have been approved the need for comparative studies in the add-on setting, as already foreseen in the current guideline, may be reinforced. Further the current endpoints may need to be reinforced more explicitly.

However, the guidance dominantly focuses on partial seizures in adults. Although many items dealt with in the current guidance may be extrapolated to other seizure types, some seizure types may need more attention e.g. generalised seizure types. Furthermore for some seizure types, study design may deviate from the overall pattern e.g. absences.

In current practice the choice of anti-epileptic depends on the diagnosis of the epileptic syndromes and not on seizure type. It needs discussion whether this should be taken into account in the trial design. A related discussion is whether efficacy in symptomatic and idiopathic epileptic seizures should be dealt with separately.

Recent applications, of AED in children indicate that special epileptic syndromes, syndrome-specific seizure may need to be extended. In addition, base on experiences in the EU paediatric work share programme indicates that studies in the very young children may warrant different study designs.

Likewise the need for special studies in the elderly and their design may need to be re-discussed and revised.

The NfG does not cover status epilepticus and it may be wise to have a position statement for this serious, life threatening condition that needs to be addressed.

There is a need for more than one formulation (for instance parenteral formulation, child-friendly and adapted formulation). It may be discussed whether this should be requirement and if so subject to a pre-approval or a post-approval commitment.

Summarising the current guidance largely holds, the current content may need to be refined but dominantly some extensions are considered appropriate.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The main topics to be revised or added relate to the above-mentioned issues and may affect several parts of the NfG.

4. RECOMMENDATION

It is proposed to revise the CHMP NfG on clinical investigation of medicinal products for the treatment epileptic disorders, to provide an updated EU consensual regulatory point of view on the

above-mentioned issues. In addition, it is proposed that the term “Guideline” is used instead of “Note for Guidance” as stated in the procedure for European Union guidelines and related documents within the pharmaceutical legislative framework.

5. TIMETABLE

It is anticipated that a draft revised CHMP guideline will be available 6 months after adoption of the recommendation document for 6-month release for external consultation, before finalisation within 6 months.

6. RESOURCE REQUIREMENTS FOR PREPARATION

Preparation of this Guideline will involve the EWP, the CNS drafting group and the Paediatric Committee.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is anticipated that a guideline will facilitate the interaction between regulatory agencies within Europe and Sponsors developing products for the treatment of CHC.

Until such time as this guideline comes into operation, EMEA/CHMP scientific advice is recommended.

8. INTERESTED PARTIES

ILEA

EFNS

9. REFERENCES TO LITERATURE, GUIDELINES ETC

Note for guidance on clinical investigation of medicinal products in treatment of epileptic disorder:

http://www.emea.europa.eu/pdfs/human/ewp/056698en.pdf

Procedure for European Union guidelines and related documents within the pharmaceutical legislative framework (EMEA/P/24143/2004):

http://www.emea.europa.eu/pdfs/human/regaffair/2414304en.pdf